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RESEARCH ARTICLE

Automatic Cell Detection and Segregation in Microscopy Images using Image Processing Toolbox

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ABSTRACT

Cell biology is an extensive research area to detect different diseases like malaria, diabetics as well as some types of cancer. Even it plays vital role to develop vaccine for some diseases. The basic step in the cell analysis is to detect of cell and segregate themselves in the microscopic image of cells. This can be done manually, but it takes much of time with less accuracy. In this paper it has been developed a simple algorithm using image processing tool such as image segmentation and mathematical morphology to detect the cells and segregate them automatically which takes very less time with more accuracy. The discussed method has been tested over microscopic cell image data set and observed that provide accurate and quick detection of cell in almost all the data set images.

Key words: Cell Biology, Edge Detection, Image Morphology, Median filtering, Connected Components

INTRODUCTION

A cell is the basic structure and the biological unit of living organism. The cell biology focuses on the study of these smallest unit call cell. The cell has many bimolecule like protein and nucleic acid which are inside the cytoplasm enclosed by a membrane. These cells made visible under microscope only. The study of cell is most required to detect disease like malaria, diabetes, or some type of cancer, because the diseases are caused by problem in cell or molecular level. Even during invention of any vaccine of some diseases the study of cell plays a vital role [1-3]. The cell biology research which going on are based on microscopy image analysis of cell culture. The analysis can be done manually, but this leads to more time consumption and may leads to error [4]. So the automation which involves the field of computer vision with image processing can save time with more accuracy. The study of cell plays a vital role for a healthy living body. The cell can be studied under specified range of microscope. During the analysis or study of cell, it is the very first step to detect the cells in the microscopic image and segregates the cell

from one another. This process is called as cell detection and segregation from each other [5]. This process can be done automatically with the help of computer vision and image processing. The microscopic cell images are used as the input source for the image processing system or model where the output is the detected cell and the segmentation of cells from each other.

COMPUTER VISION AND IMAGE PROCESSING

The computer vision [6] which takes image as an input and using image processing algorithm, it perform the required processed image output. The main aim of computer vision research is to provide computers with analogous abilities. The computer vision is just a replica of biological vision system but in a different approach [7]. When the image processing is applied to the field of biomedical it termed as biomedical image processing [8, 9]. There are radiological imaging which include radiography, thermography, ultrasound, nuclear medicine and CT, these all are source for the biomedical image processing. But on the other hand microscopic imaging technique is very different from the radiological imaging technique in the sense that interaction between the operator and the imaging device is very essential [9]. In the recent research trends where lots of research has been done on biomedical image processing so far till date.

An image is represented in two dimensional plane as f(x, y), where the value at each spatial coordinate represent a gray scale value of the pixel. There are different Image processing steps starting from image acquisition to image recognition, but in the discussed approach the analysis was focused on image restoration, image segmentation and morphological image tools [10, 11].The image restoration attempts to reconstruct or recover an image that has been degraded by using a priori knowledge of the degradation phenomenon. While capturing image using capturing device there may be possibility of addition of noise. The noise can be reduced by either mean filter or order statistic filter [10, 11]. Order-statistics filters are spatial filters whose response is based on ordering (ranking) the pixels contained in the image area encompassed by the filter [10-11]. The median filter is a kind of filter where the response replaces the value of a pixel by the median of the gray levels in the neighborhood of that pixel.

$$\hat{f}(x,y) = \underset{(s,t)\in S_{xy}}{median}\{g(s,t)\} \tag{1}$$

Segmentation subdivides an image into its constituent regions or objects [10-11]. Edge detection is by far the most common approach for detecting meaningful discontinuities in gray level. The edge can be detected by implementing first- and second-order digital derivatives in an image; the first order derivative is computed by gradient operator
The gradient of an image f(x, y) at location (x, y) is defined as the vector

$$G[f(x,y)] = \begin{bmatrix} G_x \\ G_y \end{bmatrix} = \begin{bmatrix} \frac{\partial f}{\partial x} \\ \frac{\partial f}{\partial y} \end{bmatrix} \tag{2}$$

Where Gx is the gradient in x direction and Gy is the gradient in y direction
The magnitude of this vector denoted as

$$G = \sqrt{Gx^2 + Gy^2} \tag{3}$$

The gradient can be determine by using sobel mask (Figure 1)

The mathematical morphology is a tool for extracting image components that are useful for representation and description of shape of a region in terms of boundaries. The basic tool used for morphological operation is mainly dilation and erosion. Both dilation and erosion are produced by the interaction of set of pixels of interest in the image with a set called a structuring element. The basic effect of the operator on a binary image is to gradually enlarge the boundaries of regions of foreground pixels where as the erosion operators it erodes the boundaries of regions of foreground pixels [10-11].

METHODOLOGY

The approach of detecting cell and segmenting from each other can be summarized as the flow diagram given below in figure 2.Initially the microscopic image has to given as an input, proceed by a median filtering operation to remove any unwanted noise in the image. The de-noised image will give good result for further processing. The edges of the de-noised image are determined by gradient method using Sobel mask [12]. Both sobel mask used where one gives gradient in x direction and other gives in y direction. Then the resultant of both can be determined by finding the magnitude. The edge detection even gives more customize output if it is perform by taking some thresholding value (Figure 3).

The edge detected image gone through a morphological dilation operation by selecting a flat linear structuring element, here the two different structuring elements were taken, one with 0 degree and other at 90 degree clockwise direction. After dilation the edges have been expanded to achieve the shape of the cell. The dilated image may leads to have some holes inside the shapes; that can be fill by implementation of morphological region filling operation as shown in figure 4, to get the proper shape [10]. After getting the cell shape there may be some sharp boundary, so it should be smoothed. That can be achieved by the morphological erosion operation, which erode out the unstructured boundary of the cells by selecting a disk type structuring element (Figure 5).

The cell shape is connected within itself, so connected components are determined to make different groups and then has been labeled with different color scheme [13], then the shape objects are covered with rectangle bounding box to segregates each cell. Finally the perimeters of the cells are detected and each cell detected and segregated from each other with the help of edge detection and morphological operation (Figure 6).

RESULTS AND DISCUSSION

The dataset of microscopic image has been downloaded from Murphy Lab - Software - ISBI 2009 Nuclear Segmentation [14]. It contains a set of 50 images each with dimension 1349x1030, available with portable network graphics format, but for simulation it has been resized to 500x350. For experimental simulation MATLAB version 8.3[R2014a] has been used.The microscopic image has been taken and performs the median filtering operation. The median filtering helps to remove presence of any noise. The de-noised image shown in figure 7. The edge detection operation has performed using the gradient operator where the Sobel mask has been used. The edge detected image as shown in figure 8. For better performance a global thresholding method has been implemented which make the edge points more accurate.

The morphological dilation operation has been performed to get the binary image with extended boundaries, after that if some holes are present then it can be filled using morphological region filling operation. Both the dilated and filled holes region images are shown in figure 9.For smoothness of the cell region again the morphological erosion operation has been done followed by connected components labeling. The eroded and labeled images as shown figure 10

The labeled image has shown the cells with different color for proper segmentation. Finally the detected cell regions are represented with bounding box and the exact cells with highlighting with their perimeter (Figure 11).The cell are now properly detected and segmented from each other. These outputs now can be used for further details analysis of cell by extracting each cell separately.Some sample result has been shown below in figure 12.

CONCLUSION

The proposed algorithm is applicable for fast and accurate detection of cells and segregation of cells from each other. This is an application of image processing in the field of biomedical which termed as biomedical image processing. This process gives advantage in detection over the manual detection in terms of accuracy and time consumption. It involved image segmentation and morphological tool of image processing tool box to implement the method. It was giving good result while tested over a set of microscopic cell images. This study can be further extended to nuclei detection as well as classification of some types of cancer using the image processing tool box.

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X – Direction Kernel			Y – Direction Kernel		
-1	0	1	-1	-2	-1
-2	0	2	0	0	0
-1	0	1	1	2	1

Figure 1.Sobel Mask/Kernel

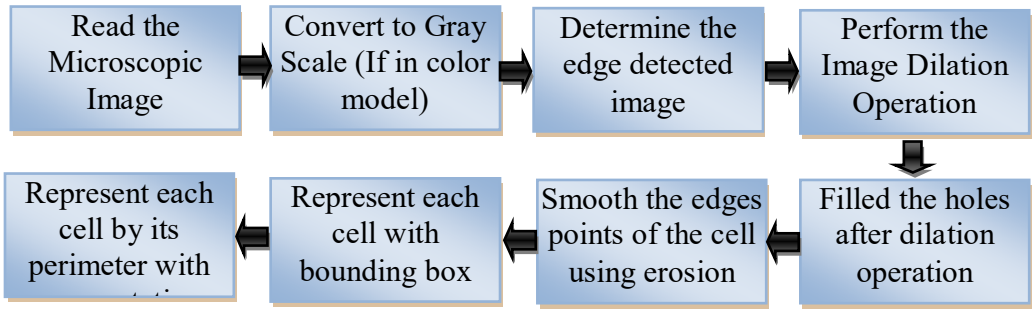

Figure 2.Flow Diagram of Implemented Method

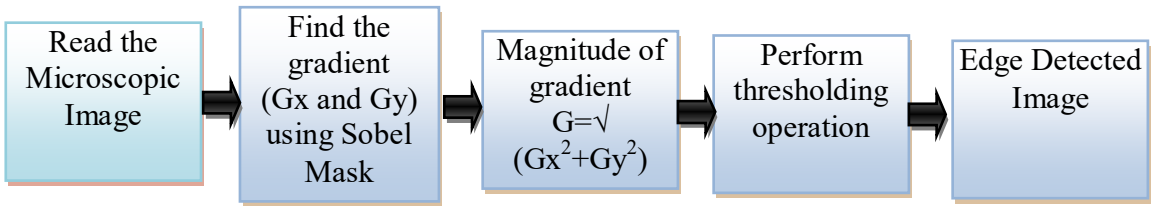

Figure 3.Process of Edge Detection

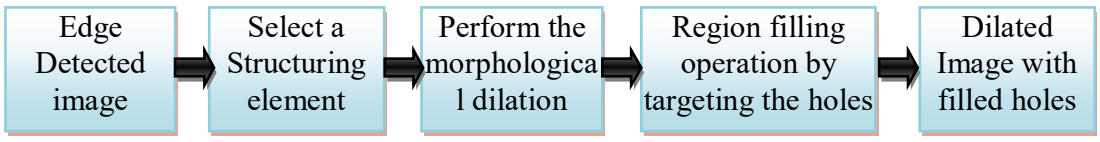

Figure 4.Flow Process of Dilation with Region Filling

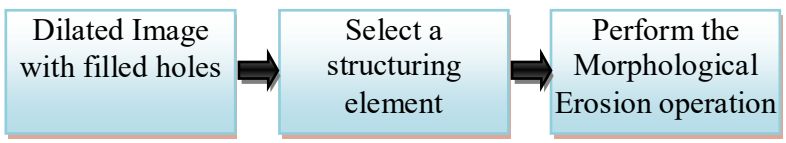

Figure 5.Erosion Operation

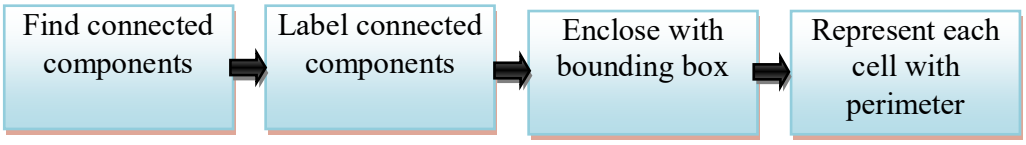

Figure 6.Connected Components and Labeling

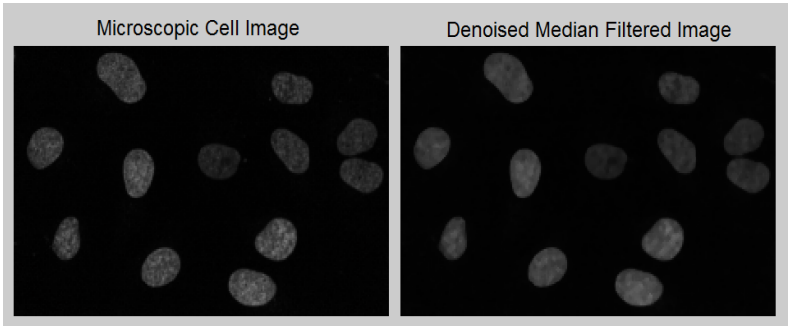

Figure 7.Result of Median Filtering

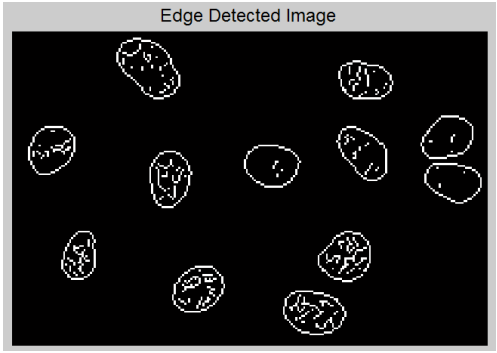

Figure 8.Edge Detection Output

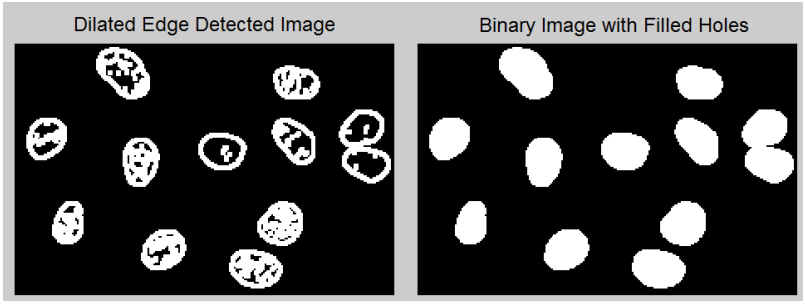

Figure 9.Result of Dilation and Region Filling Operation

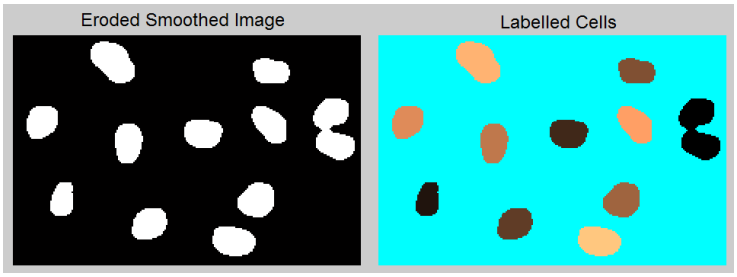

Figure 10.Result of Connected Components and Labeling

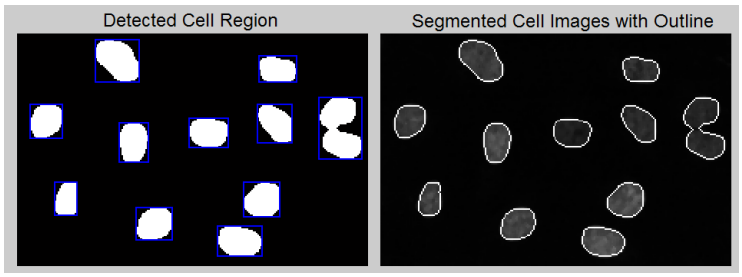

Figure 11.The segmented cell with bounding box and outline

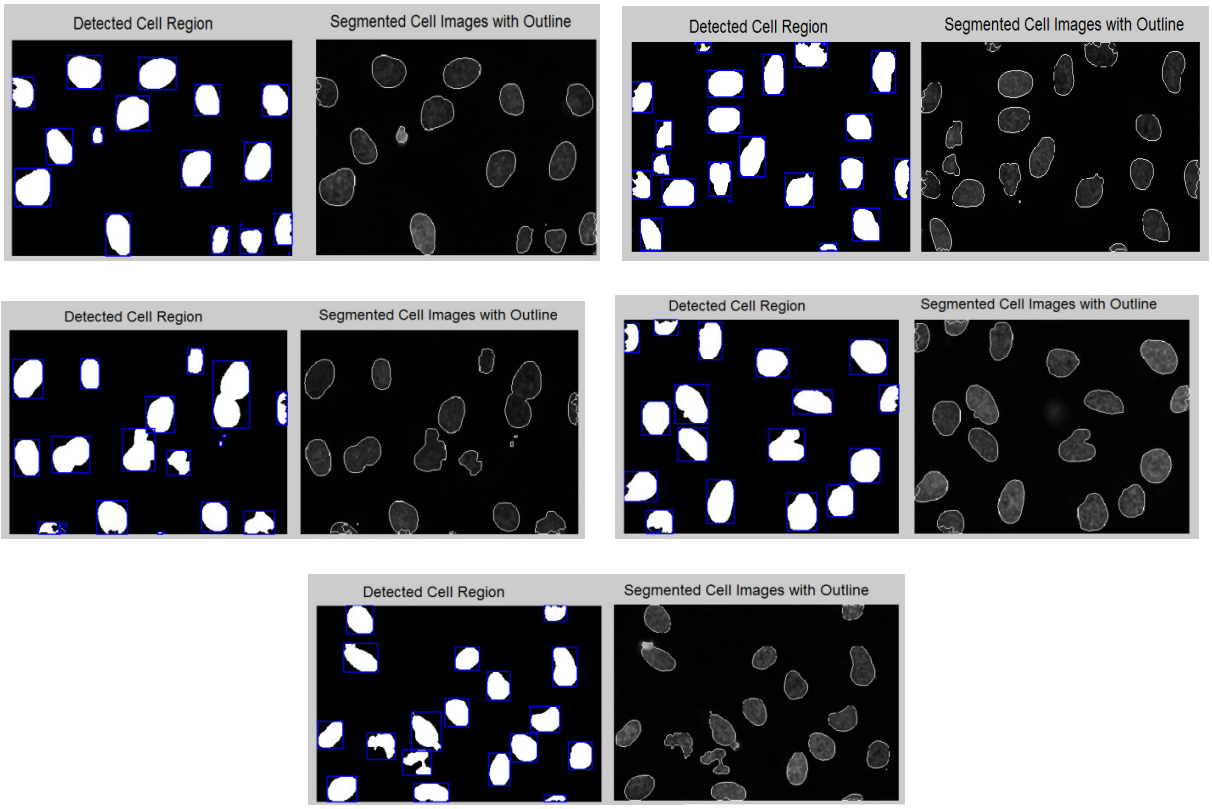

Figure 12.Sample of output using the implemented method

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RESEARCH ARTICLE

Comparative Analysis of Nutrient and Mineral Content Present in Fresh Fish (Hilsa) with that of Dried Fish

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ABSTRACT

The purpose of this study was to compare the proximate composition and minerals value of fresh fish and with that of dried fish. Fish species were collected from the market and brought into the laboratory of Department of Zoology Centurion University of Technology and Management Jatni, BBSR. Then the nutritional value and mineral content were done by using the standard method. The result of this study determined that the highest amount of protein, carbohydrate, fat moisturecontent was found in fresh fish than dried fishand the mineral content was present in between same range in fresh and dried fish.

Key words: Hilsa ,Proximate composition , Mineral.

INTRODUCTION

Fish are rich source of vitamin and mineral for the consumers[1].Composition of fish are different from other food product because fish content some usual features which was differ from other [2].Presently fish is said to be healthier and cholesterol free source of protein[3]. And it contain most important nutritional components which is help to serve as a source of energy for human being .But in developed country there are some domestic consumers who prefers to consume dried fish. Drying increases the service life, enhance the quality, provide ease of handling, further processing and sanitation .But during rainy season the fisherman is not able to dry the fish properly as they rapidly absorbed moisture and mites .Moisture which can cause extensive damage resulting in heavy financial loss. However some people consider dry fish as low coast dietary protein which is easily accessible to people of low income groups. A well balanced of fish diet can contribute to heart health and children proper growth and development so it occupies most important place in human daily life[4]. Chemical composition of fish varies from each individual according to their species in depending of their sex, age, environment and season.omega-3 fatty acid

are highly present in fish and fish oil which prevent cardiovascular disease and which have sparked intense interest in both epidemiological studies, which have favorable effect on CHD, and metabolic ward studies and improve in lipid profiles in HYPERLIPIDEMIC patients. Due to composition of essential amino acid and palatability fish meal has been the most important feed stuff used as a source of protein. In aquaculture due to high demand for protein ingredients it is expected to exceed supply in the next decade. Fish have high biological value which is found mostly in coastal communities in developing countries .Due to the presence of high biological value many Doctors advice to take fish instead of meat several times in a week[5].Many researcher assessed the nutrition and mineral value of fish[6] [4][7][8][9].Mainly the nutritional value of fish (both fresh and marine fish) are directly depend upon its proper shipping ,handling and storage period .Fish is one of the most important source of animal protein and other vital nutrient source .Lipid have a great role in human life because it can commonly obtained from the diet [10]. Which is rich source of omega-3 fatty acid.

Drying is a preservation of food process in which it remove water from the food product and enhance the rate of micro-organisms growth and their quality .For this process energy and wind is must be used to evaporate the water from the food. Evaporation is a process like air drying, smoking, wind drying, and sun drying.Dried fish is an inexpensive food which is filled with dietary protein source. Dried fish is a very popular among the Bangladesh market because their people does not like to consume the fresh fish but they prefer to consume dried fish in their daily life. Dried fish is a good protein source essentially fatty acids, vitamin and many minerals, so the present study is undertaken in the developing country. Drying is a process of preservation of fish for a long time to reduce its spoilage in their quality help in post-harvest losses and available the product during the time of fish storage. According to [11] drying is a process of vaporize moisture or remove the water from the product. It ensues cheap protein availability to people. Shelf life can be increased by drying .It also can enhance the quality, provide east of handling, further processing and sanitation [12]. Release of water vapor put impact in the microbial growth activity oxidation of fat and acetolytic activities in the fish resultant reduction in weight and volume. Hilsa is a type of species which have the ability of migrating far distances and able of withstanding a broad range of salinity. At the time of breeding it displaces to fresh water. So it choose to live in the sea where they stay maximum time of their life. It arises Shatt al. Arab river in Iraq and other rivers in Iran. It has a big breeding season which lasted from May to August [13].

It has two periods of breeding in the Bay of Bengal. One is from February to May during spring warming and another is major breeding that continue from July to October[14] which is overlaps with the heavy monsoon. It is very important species in the drift gillnet as well as fixed stake—net fishery in Kuwait [15]. In Bangladesh it is the biggest single fishery which contributes 11% of total production approximately (2899, 198 metric tons) and 24% of 115, 179 metrics tones from inland fisheries and 198, 574 metric tons from marine fisheries[16] owing to its popularity and economic importance it is celebrated as the national fish of Bangladesh. It is absorbed all over Bangladesh.

The fatty acid and lipid content of fish differ between in dark muscle and white muscle. They are high flown by various sources like temperature ,salinity, season, life stage, age, size and the kind of various food ,mainly if a species is carnivorous or omnivorous and herbivorous[17]. In Arab Tigris and Euphrates of Iran, the Indus of Pakistan, Iraq, the rivers of Eastern and Western India, Padma, Jamuna, Meghna and other coastal rivers of Bangladesh mainly the sea site habitat are occurs which has a broad range of distribution and takes place in estuarine, marine and riverine environment. In Bangladesh and Kuwait Hilsa, TenualosaIlisa[18] are locally known as Ilish and Sbour which is belonging to the family Clupeidae. The fatty acid data of Hilsa is limited information through there are abundance studies. Which are form various geographical regions have reported fatty acid data of difference fish species. From the Sundarban estuarine zone, Hoogly estuarine system and Godavari river and West Bengal coast of India have been reported[19][20][21][22]. During monsoon season which contains from June to August fishing of HILSA takes place. For breeding the adult fish displace to the rivers [12]. Both in Bangladesh and Kuwait the opportunity of Hilsa in the market is high during August to September and in order to collect the samples during the month of August we choose. The expatriate Bangladeshi communities in Kuwait have faith that the taste of Hilsa from the Bay of Bengal is

separate from Arabian Gulf due to popularity of Hilsa fish. To estimate and contrast the proximate composition, mineral composition as well as fatty acid profile of Hilsa muscle was the objective of this study and also to address the nutritional specialty of this species.

The fisherman dry the fish in the fishing vessels after catching fish in the sea. This is the best method to compare as the fisherman have not use any kind of salt or chemicals. For auctioning fishes were dumped in the whole sell, after fishing. As requirement raw fishes were transported and purchased to the Khati. Some dry fish produces have their own boat. They catch fishes in the sea with the help of the boat. Dry fishes were made through the methods of by salting and washing in a separate chamber. To remove water from the fish body the dry fish producers used salts and they dried under direct scorching sunlight on chamber. Generally it takes 3 to 7 days for full drying. It may increase up to one fortnight at the time of cloudy weather fisherman grind the fish after drying and sieve them. Then fisherman kept them on chat Basta and sell them to Beparis.

MATERIALS AND METHODS

Study area

The experiment was performed in Department of Zoology , Centurion University of Technology and Management, Jatni BBSR.

Collection of sample

For that experiment both fresh and dried fish was needed. Fresh fish and dried fish were collected from the market. Then both the fish was cleaned and take their muscle part for analysis the nutrient and mineral. After that muscle was grinded by the mortar and pestle,weighed by winning machine and kept it inside the oven for 2 days at 1050C. After 2 days these sample were grinded and prepare it in to power form.

Determination of protein in both fresh and dried fish

Usually Lowry's method [23] was followed to determine the amount of protein present in both fresh and dried fish muscle.

Determination of lipid in both fresh and dried fish

Lipid was estimated by using the chemical petroleum ether by SOXHLET-apparatus.

Determination of moisture in both fresh and dried fish

The moisture content was determined by drying at 100-105 for 48 hours in a hot air oven as described by Association of Official Analytical chemistsAOAC,1990[24].

Determination of carbohydrate in both fresh and dried fish

Carbohydrate was estimated by the Hedge-Hofrieter[25] method.

Determination of mineral in both fresh and dried fish

The total amount of mineral content was estimated by XRF method in both fresh and dried fish. The XRF is a nondestructive analytical technique used to determine the element composition of materials.

RESULT AND DISCUSSION

Moisture

From the above experiment it was determined that the percentage of moisture present in the fresh fish muscle (46.94 ±4.63%) and dried fish muscle (19.25 ±4.11%). Nutrient of fish is depend upon the amount of moisture present in the

fish because nutrient is inversely proportional to the moisture so lower the moisture higher the nutrient content present in the fish and it was determined that between the fresh fish and dried fish fresh fish have more amount of moisture than dried fish so fresh fish content less number of nutrient than dried fish. According to Parazo and[26]Mazumdar[27] the amount of moisture inversely proportional to the amount of lipid present in the body like amount of moisture is decreases with increase the amount of lipid on the fish body. In that case it also determines that fresh fish have high amount of moisture than dried fish which is given in (Table-1).

Lipid

After the experiment about the lipid extraction in SOXHLET method it was known that highest amount of fat is present in Hilsa fish. In this experiment it is estimated that fat content of fresh fish (23.24 ± 0.027%) and dried fish (19.19 ± 4.11%), which is shown in Table – 1and 2 respectively. The value of lipid composition varies from each individual fish indicating that changes depends upon many factorssuch as age, maturity stage, availability of foodand environmental temperature. Higher lipid composition was found in the species from the Bay of Bengal fish species as compared to fishes from rivers such as Jamuna, Padma, Meghnaetc.This may be probably because of huge amount of nutrient in the Bay Of Bengal that helps the productionas well the nutrientcontentHilsa fish in the Bay Of Bengal. In this case the amount of lipid is more present in the fresh Hilsa fish (23.24±0.02%) as compared to dried Hilsa fish (19.19±4.11%). In addition to food quality the size of the species also put impact in their proximate combination[28].Hilsa are mainly fatty in their breeding season in the month of August. [29]had told that higher level of fat as present on the medium size of fresh Hilsa fish. Due the above cases fresh fish have high amount of fat than that of dried fish.

Protein and carbohydrate

In the process of Lowrysmethod[23] the amount of protein was estimated that protein content of fresh HILSA (20.44±0.042%) and dried Hilsa muscle is (18.18±0.075%).Fish is a good source of dietary protein so many people prefer to consume fresh fish in their daily life style. In this experiment it is determined that high amount of protein is present in fresh Hilsa fish than dried fish because during dry fish production fishermen use huge amount of salt in the fresh fish to turn it into dry fish .In that process solar energy and wind is necessary to complete that process in which salt is damages the amount of protein in the fresh fish .In this experiment from all the collected sample it was estimated that muscle of Hilsa fish containsless amount of carbohydrate. The amount of carbohydrate in fresh fish (3.06±0.178%) and dried fish is (1.8±0.083%).

Mineral

Mineral are essential part for growth of all the living organisms because it helps in the bone mineralization, energy metabolism and reproduction of all living organisms. Minerals which are present in the scales ,muscle and vertebrae part of the fish body includes phosphorous(P) , Magnesium(Mg), Copper,Zinc (Zn) andManganese (Mn)which was present in same range between fresh and dried fish.

CONCLUSION

The economic as well as the medicinal value of the fish species increases due to presence of specific nutrient content in fish .Therefore it can be emphasized that fish can also play an important role in order to fulfill the nutrient demand of the people of the country. In this studythe mineral profile and the proximate composition of the HILSA fish from their muscle was determined and it was found to be rich in protein, lipid and carbohydrate , however the nutritional value of dry fishes greatly deteriorates due to the longer storage. The present experiment provides valuable information to the people to includefish food in their daily diet. In the present investigation it is clear that the amount of protein, lipid, carbohydrate and moisture content of fresh fish is more than the dried fish but the mineral content of both the fresh and dried fish product are in same range. From the results from the present study

it can also be indicated to the dry fish industries to adapt more precautionary measures during storage of dry fish in the warehouses and sales centres.

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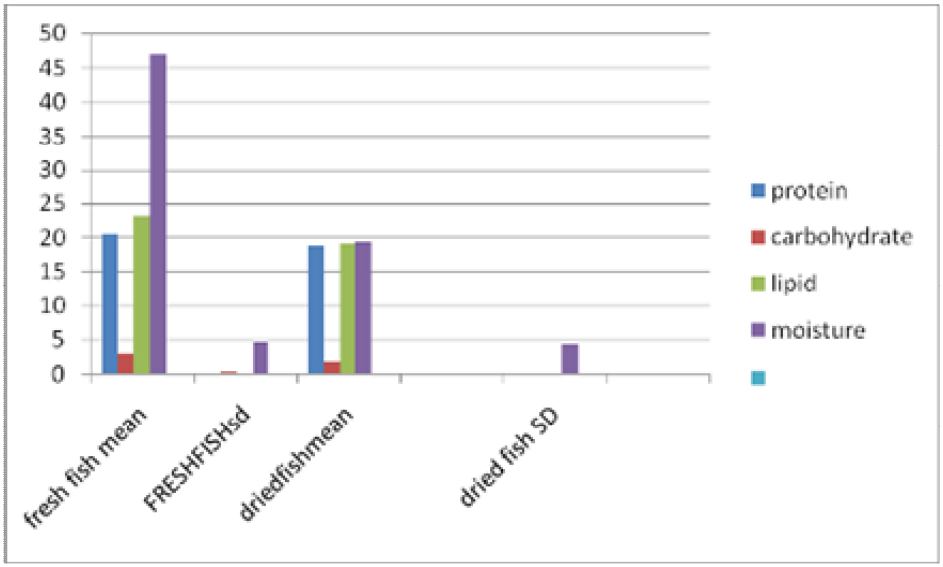
Table1.Nutritional value of fresh HILSA fish

Sample	Moisture(%)	Protein(%)	Lipid(%)	Carbohydrate(%)
1	43.75	20.46	23.25	3.8
2	44.13	20.49	23.24	3.8
3	52.22	20.38	23.27	3.6
4	51.78	20.43	23.26	3.5
5	42.85	20.47	23.20	3.6
Mean±SD	46.946±4.6396	20.44±0.042	23.24±0.027	3.06±0.178

Table2.Nutritional value of dried HILSA fish

Sample	Moisture(%)	Protein(%)	Lipid(%)	Carbohydrate(%)
1	15.67	18.80	19.15	1.8
2	18.79	18.85	19.10	1.9
3	24.53	18.92	19.21	1.9
4	22.25	18.87	19.23	1.8
5	15.02	19.00	19.26	1.7
mean	19.252	18.88	19.19	1.8
SD	4.117	0.075	0.064	0.083



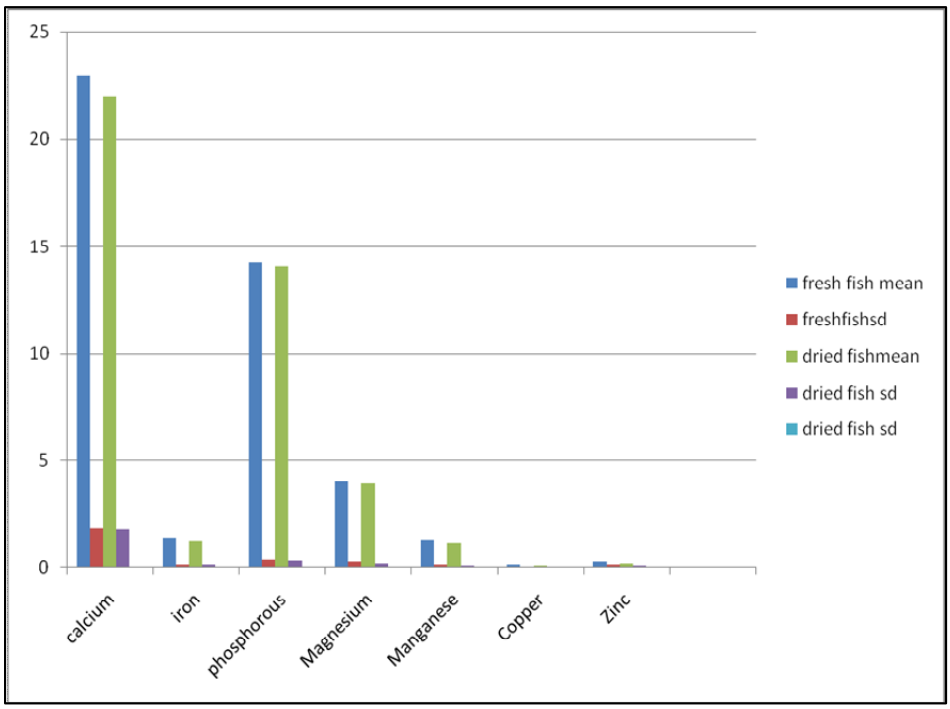
Graph 1.Represented the comparative nutritional value present in fresh and dried HILSA fish

Table3.Represents the amount of mineral present in dried fish

Sample	Calcium	Iron	P	Mg	Mn	C	Zn
1	20.04	1.10	13.51	3.80	1.08	0.11	0.10
2	22.10	1.15	14.18	3.80	1.12	0.10	0.11
3	24.20	1.34	14.20	3.75	1.18	0.11	0.21
4	20.35	1.42	14.21	4.10	1.25	0.12	0.21
5	23.20	1.31	14.30	4.21	1.31	0.12	0.34
Mean±SD	21.97 1.792	1.26 0.134	14.08 0.321	3.92 0.208	1.18 0.093	0.112 0.008	0.194 0.097

Table 4.Represented the amount of mineral present in fresh fish

Sample	Calcium	Iron	Phosphorous	Magnesium	Manganese	Copper	Zinc
1	21.12	1.30	13.60	3.82	1.15	0.15	0.15
2	22.19	1.25	14.32	3.92	1.20	0.13	0.17
3	25.93	1.45	14.40	3.82	1.32	0.15	0.27
4	22.34	1.59	14.41	4.20	1.42	0.18	0.27
5	23.25	1.48	14.48	4.32	1.45	0.18	0.40
Mean	22.96	1.41	14.24	4.01	1.30	0.15	0.25
SD	1.821	0.138	0.362	0.230	0.131	0.021	0.099



Graph 2.Represented the comparative mineral value present in fresh and dried HILSA fish

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RESEARCH ARTICLE

Evaluation of E6013 Electrodes Available in Indian Market

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ABSTRACT

Evaluation of 5(five) different brands of E6013 Shielded Metal Arc Welding (SMAW) electrodes available in Indian market like ESAB, D&H ,MODI ,FERROSEAL , ADOR are commonly used in project sites. To complete this project and evaluation work we purchased one packet of E6013 electrodes of above mention brands. Manual arc welding electrode is used extensively (80%) based on cost and availability in various project sites of Odisha. The welding was done using standard parameters i.e. constant heat input. The beads were studied to evaluate the quality of electrodes by observing slag peeling, bead look, welder's appeal etc. The bead dimensions were also measured along with deposition rate.

Key words: SMAW, E6013 electrode, Slag peeling, Bead look, Welder's appeal, Bead dimensions, Deposition rate

INTRODUCTION

Integrating or joining of different parts to make a single useful unit is known as fabrication process. In arc welding the two parts that are to be joined are brought above their melting point temperature at the interface and then solidification is done to achieve a permanent or non temporary joint. For fabrication process, welding process is mostly used because the joint achieved by the welding gives the strength nearly equal to the strength of parent metal or slightly less. Welding process can be used both for making new structures and repairing of old elements . The term weld or weldments is the joint obtained from welding. In E6013 Electrode, E signifies that the electrode is covered by flux. The digit 60 signifies that the minimum tensile strength of weld metal which is 62000 psi and a minimum yield strength is 50000 psi. The fourth digit 1 clarifies that the welding can be done in all positions i.e, flat, overhead, horizontal and vertical (upwards). The digit 3 signifies that the electrode has rutile potassium based flux coating. Based on the type the source of heat input, the welding processes can be classified as shown in the Figure below:

In welding for joining of thicker materials, the edge of the interface must be prepare in such a manner that the heat of the welding can penetrate through the entire depth. Generally welding is done on both sides of the thicker materials so that the arc can access completely into the joint, so a V or U joint is made.For thicker materials The V- joint is easier but the need of extra material is increases as the material thickness increases. Due to this reason a U- joint is preferred, because after attaining a certain thickness extra material needed to fill the joint is less. But machining of a V-joint is easier than a U- joint.The interfaces where the welding will be done should be clean. Because, if any unwanted particles such as dust, dirt or grease will be present then these will affect the welding and present in the final solidified weld and makes the joint defective and weaken the joint.

From the surface of the parent material for removal of the oily substances some chemicals with chemical processes are employed. Acetone and carbon tetrachloride like organic solvents can be used. When organic solvents are used for cleaning, cares must be taken to see that solvent is completely evaporated from the interface before any welding is attempted. Otherwise, highly poisonous gases such as phosgene may form from the solvents such as trichloroethylene and carbon tetrachloride under the intense heat of the welding.Also the presence of oxides affect the proper fusion process during welding. For this reason fluxes are used to remove oxides, the effect oxides and also the unwanted surface particles. The flux reacts with the oxides and produces low density slag which floats in the weld pool during the welding and protects the welding from oxidation that occurs due to the presence of oxygen in the atmosphere. The use of type of flux are determined according to the types of operation and parent materials being welded.A filler metal is also used during the welding process. The gap between the joining parts are filled by these metal, except the resistance welding. The filler metals are made up of same materials as that of the parent materials. To increase the strength of the joint some alloying materials also can be added.

MATERIALS AND METHODS

Welding Operation, Process Parameters and Experimentation

Process of welding operation and experimentation consists of three steps as shown in Fig. 2 [5, 6]:

1. Welding operation
2. Parameters included for Arc welding operation
3. Experimentation

Welding Operation

To start the arc welding process, first it is required to initiate the arc. The slight touch of the electrode with the work and then withdrawing it initiates the arc. After the arc initiation the consumable electrode starts to melt and the molten metal of the core wire passes to the weld pool. When melting of electrode starts, the flux that covered the electrodes comes into action, these flux disintegrates and generates shielding gases around the weld pool, which protects the weld area from the surrounding atmospheric gases and mainly from oxygen. Additionally, the molten slag are provided by the flux and the filler metal is covered by the molten slag because it travels to the weld pool from the electrode. In the weld pool surface the slag floats and keeps the contamination away during the whole solidification period. After the proper solidification process the chip or slag removal is done to observe the finished weld. With progression in welding, electrodes melts continuously, so periodically checking, removing the end stub of electrode and inserting of new electrode is done by the welder to the electrode holder.

Based upon the types of the electrode, work piece composition, and the welding position the welding techniques are used. Again the types of electrode and position of welding, decides the welding speed. For Flat welding where quick melting electrodes are generally used with slower solidification rate, least skill of the operator is required. But more

operator skill is required for faster welding speeds, Sloped, vertical or upside-down welding and with faster solidification rate. Also the melting of electrodes occurs somewhat slowly in this.[2], [3]

Position of Welding

Ideally, the work should be positioned during the welding, so that the molten weld metal is held in placed by gravity. It also enables high currents to be used, leading to faster welding. This implies that the work can be turned. Many fabrications do not lend themselves to this treatment, and much of the welding in industry is done "in position ". The welder controls the weld by lowering the heat input to reduce the fluidity and to give a small pool which solidifies before it has time to run out of the joint. At the same time the direction of the arc, i.e. the angle between the electrode and the weld surface, can be varied to the position the weld pool to the best advantage.

Parameters included for Arc welding operation

At the starting of the welding operation, there are a few parameters that must be set up to make sure that the welding process can be easily operated smoothly. The parameters that must be set up are:

1) Amperage
2) Arc voltage
3) Travel speed
4) Heat input

The size, shape and quality of the weld affected by different welding parameters.Weld current, arc voltage and travel speed are the main parameters. The arc voltage requirements and the amperage requirements are depends upon the selection of size and type of electrodes for SMAW. Alternating or direct current can be used for the purpose. For welding of thin metals direct current electrodes are used as these electrodes at low amperage also performs well. For the deepest penetration, covered electrodes are generally used with electrode as positive and Higher melting rate generally produced with electrode as negative. The angle between the work and electrode, flux layer thickness and arc length are taken as secondary variables.

Amperage

Basing upon the size and classification of electrode the correct amperage value is decided, the position of welding and joint types are also considered. Sufficient current is required to melt both electrode and base metal. Deeper penetrations achieved by higher current. But too high amperage also causes welding defects like excessive spatter, electrode overheating and cracking.

The normal operating range and current are recommended by manufacturers of electrodes. As a basic rule an electrode will require around 40 amp / millimeter (diameter). So 160 A is taken here for 4mm diameter electrode, but the acceptable operating range is 140-180. The Figure 5 has shown the required value of current for different diameters of electrode.

Arc voltage

The arc voltage varies narrowly unlike the current. It defines the bead width and shape. Wider and flatter beads produced due to high voltage. Cracking can be produced due to the use of very high voltage. Stiffer arc improves penetrations that can be produced at low arc voltage. Very narrow beads are result of too low voltage.[4], [5]

Travel Speed

The travel speed of electrode affects the shape of bead, fusion depth, cosmetic appearance and heat input to the work. Narrow bead gives less penetration that produced due to faster travel speed as required for sheet metal welding. The heat input also affected by travel speed, which changes the metallurgical structure of the weld metal. The cooling rate increases or decreases proportionally with the travel speed. Also, the heat affected zone will increase in the size and the cooling rate decreases. Undercut and porosity are produced due to too fast travel speed, as the weld freezes quicker.

Heat Input

The rate of travel of the electrode along the seam or the rate of travel of the work under the electrode along the seam is called as welding speed.
Welding Speed = Travel of electrode mm/min.
Heat input rate or arc energy = V×I×60/S Joules/mm

Where,
V is arc voltage in volts
I is welding current in ampere
S is speed of welding in mm/min.

Experimentation

In the construction sites of Odisha various types of E6013 electrodes are used. We only selected 5(five) brand varieties of E6013 electrodes which are popular in the construction sites. The electrodes are manufactured by companies and brand like"ESAB-Ferroking, MODI-Steelon Standard, FERROSEAL, D&H-Econotherme, ADOR-Superbond". A mild steel plate of 220 X 95mm was selected for experimental beads using standard parameters mentioned in TABLE: 2 below**.** An ESAB welding machine model RS -400, 3X415 ±10%, 50Hz was selected to conduct the experiment.The experimental beads were laid in the plates with using standard parameters. All together 5 (five) beads were laid.

RESULTS AND DISCUSSION

After the welding beads being welded on the mild steel plate we have done the following observations:

Weight of work piece before welding bead formation=1.600kg
After 1st bead formation weight=1.650kg
After 2nd bead formation weight=1.700kg
After 3rd bead formation weight=1.750kg
After 4th bead formation weight=1.800kg
After 5th bead formation weight=1.850kg

Results of spatter formation, noise generation, fusion, crater depth,weld look, feed and under cut defect details described in the table 3

Results of Penetration, Bead height and Bead width

The following formulas are being used for the calculation of Penetration, Bead height and Bead width:
Calculation procedure for penetration
: (x+y)/2 where x & y are the penetration rate at both ends of the plate.
Calculation procedure for bead height

: (x+y)/2 where x & y are the height of the bead at both ends of the plate.
Calculation procedure for bead width
The given bead on the plate is subdivided into 5 sub parts and the averages of 5 subparts are taken into account.

CONCLUSIONS

It was observed that all the brands are giving almost equal deposition rates of 50gm/electrode. The bead height was varying from 2.9mm to 3.45mm& bead width varying from 1.10mm to 1.14mm for all brands. The prices of ADOR WELDING LIMITED, SUPER BOND electrode is the highest/piece Rs.12.11&FERROSEAL is lowest/piece Rs.5.83. The penetration of ADOR WELDING LIMITED, SUPER BOND electrode is the highest i.e. 1.75mm and all other brands gave a penetration of 1.5mm approx. ADOR WELDING LIMITED, SUPER BOND performance was the best with a **score of 18 (Eighteen)** - slag peeling & bead look, welder's appeal.

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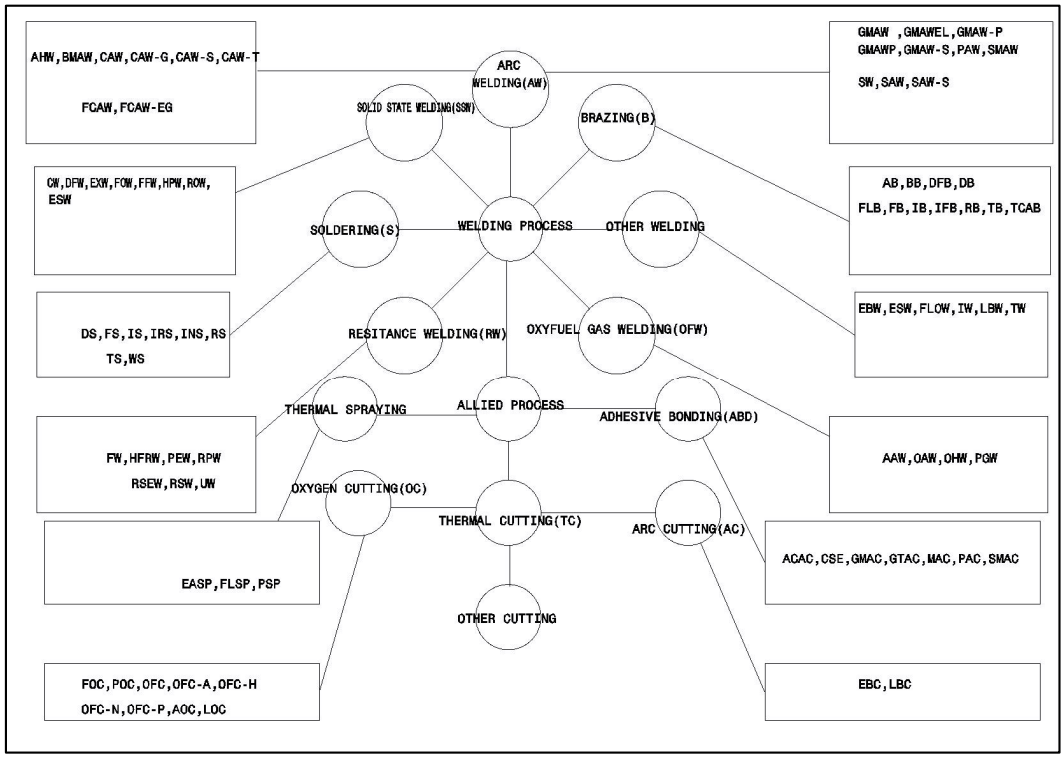

Fig. 1. Welding process classification

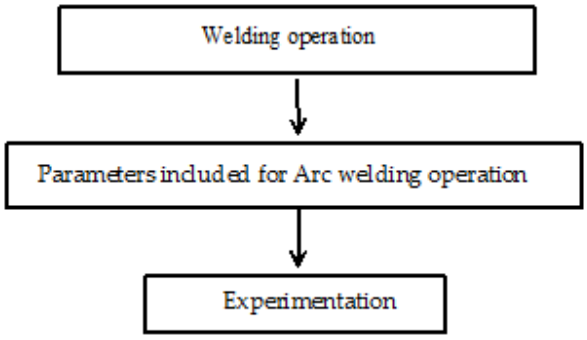

Fig.2.Process of welding operation and experimentation

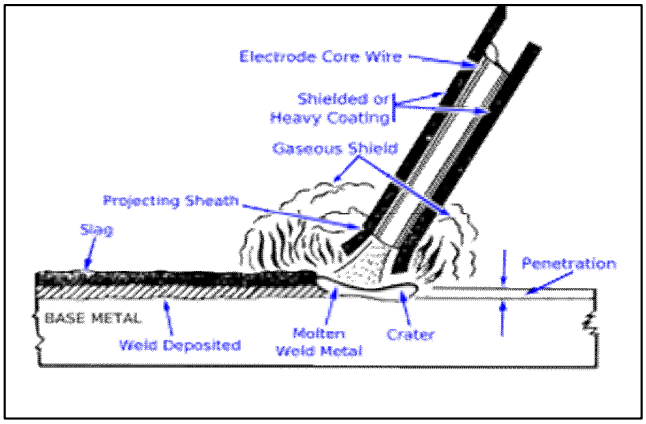

Fig. 3.Welding Operation

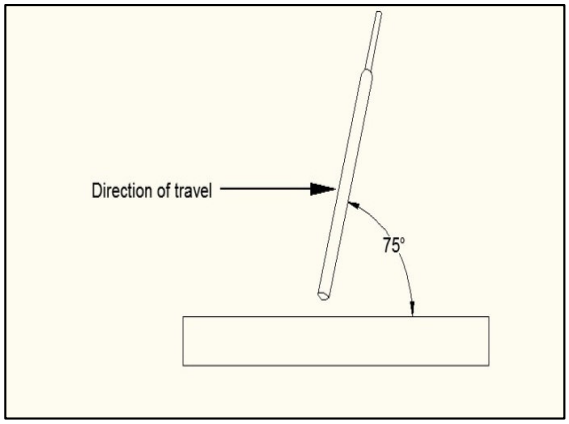

Fig. 4.Suitable angle for flat welding for SMAW

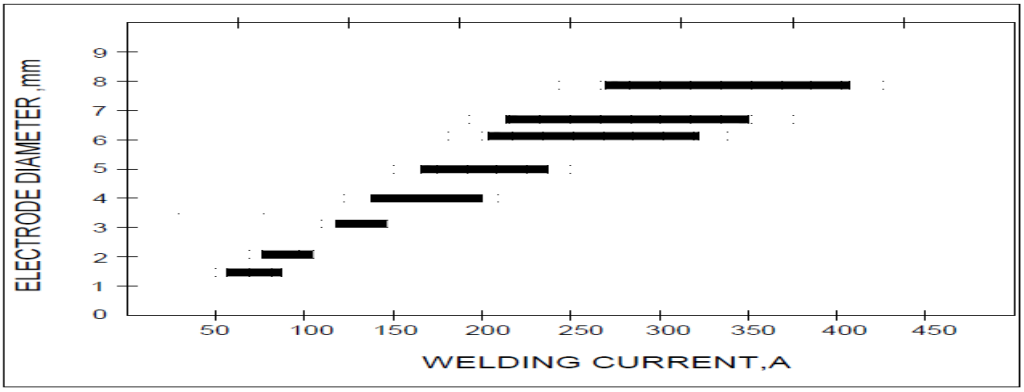

Fig. 5.Welding current for different diameter of electrode

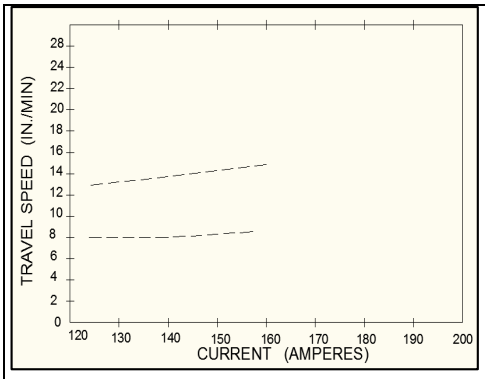

Fig. 6.Travel speed Vs Current (E6013 SMAW electrode)

Fig. 7.Welding machine used

Fig. 8 Welded beads by five types of electrodes

Table 1.Voltage limits for different types of electrodes

ELECTRODE	VOLTAGE LIMIT, V
E6010	28-32
E6011	28-32
E6013	22-26
E7018	25-28
E7024	26-32
E8018	22-28
E11018	25-30

Table 2.Standard Welding Parameters used

SL. No.	CURRENT (ampere)	VOLTAGE (volts)	Bead Length	Time (Seconds)	SPEED mm/min	HEAT INPUT (J/mm)
1.	150	22-24	95mm	41-42	135.71	1459

Table 3.shows the results based upon spatter formation, noise generation, fusion, crater depth,weld look, feed and under cut defect.

BRAND NAME	
ESAB	Fewer Spatters, More Noise, Good Fusion, Crater Defect
MODI	Less Spatter, Medium Noise, Good Fusion, Weld look is very good (Shiny Bead), No Defect
FERROSEAL	More Spatter, More Noise, Under cut defect, Crater defect, Fusion is ok
D&H	Less Spatter, Less Noise, Fusion is not very well, Undercut defect
ADOR	Less Spatter, Smooth Noise, Good Fusion, Uniform feed, Undercut defect

Table 4 .Scoring and Grading based on slag peeling, bead look and welder's appeal

BRAND NAME	Slag Peeling	Bead Look	Welder's Appeal	Score #	Deposition grams	No. of Electrode*	Cost (Rs.)	Cost/pc (Rs.)
ESAB	B	C	B	11	50	85	590	6.94
MODI	A	A	A	15	50	100	956	9.56
FERROSEAL	C	B	C	10	50	60	350	5.83
D&H	D	D	D	06	50	80	630	7.87
ADOR	O	O	O	18	50	90(5Kg)	1090	12.11

*Per Packet
#O: Out Standing (6) A: Very Good (5) B: Good (4) C: Satisfactory (3) D: OK (2)

Table 5 .Different parameters studied about electrodes

BRAND NAME	WEIGHT OF ELECTRODE (in grams)	WEIGHT OF CORE WIRE (in grams)	WEIGHT OF FLUX (in grams)	COATED ELECTRODE Diameter in mm
ADOR	56.70	43.76	11.21	5.0
D&H	54.68	43.60	10.29	5.1
FERROSEAL	58.70	43.42	14.22	5.1
ESAB	54.62	43.35	9.51	5.1
MODI	57.18	44.03	12.03	5.09

Table 6. Bead on the plate is subdivided into 5 sub parts and the averages of 5 subparts are taken into account.

BRAND NAME	PENETRATION mm	BEAD HEIGHT mm	BEAD WIDTH mm
ADOR	(2+1.5)/2=1.75	(3.4+3.5)/2=3.45	(1.1+1.05+1.12+1.2+1.18)/5=1.13
D&H	(1.5+1.5)/2=1.5	(3+2.8)/2=2.9	(1.05+1.15+1.2+1.2+1.1)/5=1.14
FERROSEAL	(1.5+1.5)/2=1.5	(3.5+2.5)/2=3	(1.05+1.1+1.08+1.15+1.18)/5=1.11
ESAB	(1.5+1.5)/2=1.5	(3.5+2.8)/2=3.15	(1+1.1+1.1+1.12+1.2)/5=1.10
MODI	(1+2)/2=1.5	(3.5+2.5)/2=3	(1.02+1.15+1.15+1.2+1.18)/5=1.14

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RESEARCH ARTICLE

Coping Mechanism for Natural Disaster: Insights from Cyclone Fani in Odisha

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ABSTRACT

The paper discusses coping mechanism for natural disasters among different actors of the society and their interaction to develop a sustainable approach. By referring Fani as the case, the study discusses coping strategies adopted by individuals, government and institutions.To understand the coping mechanism of different actors, the paper obtained information from both secondary and primary sources. To understand the coping mechanism of the government, the study uses secondary data and to understand the coping mechanism of individuals and institutions, we have done a case study in Balukhanda area of Puri district. We had done two visits to the study area- one is on 2nd of May, 2019 and another one is after one week of landfall of cyclone. The study found that individuals and youth of the affected area were helping each other in disseminating information about the cyclone. They were also helping people, who stay in kachha house, to move to a safer place.Similarly, different organizations particularly non-government organizations werealso working in disseminating information regarding cyclone, its landfall and probable consequences thereafter.

Key words: Natural Disaster, Coping Mechanism, Institutions

INTRODUCTION

Natural hazards have recently become a global concern. Over the years, natural hazards have increased not only inoccurrence, but also inenormousness leading to financial and human loss (Costanza& Farley 2007; IPCC 2012). Disasters whether natural or human-made are shocks to the functioning of the economic system and also cause socioeconomic deviations (Das, 2016). The United Nations (UN) defines a disaster as "a serious disruption of the

functioning of a society, causing widespread human, material, or environmental losses which exceed the ability of the affected society to cope using its own resources" (UN 1992). Developing nationsare witnessing an increasing occurrence of natural hazards. As per the estimates, India is now the third worst-affected country due to naturaldisasters (Retrieved from https://economictimes.indiatimes.com/news/politics-and-nation/on 10th July, 2019). The country's coastal regions, in particular, are highly vulnerable because of growing urbanization, high population densities and increasing economic activities such as agriculture, aquaculture, tourism, industries and trade etc. (Roy, 2019).Odisha, a state in India, is prone to cyclones because of its geographical situation. Of the 30 districts in Odisha, 14 are cyclone-prone out of which 6 are coastal districts adjoining Bay of Bengal(Mohapatra, et. al., 2012). Over a period of 120 years, these coastal districts have beheld11 severe cyclones and 55 cyclonic storms (http://www.ncscm.res.in/cms/more/pdf/ncscm-publications/orissa_final.pdf; Gupta & Sharma, 2000). From 1999 till date, the state has experienced three disastrous tropical cyclones, the first in 1999 (Super Cyclone) and the second in 2013 (Phailin) and third in 2019 (Fani).

Given the highly climate sensitive nature of Odisha, the question is whether or notpeople of Odisha are equipped to withstand the impacts of these natural disasters? Do they have the capacity to cope and recover? The present article aims to describe the coping strategieswith respect to disaster management to develop a meaningful understanding of lessons learned fromFani.Specificallythepaperexaminestheefficacyof various coping strategies adopted by government as well as by individual households in Odisha to hedge the negative impacts of Fani.

Literature Review

Natural hazards are becoming more frequent, resulting in damage to both family and communities (Ogata and Sen 2003). Changes in temperature, rainfall have increased not only the frequency; but also intensity of natural disasters on the earth. With the increase in the frequency and severity of disasters, a large number of populations have been hit during the last decades according to the data from EM-DAT, 2008 reference (Retrieved fromhttp:// www.emdat. be/Database/ Trends/trends.html. on 10thJuly, 2019). For example from 2000-04, one in every 19 people living in the developing world was affected by a natural hazard, whereas the figure stands at 1 to 1500 in the Organization for Economic Co-operation and Development (OECD) Countries (UNDP, 2007).

Along with the increase in natural calamities, the capability to cope especially human mortality, is also improving. However, the developing world is still susceptible to severe economic losses (Intergovernmental Panel on Climate Change 2014). For example, the middle income nations lost 1 % of GDP (Gross Domestic Product) due to natural hazards during 2001–06, whereas it was around 0.3 % for low income nations and less than 0.1 % for high income nations (IPCC 2012). In a study by Mirza (2003) the developing countries during 1990slost US$ 35 billion directly from natural calamities, and this waseven eight times higher in comparison to the corresponding figure in the 1960s. Roy (2019) claims that India is among the top five countries in the world that was most frequently affected by natural disasters from2006-2015. Based on EM-DAT international disaster database, Bahinipati&Patnaik (2015) have found that for India, lost around US$ 35.95 billion and US$ 11.41 billion between 1970 and 2012, respectively for natural hazards only.

The Bay of Bengal is one among the six main cyclone-prone regions in the world (Iwasaki, Razafindrabe, Shaw, 2009). Odishawith a coastline approximately 480 km. along the Bay of Bengal (Chandramouli, 2011) is therefore prone to natural disasters. For a poor state like Odisha, natural disasters have always hurt the economy. For example the loss of the state which was INR 1.05billion during 1970s, has increased to INR 8.51 billion, INR 68.81 billion and INR 105.04 billion during 1990s, 2000s and 2001–2009, respectively due to natural disasters such as cyclone, flood and drought (GoO 2004, 2011). Over a period of time the households have been able develop a variety of ex-ante and ex-post risk coping mechanisms to withstand the hazards.Somemechanisms have been developed for mitigating risk by reducing income;ex-post coping mechanisms are planned on top down hierarchical approach likeinfrastructuralresolutionsandfocus of solid resilience resolutions (Patnaik& Narayanan, 2010). While the upgrade

of disaster preparedness mechanisms in many of India's coastal states has led to drasticreductioninthemortalityrate, the number of people affected and the impacts on physical assetshave remained unchanged (Roy &Chatterjee, 2019). For example,from casualty count, the number declined fromover 10,000 in 1999 Super cyclone, 24 in 2014 because of cyclone Hudhud.Thegreatestimpact of the extreme weather events are increasingly being feltinterms of the loss and damage to the critical infrastructure in India's coastal regions (Retrieved fromhttps:// www.dni.gov/ files/ documents/ climate2030_india.pdf on 10th August, 2019). The trauma of Super Cyclone forced people of Odishato considers disaster preparedness, coping, and prevention strategies. The Odisha State Disaster Management Authority (OSDMAwith the support of the Government of India (GoI) and the United Nations Development Program (UNDP))has implemented the disaster risk management program (DRM) in many disaster prone districts of the state during 2002–08 to reduce possibleill-effects, (Das&Smith2012).Under the DRM program, interventions comprisingboth hardandsoftresilience enhancing actions are carried out.

Capacity building programs have been implemented by both governments and NGOs in order to increase responsiveness and understanding of disaster hazards at the community level. For example, OSDMA encouraged local people to establish committees for cyclone shelter management and maintenancein addition to the creation of multi-purpose cyclone shelters. Communities have also been skilled to increase their preparedness through mock drills. Moreover an accurate forecasting system was developed mainly as an initiative of the India Meteorological Department. With this background, the present paper attempts to understand the several coping mechanisms adoptedby government, households, and institutions living in Fani affected areas to hedge against the risks.

METHODOLOGY

This paperdiscusses the general process of disaster management through coping strategy to develop an understanding of the lessons learned from Fani. Taking clue from the literature, the study considers coping strategy as those mechanisms adopted by government as well as households to handle the disaster. The main source of empirical evidence for this paper is derived from contents of local daily, local magazines. In addition,YouTube videos, Facebook posts have been referred. The study highlights coping strategy of individuals, of institutions such as community, civil society, NGOs, and of Government.Content analysis of the materials is done and some case studies are presented in the paper.In addition, to strengthen the analysis, the study has done a case study in Balukhada area of Puri district. To understand the coping mechanism of individuals and communities, we have made two visits to the study area. One is before landfall, that is 2nd of May, 2019 and another is after one week of landfall. To obtain information on coping strategy of individuals and institutions, personal interview, group discussions and contain analysis are being done.

DISCUSSION

Fani (pronounced as Foni) has been considered as the strongest tropical cyclone that Odisha experienced since Phailin in 2013. Fani originated from a tropical depression that formed west of Sumatra in the Indian Ocean on 26th April. Cyclone Fani is different from all cyclones that had hit Odisha in the past because of its unusual timing, according to data from the Meteorological Department. Most extremely severe cyclones that hit India's east coast occur in the post-monsoon season between October and December. But Fani strike Odisha in May, therefore is termed as one of the 'rarest of rare summer cyclones' – the first in 43 years to hit the state, Odisha.

Government level of coping

With the forecasts that Fani would make its landfall in Puri, Chandrabhaga,state governmenthad held several meetings to check the preparedness in dealing with the cyclone. The evacuation process started as of 30th May'19 to ensure zero causality in mind. The state government had instructed all the district collectors to evacuate people from

the susceptible and low-lying areas to safer places. People living near the coast or in low-lying areas were evacuated and placed in multipurpose cyclone / flood shelters and other safe shelters.As of 3rd May '19, a record of 1.2 million people had been sheltered in over 4000 shelters which included 880 specially designed cyclone shelters. The coping strategies adopted by government are given in Table 1.-

Timely warning system, disaster preparedness, farsighted action, and well-planned large-scale evacuation strategies helped 1.2 million people in the sensitive coastal regionmove safely into nearly 4,000 cyclone shelters. The whole process of rescue, relief and management this time is very different from what had happened 20 years ago, when the super cyclone of 1999 had occurred. In the supercyclone of 1999, officially around 10,000 people had been killed. There was severe damage to life as well as property. Since then the government has been taking stringent actions so that a situation like the super cyclone is managed properly.

Individual Cases of Coping

The warnings of the cyclone were spread to residents in various ways. Constant news coverage in the broadcast and print media, online news networks, telephone, fax, email, and loudspeakers before the onset of the cyclone helped people realize the severity of the danger.

Institutional Coping

Organizations such as National Disaster Response Force (NDRF), Odisha Disaster Rapid Action Force (ODRAF), Panchayat Raj Institutions (PRI) agencies, teamed up to work tirelessly to evacuate 1.2 million people. More than 45,000 volunteers, 2,000 emergency workers, 100,000 officials, youth clubsextended their hands to the organizations. The preparation included sending three million targeted messages and setting up around 7,000 kitchens and 9,000 shelters.

Along with Government, several organizations have come forward to help in reviving the devastated state. The World Bank, SOS Children's Villages of India, ActionAid Association, SEEDS India, Paytm, Amazon, Zomato, Habitat for Humanity, SOS Children's Villages of India, ActionAid Association, Goonj, Ketto, Milaap, Oxfam India, HelpAge India, World Vision, DonateKart, ImpactGuru, Khalsa Aid, Hamara Bachpan etc. are only few to name who have come forward to help the state get back to normal cycle.

Government, Individuals and Institutions: An interactive Learning and competence Building

From different secondary sources, it is found that in Odisha government had taken all efforts in evacuating people from vulnerable places and creating awareness among the backward section of the society. However, from our field survey, we found that, individuals and youth also played a major role in creating awareness in their localities. They were helping elderly people in shifting their valuable belongings to the safer place. However, it is reported that people found difficulties in shifting their domestic animals. It is found that, some families were not convinced to shift from their houses, because of their domestic animals. However, with the help of different formal as well as informalinstitutions, millions of people were evacuated. NDRF, ODRAF, Indian Navy and several others were engaged in disseminating information about the cyclone, its landfall area, wind speed, landfall impact and many more. Similarly, different non-government organizations (NGOs) were also working in disseminating information and evacuating people. Since, different workers were working for the same objective, the study found that through interaction among these actors, villagers of affected areas receive different sorts of do's and don'ts starting from pre-disaster, during disaster and post disaster phase. In pre-disaster phase, whether it is government, individual or communities, all of them were trying to save lives of people by evacuating the vulnerable society to safer place. During disaster, dry foods and emergency lights with all necessary equipment were arranged. Soon after disaster, every actor of the society was involved in providing foods, clearing roads, cutting trees and in many more activities.

No doubt, disaster has been a regular phenomenon in Odisha. However, now time has come to put a combined effort in coping up with the disaster.

CONCLUSION

Cyclone Fani has left people of Odisha in severe distress. According to official estimates, 64 people lost their lives for Fani. But what considering the supremacy of the cyclone, it is noteworthy that more lives have been saved. A record 1.2million people were evacuated timely, and almost 7,000 kitchens, catering to 9,000 shelters, were made functional overnight. This mammoth exercise involved more than 45,000 volunteers. The government's "zero casualties" policy for natural disasters, strong plan, effective synergy of groups, strongcyclone shelters in vulnerable pockets of the state, along with early warning systems kept the fury of damage only to properties and public infrastructure. Over a million trees, hundreds of miles of power lines, and innumerable homes and schools have completely been destroyed. The United Nations office for Disaster Risk Deduction (UNISDR) and other organizations have hailedthe efforts of Odishafor its dainty task in dealing the fury and wrath of the nature.

Though the relatively low death toll hides extensive damage to infrastructure and livelihoods, such cyclones call for development of a bettercapacity of the people to be able to minimize the loss of assets and livelihood. In the wake of frequent natural disasters in Odisha, communities need to be prepared to withstand damages, in addition to saving lives.The present study reveals that the coping strategies have improved a lot in a disaster prone region like Odisha. But still there is long way to go. Steps need to be taken to strengthen a resilient society. Mostly people in low lying areas are vulnerable to natural disasters and problem is that with their bare minimum existence, they don't have the capacity to afford safe buildings and other better entitlements. Therefore, linking disaster management to livelihood security and capacity building of the community should be given more importance.

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Table 1: Coping Strategies of Government during Cyclone Fani

Preparedness	Early Warning	Response and Recovery
Infrastructure Development (Cyclone Shelters Promotion of Capacity building programs Training Anganwadi, Asha workers, SHG	Timely dissemination of warning Diverse communication system for early warning Do's and Don'ts during Cyclone Cautions to Fishermen	Suspension of trains and flights Stock of medicines and food supplies Measures for uninterrupted Electricity and Telecom service Activating District Emergency Operation Centers and control rooms Evacuation of people from low lying areas Advising tourists in Puri, Konark to leave Special care to vulnerable people and pregnant ladies Restoration work by NDRF, ODRAF and one lakh officials

Case 1: Benevolent effort of Police

Nothing can be more appreciating than a prompt and effective action taken by Odisha authorities that helped in the evacuation of 12 lakh people within a day, minimizing the scale of devastation.
Several departments worked together to make the herculean rescue effort a possibility and personnel extending their services, going beyond the line of duty at times.

The picture is of Superintendent of Police ShriPinak Mishra, IPS, requesting villagers living in low-lying areas to take refuge in the shelter houses built to restrict the calamities of Cyclone Fani.

Shri Mishra's gesture with folded hands to cooperate & move to the safe zones shows the humanitarian approach of police who are often criticized by common people. The compassion and commitment of police for the safety and security of the citizens are certainly admirable.

Source: https://www.news18.com/

Case 2: Tireless work of NDRF Team

NDRF had deployed 50 teamsto carry out rescue works in Cyclone-Fani hit areas in Odisha. This is the second largest deployment after Kerala floodswhere 58 teams had been engaged. From 'seven quick deployment antennas (QDAs)' for mobile telephony to cutting edge cutters, both men and machine worked tirelessly to bring Odisha back to normalcy. In the first three days, NDRF teams were in field day in and out to respond the call of the hour. In all, there were 19 senior supervisory officers, over 100 local supervisors, six doctors and paramedics, signals men, drivers, etc. There were 1,500 operations men in orange uniforms of fifty teams from four battalions-Mundali, Guntur, Kolkata and Varanasi.

DIG Singh and his entire team believes that Odisha has put in place an excellent disaster preparedness system, which according to them is 'the best in the country' and is prepared to meet any disaster.

Source: https://www.firstpost.com

Case 3: Female cop hero Ms. PritismitaParida

The constable of Talachua Marine Police Station single handedly evacuated around 300 women and children on her motorcycle. Working tirelessly and going beyond the duty hours, the 23-year-old policewoman rode her bike for three days from May 1 to 3 to shift the women, children and elderly to the cyclone shelters.

She shifted the most vulnerable ones to safety from remote areas of Talachua, Rangani, Khasmunda, Pataparia, Baghamari, Manjulapali, Dolasahi, Keruapala and other villages. She also convinced women about the necessity to move out of their homes and shift to cyclone shelters.

"After the authorities warned that cyclone Fani would hit coastal pockets, I decided to shift women and children on my motorcycle. It was dangerous to drive a motorcycle with two pillion riders on slippery village roads but, I was determined to rescue them. As many villagers were getting restless, I had to shift two at a time," said MsPritismita.

Source: Indian Express, 9th May

Case 4: Samaritan PratapSahu

After Fani left behind a trail of devastation and plunged all affected areas into darkness, ShriPratapSahu from Bhubaneswar decided to visit these areas on a bike carrying a generator to help people charge their small inverters, mobile phones and torches.

Since most of the electric poles were uprooted in most of the areas where Fani caused havoc, ShriSahu, took out his generator on bike and began visiting various villages to help people charge their phones and other gadgets for free. He began on May 4, continued even after 10 days.

"I knew that there would be many people who need to charge their gadgets. Hence, I kept around thirty connectors which would help multiple people charge their gadgets at the same time. I even asked the villagers to bring extra connectors to enable more people to charge their phones and inverters," he informed. The man spent from his own pocket to put oil in the generator and visit villages on bike. Despite the fact that Fani damaged his house too, Pratapwas determined to help people in remote areas first.

Source: https://www.mycitylinks.in

Case 5: Death-defying acts of doctors, nurses in Odisha's Capital Hospital

On 3rd May, when the cyclone began to bring down the ceiling of the SNCU, Capital Hospital, Bhubaneswar, the 13-member team stood strong in resolve to let no harm come in the way of the babies. As ceiling collapse became imminent, the nurses came together to make an umbrella formation and provide a protective shield over the babies.

Defying all odds, 23 new born babies were shifted to Paediatric Intensive Care Unit (PICU) through the inner stairs and located the, which was better placed as neither wind nor rainwater was entering it.

The team members formed a human chain and with the help of their parents successfully shifted the babies. All babies were immediately provided oxygen from the portable cylinders. Later, 11 babies, who were in critical condition, were shifted to other hospitals.

Source: Indian Express, 10th May

Case 4: Humble gesture of Marwadi Yuva Manch

A group of young people from MarwadiYuva Manch, extended their helping hand to provide voluntary services. The Yuvamanch provided services at many places of Puri and Khordha district including Nimapara, Delanga, Balanga, Bamuna, Motari, Kanasa, Jatni, Alarakud, Brahmagiri, Nirakarpur, Kalamati, Podpada and Jatni.

From 4th May till 18th May, those group of young people distributed food, glucose, mosquito coils and drinking (mineral) water, provided dinners to the NDRF members, donated blood and helped others in the rescue operation. Importantly, this team was the first to reach out a few villages to provide relief materials. In some villages in fact, this team was the first to reach to provide relief materials. Their tenacious service to people received admiration from all.

Source: https://kalingatv.com/

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RESEARCH ARTICLE

Simulation Study of Collimators to Use at Low Energy Facility

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ABSTRACT

Accelerators are very much important in the present days starting from the research to the application to the society. As the important job of the accelerator is to deliver the required ion beam of desired energy it is also important to produce mono energetic, focused ion beam. Naturally as the ions are same charge they repeal and diverge where as to get a desired small focused beam one need to collimate the diverge ions. Here we have shown a simulation of a collimatorarrangement consisting of 3 metallic discs and found that a particular arrangement will produce a suitable focused ion with less loss in the ion beam. It can be used for any accelerator which generates ions of low energy.

Key words: Accelerator, low energy, simulation, collimate.

INTRODUCTION

Improvements in accelerator technology over the past many decades have provided opportunities for increasingly sophisticated investigations into the fundamental properties of matter. Over the years, the size and complexity has grown to include a vast range of beam energies and detection equipment spanning the disciplines of nuclear physics and high energy particle physics. For low energy nuclear physics, two accelerator facilities are currently available to users in the country: the 14UD BARC-TIFR Pelletron, TIFR [1], Mumbai and 15UD IUAC Pelletron at New Delhi [2]. Both are mature facilities with limited scope for hands-on training of entry level students and young faculty in accelerator science. In addition with big machine there is also small accelerator like Table top accelerator (TTA). This produces ions of low energy. One TTA is exist at IUAC delhiwhereas the other is at Nuclear Physics group at the Manipal Centre for Natural Sciences (MCNS) [3-5]. It provide an easily accessible tool for training students and beginning researchers in the most basic aspects of accelerator design including critical components such as ion optics, beam transport and vacuum systems, became evident.In both the cases they have an experimental chamber in addition with many other units.One of the main important aim is to get a focused ion beam from the machine. So the use of collimator is the must. The main problem is the arrangement of the collimator or slits. The figure of both the machine has shown in Fig.1. There are many componenet of the machine out of which some few important parts are

a) Ion source: The cold plasma-based PIG ion source has been used in both the machine which provide proton upto 60 keV. With this, it has been possible to get a stable beam with 300 micro amps. The full ion source is assembled in nylon housing and connected to 60 kV power supply. It is suitable for many ions. Presently the charge state is 1. Since E=qV, for hydrogen as q=1 and V = 60KV so the energy of the proton is 60 keV. The higer ions can also possible to get but with lower energy range.

The other importantcomponent of the acceleratoris b) The focusing unit: The electrostatic quadrupole triplet (QT). The QT assembly is inside a stainless steel (SS) vacuum jacket. The mian purpose of the QT is to focus the beam and provide to the input to the bending magnet.C) Bending magnet:A 90^0 bending magnet is mounted on the beam line. The magnet is created by assembling a number of small permanent Nd magnets arranged inside a housing. The B field is uniform and it can be measured by using Hall probe. All the Nd pellets are inserted in the magnet housing which has been made up of thick MS plates. There is a hand wheel to control the height of the shorting plates. The shorting plates are used to vary the B field. d) Scattering chamber: A large scattering chamber for multipurpose use with many ports. A up and down movement including angular rotation system has been coupled with the target ladder to keep it in any direction. A faraday cup is there to measure the beam current. There are also view ports and electrical feed-through port.

METHODOLOGY

Simulation of the collimator

The currently simulated collimates can be placed before the scattering chamber and after the bending magnet. To reduce the beam spreading. This will cut some beam so the beam current will go down which requires an optimized position for the disc to be placed. In order to understand this a simulation has been performed using SIMION [6] package. All the discare grounded and the beam of 10mm dia has been fall on the disc. The three disc position has been varied and found the optimum distance for the minimum loss and maximum transmission. The disc arrangement has been shown In Fig.2 in addition the ion trajectory also. One can see also from Fig.2 the cross sectional view of the setup and One can see that the ions are very much focused say ~4mm dia at very far (~30cm) from the originatingpoint.Which is the requirement of the experiment.

RESULT AND CONCLUSION

A simulation has been performed for the position of the metallic disk having circular shape to reduce the beam spread in low energy accelerator. Using SIMION it has shown that a specific position of the disc are very important for this purpose and the disc can be used for any low energy ion beam facility to reduce the beam spreading. The metallic disc can be used as collimator or slits.

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The other is very much thank full to the SIMION group and IUAC people for providing opportunity to visit their lab and give idea about the component including the operational principle. Author also thanks to MCNS-MAHE to provide image of existing TTA on newspaper.

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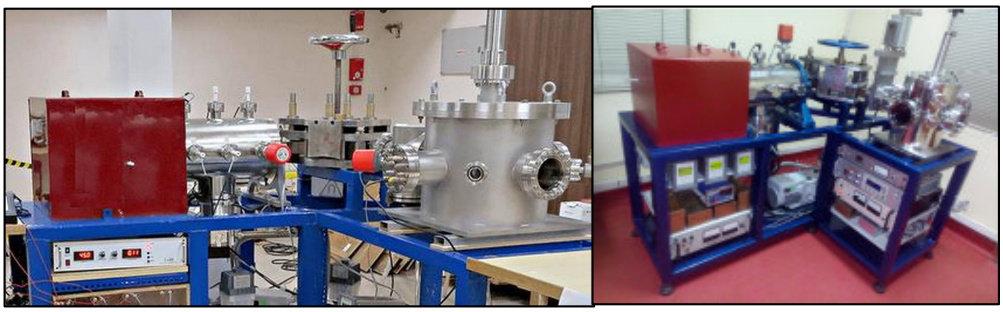

Fig.1.The existing small Table top accelerator of Manipal (left) [7] and IUAC Delhi (Right) [8]. Both have the scattering chamber including other component.

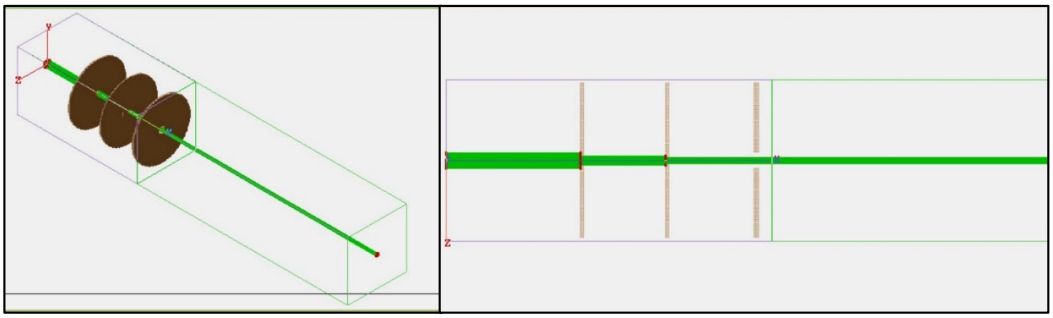

Fig.2.The 3D view of the metallic disc used for the simulation (left). The cross sectional view of the same (Right)

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REVIEW ARTICLE

The Role of Small Millets as Functional Food to Combat Malnutrition in Developing Countries

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ABSTRACT

Small millets comes under a group of coarse cereals that are considered as staple food for the tribal people in Asia and Africa, where cultivation of major crops like rice, wheat, maize fails to produce substantial yield. Small millets are valued for their nutritional properties as well as due to their high resistance to abiotic stresses and ability to grow with minimum nutrient input. Minor millets can grow anywhere without exploiting much of the natural resources which in turn leads to sustainable agriculture and environment friendly farming. Small millets are rich source of carbohydrates, dietary fibres, fats, proteins, vitamins essential minerals and trace elements, essential amino acids, anti-oxidants and hence can be regarded as functional foods. Despite its excellent nutritional property and ease of cultivation method, very less scientific research have been done till date on minor millets. They are always being neglected and thus referred as "orphan cereals" by scientists.The presence of phenolic compounds, soluble fibers and starch–lipid–protein interactions in minor millets attribute to theirhypoglycemic properties. These neglected crops can assure both health and food security issues due to their therapeutic properties as well as their capability to resist severe weather conditions.

Key words: Small millets, functional foods, anti-oxidants, nutrition.

INTRODUCTION

Millets are the coarse cereals cultivated by smallholders and tribal farmers mainly under rainfed conditions. The distribution of millets is mainly noted in the Asian and African continents and some portions of Europe. These are among the foremost ancient cultivated crops in India. Millets are categorized into two, namely, major and minor or

small millets. Sorghum (*Sorghum bicolor* L.) and pearl millet (*Pennisetum typhoides* L.) belong to major millet group, while finger millet or *ragi* (*Eleusine coracana* L. Gaertn), barnyard millet (*Echinochloa frumentacea* L.), foxtail of Italian millet (*Setariaitalica* L.), *kodo* millet (*Paspalum scrobiculatum* L.), little millet (*Panicum sumatrens* L.), proso millet (*Panicum miliaceum* L.) and brown-top millet (*Brachiaria ramosa* L. Stapf; *Panicum ramosum* L.) are known as small millet (Maitra, 2020). The grains of small millets are nutritionally superior to rice and wheat, as these are rich in dietary fibre, proteins, minerals and vitamins and hence these are re-evaluated as nutri-cereals. Agricultural sustainability is comprised of food and nutritional security and in developing world malnutrition is a major concern where majority of human population is habituated in cereals-based diet. In this context, millets can be a suitable option for nutritional security of undernourished people of developing countries (Maitra and Shankar, 2019). Apart from nutritional importance, small millets have the qualities to ascertain agricultural sustainability in resource-poor and fragile ecological conditions. Small millets in cropping system provide multifaceted benefits like yielding of grains and forage, enriching of agro-diversity, checking of erosion in arid regions and assuring higher C sequestration. Under the adverse impacts of global warming and climate change ecologically hardy small millets can withstand under hostile climatic conditions (Brahmachari *et al*. 2018).

In India and Africa,small millets as whole or flour form are mainly used for food and allied purpose, whereas in Japan they are mainly used as birds' feed (Asharani *et al*., 2010). India is one of the major producers of these minor crops. According to Chandel *et al*.(2014), the world total production of millet grains was 762,712 metric tonnes and India being at top position with an annual production of 334,500 tonnes contributing 43.85% of world's production. Small millets are excellent source of nutrients and contain 60–70% dietary carbohydrates, 6–10% protein, 1.5–5% fat, 12–20% dietary fibre, and 2–4% minerals, many essential phytochemicals (phenolics, flavanoids, tocopherols and carotenoids)compared to rice or wheat (Hadimani and Malleshi, 1993) and have several health benefits to the consumers. There is a huge scope of developing value added products from minor millets, which may have health benefits to human beings.

Millets may be considered as functional foods. Functional foods contain bioactive ingredients which are beneficial for physiological benefit of human beings and can combat with chronic diseases (Banerjee and Ray, 2019). The flavonoids like tannin, anthocyanin; phenolic compounds; tocopherols and carotenoids- found in small millets, are natural antioxidant that protect the phospholipid membranes around nerves, heart, muscles and red blood from the attack of reactive oxygen species and thus prevents from carcinogenesis, cardiovascular diseases and aging (Theriault *et al*., 1999). Carotenoids are reported to prevent atherosclerosis (Dwyer *et al*., 2001), maintain normal functioning of immune system, retina of eyes (Beatty *et al*., 1999) and serves as precursors of vitamin A.

Importance of Small Millets in Food Chemistry

Minor millets contain all essential nutrients carbohydrates, dietary fibres, proteins, fats, vitamins, essential elements and anti-oxidants. Nutraceutical research is gaining popularity due to public awareness of health and nutrition. As the importance of dietary fibres, anti-oxidants, phytochemicals are proven by scientific research; there is a constant search of newer sources of nutraceuticals. Minor millets, in this context, is highly valuable natural resources that contain all essential nutrients and can be used as functional food. In some parts of India, small millets are staple food among the people who belongs to low-income group. The biochemical components of these millets can justify why they are considered as functional food and how they are effective against diabetes, tumour, atherosclerosis and microbial action. This review article will deal with biochemical constituents of minor millets and their role in human health. These cereals are one of the oldest crop known to human civilization butdeprived of scientific attention for a long period of time. A brief description of important biochemical components of small millets are listed in Table 1 (Shobana *et al*., 2013; Maitra, 2020).

Carbohydrates

Finger millets are rich in carbohydrates and contains free sugars (1.04%), starch (65.5%), non-starchy polysaccharides or dietary fiber (11.5%) (Gopalan et al., 2009). The dietary fiber content of brown rice, polished rice and all other millets such as foxtail, little, kodo, and barnyard millet is lower than finger millets (Shobana et al., 2013). Starch is a polysaccharide which has two components, namely amylose and amylopectin. In finger millets, the amylose content is found to be lower (16%) than other millets such as sorghum (24.0%), pearl millet (21.0%), proso millet (28.2%), foxtail millet (17.5%) and kodo millet (24.0%) (FAO, 1995).

Proteins

In finger millets, a variety of proteins can be found. Prolamins, a group of plant storage proteins, rich in prolines are main fraction obtained from finger millet protein. Generally, cereals and millets have lower amount of lysine than that of legumes and animal protein (ICMR, 2010). Albuminand globulin fractions of finger millets contain many essential amino acids while the prolaminfraction consists of higher proportion of glutamic acid, proline, valine,isoleucine, leucine, phenylalanine but low lysine, arginine, and glycine (Shobana et al., 2013).The chemical score (i.e., a measure of protein quality, calculated as the ratio ofamount of amino acid in a test protein over reference protein expressed as percentage) of finger millet protein is 52 compared to 37 of sorghum and 63 of pearl millet (FAO, 1995). Higher levels of sulfur containingamino acids are present in finger millets compared to milled rice. The protein digestibility of finger millet is affected by the tanninconten of the grain.Another minor millet, foxtail millet is known for its high amounts of proteins and minerals (Suma and Urooj, 2012).

Fats

Finger millet lipids consist of 70–72%neutral lipids mainly triglycerides, traces of sterols, 10–12% of glycolipidsand 5–6% of phospholipids (Shobana et al., 2013). In finger millets, 46–62%oleic acid, 8–27% linoleic acid, 20–35% palmitic acid and traces of linolenicacid are present. Oleic, linoleic and linolenic acids are unsaturated fatty acids containing 18 carbons whereas palmitic acid is a saturated fatty acids containing 16 carbons. Fat content of finger millet is lower compared to pearl millet, barnyardmillet, little millet, foxtail millet, which may account for the better storage properties offinger millets compared to other millets.

Essential nutrients

Finger millet is an exceptionally rich source ofmicronutrients. It contains calcium (344 mg), phosphorus (283 mg), potassium (408 mg), iron(3.9 mg) (Gopalan et al., 2009), and many othertrace elements and vitamins. Nearly 49 % of total calcium is found in husk of finger millets. "Hamsa"variety of finger millet is known to contain much higher levels of calcium(660 mg). The phytic acid contentof finger millet is somewhat lower than common (proso) millet and foxtail millet. The oxalates are also found in finger millet inthe range of 29–30 mg. Platel et al., 2010and Rateesh et al., 2012 observed increased bio-accessibility ofminerals (iron, calcium, zinc, manganese) on malting of finger millet. Thus finger millets can be considered as a good supplement for children and adolescentsfor improving bone health and haemoglobin.

Vitamins and Amino Acids

Small millets contain important vitamins like thiamine, riboflavin, niacin, vitamin C and essential amino acids like arginine, histidine, lysine, tryptophan, phenylalanine, tyrosine, methionine, cysteine, threonine, leucine, isoleucine, valine. Among these, tyrosine is only found in foxtail millets and barnyard millets are deficient in all of the essential amino acids (Shobana et al., 2012).

Phenolics compounds

Millets contain phenolic acids, which are located in the pericarp, testa, aleurone layer and endosperm. The richness in phenolics acids, tannins and phytate can reduce the risk for colon and breast cancer in animals (Graf and Eaton 1990). Variations can be observed in phenolic content of finger millet depending upon their varieties (Chethan &

Malleshi, 2007). Higher levels of phenolic compounds are reported in Brown variety contains higher level of phenolic compounds compared to white variety as reported by Chethan & Malleshi, 2007. Finger millet is reported to contain many phytochemicals which are have health benefits (Chethan,2008; Shobana, 2009; Shobana, Sreerama, & Malleshi, 2009). A phenol compound exists in both free and bound forms in fingermillet (Subba Rao & Muralikrishna, 2002). Important phenolic compounds found in finger millets are caffeic acid and catechin. Caffeic acid is known to decrease the fasting glycemia and increasethe glucose uptake in rat adipocytes and mice myoblasts; whereas catechin was found to improve the glucose tolerance in rats and quercitin inhibited glucose transportin transfected oocyte model in rats (Scalbert et al., 2005). There is not enough literature available on the bioavailabilityof phenolics in finger millet which is utmost necessary to studythe nature of phenolic compounds in in-vivo models to detect their anti-oxidant function and the long-term effects of thesephenolicsin human health.

Rao et al., 2010 reported that the phenolic contentof khodo-millet (10.3%) was highest, followed by finger millet (7.2%) and foxtail millet was found to contain minimum phenolics (2.5%). As far as reducing capacity is concerned, finger millet was having the highest (5.7%) followed by foxtail millet (4.8%) and the prosomillet was found to have least reducing property (2.6 %). Davies Oxidative damage of cellular-free radicals can lead to damage of cellular constituents and the repair mechanism depends on presence of antioxidants. The antioxidants donate either an electron or hydrogen to cellular molecules oxidized by free radicals and thereby prevent the damage of cellular constituents, including DNA, proteins and lipids membranes from free radicals (Davies, 1991). With respect to the above observations, it can be assumed that the reducing property found in all the millets can help in reducing the oxidative damage caused by free radicals.

Role of Small Millets as Functional Food

The concepts of food consumption have been changed and presently health conscious people having higher purchasing capacity are in search of nutritious foods. The intake of food with nutraceutical ensures health benefits and well-being reducing hazards from chronic sickness like cardiovascular disorders, some cancers and fatness. The nutraceuticals actually contain “antioxidants” which are micronutrients having the ability to neutralize the actions of free radicals, the potentially harmful products generated during a number of natural processes in the body and associated with ageing of cells and tissues. Small millets contain enough of phenolics, a powerful antioxidant and thus small millets and their value added products are fetching considerably good demand among the consumers. Further, the consumption of finger millet based diets showed significantly lower plasma glucose levels due to the rich fiber content with it compared to rice and wheat. The small millets are rich with bound polyphenols which reduce of the action digestive enzymes (Rohn *et al*., 2002). Flavonoids, phenolic acids, and proanthocyanidins are some polyphenolic compounds known to forage the radical and thus prevent many diseases and morbid states (Himansu *et al*., 2018). The nutritionally rich millets are having enough potential to ensure health benefits when consumed as staple cereal as well as value added products and hence these small grains truly deserve the recognition as nutri-cereals.

CONCLUSION

Small millets are having a potential to serve as an important source of nutraceuticals. They can be used to treat diabetes, tumour, obesity, pre-mature aging and serve as an important source of calcium, essential amino acids and vitamins. A variety of value added product can be derived from small millets and thus there is always a huge scope of research to evaluate the nutritional property of these value added products. The nutraceutical and nutrigenomics field of research always look for natural source which are rich in nutrients. Small millets are cheap, easy to grow, environment friendly and excellent source of nutrition which supports sustainable agriculture.

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Table 1. Nutritional value of small millets (all values are per 100 g of edible portion)

Millets	Moisture (g)	Protein (N*6.25)	Fat (g)	Mineral (g)	Dietary Fibre (g)	Carbohydrate (g)	Energy (kcal)
Finger millet	13.1	7.3	1.3	2.7	11.5	72.0	328
Proso millet	11.9	12.5	1.1	1.9	-	70.4	341
Foxtail millet	11.2	12.3	4.3	3.3	2.4	60.9	331
Little millet	11.5	7.7	4.7	1.5	2.53	67.0	341
Kodo millet	12.8	8.3	1.4	2.6	2.47	65.9	309
Barnyard millet	11.9	6.2	2.2	4.4	1.98	65.5	307
Brown-top millet	11.3	9.0	1.9	3.9	-	71.3	338

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RESEARCH ARTICLE

Empirical Measurement of Risk and Return of Indian Sectoral Indices with Special Reference to Bombay Stock Exchange

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ABSTRACT

Investors always invest in different investment avenues on the basis of risk and return. Investors who don't want to take more risk by means of return usually invest their money in secured financial securities.However investors those who can take more risk prefer to invest their money in stock market to get high return. Investors by means ofmaximum risk-taking ability have to evaluate the security market on the basis of risk as well as return consequently they can modify their portfolio as per current market situation. The study investigates tomeasure the risk in additionto return of the Sensex as well asselected sectoral indices of India's most important stock market i.e. Bombay Stock Exchange (BSE) . This research article has been analysed to find risk and return and ranking the sectoral indices according to their performance. Eventually, the linear association has been recognized among selected sectoral indices with Sensex. Regression analysis has been applied betweenselected fifteen sectoral indices to find out the effect of the sectoral indices on Sensex. Data has been taken from secondary sources for the study. To find risk-return trade-off the different indices data have been composed from the official website of BSE for a period of ten years from 1st January 2010 to 31st December 2019.

Key words: Sectoral Indices, Sensex, Risk, Return, Beta, Trade-off, Regression Analysis

INTRODUCTION

Nowaday's most of the investors are interested in investing in the stock market because of its growth rate and high yield. Investors can also invest in mutual funds, bank deposit, real estate, gold etc. But stock market is more attractive for the investors, because of its expected high return (Akhila and Neeraja, 2018). From the starting of the

1990s in India, important stepsimplemented for economic liberalization. Moreover many steps have been taken to increase the activities of stock market. Power of SEBI is increased to control the stock market. Regulations for international investors are also changed. (Shanmugasundram, Benedict, and John, 2013). These major steps have led to in substantial developments of stock markets in India to play an outstanding part in Indian economy. Pursuing the underlying forces of the Indian stock market is very much suitable for traders, investors, and policymakers. The SCRA recognized for the resolution of supporting, regulating as well as controlling the business of trading and dealing in securities (Ahmed, 2008). The sectoral indices give a single value for group of companies in same industry. These market indices are suitable devices of the stock market whichspecify the trend of the security market for a time horizon. By means ofconsidering the sectoral indices, investors canassociatein what mannerparticular stocks in addition mutual funds have performed against market displays for the same time horizon.

Market indices provide historical data of stock market performance, which provides information to the investors for a better understanding of their investment decisions. Investors, who do not have enough information regarding different stocks to invest, can use the indices for their investments in the security market. Stock market indices also deliver a benchmark through which investors can associate the performance of their stock portfolios. Stock market indices are also used as a forecasting tool. Stock market trends can be forecasted by understanding the historical performance of the stock market indices (Shanmugasundram and John, 2013).Sensex deals with the stock prices of thirty listed well-established companies of the Bombay Stock Exchange. The thirty companies are nominated on the foundation of their financial accuracy and performance. Sensex consists of large and entrenched companies that are representatives of the numerous industrial sectors. Sectoral indices are compiling of stocks assembled in such a manner to trajectory a specific market or sector. A Sectoral index includes the stocks which are part of the same industry or sector. Companies from same industries are present in a sectoral index. So when company's stock price changes, that particular index also changes. So this paper analysed to find the return and risk of different indices including SENSEX.

Literature Review

Bhunia (2012) used capital asset pricing model for the analysis. He found that risk and return is the most important factor in Indian stock market. He has calculated beta of Sensex and also of the stocks of different bank indices.On the other hand Patjoshi (2011) analysedvolatility in Indian stock market by taking various indices of BSE and NSE. Similarly Nandini, Patra, Mishra (2012) studied the volatility by finding month of the year effect and also day of the week effect. They have used statistical techniques and GARCH (1,1) model for the analysis. They found there is a significant difference in the return of the days of the week. SimilarlyNandini (2013) analysed to find the volatility in the Indian stock market. She also found that there is a significance difference in the return of days of the week in different stock exchanges. Conversely, Shanmugasundram, John (2013) measured risk and return in the Indian Sectoral indices in addition to Nifty for different time periods. In this study five Sectoral indices (Auto, Bank, FMCG, Infrastructure and Information Technology) and Nifty from 2004 to 2012. Here ANOVA and t test employed to find the risk involves among the Nifty and other sectors in different time interval.They didn't get any significant difference in the standard deviation of different sectoral indices. But they found a significant difference in the mean return for the study period. On the contrary, Lakshmi (2013) tried to find the volatility in different sectoral indices of Indian stock market. She has used ARCH model for a period of 2008 to 2012 for the study. She has taken 11 sectoral indices for the analysis. She found highest volatility in reality sector. There was 80% volatility in reality sector, when 20% volatility is in NIFTY. She also found that banking sector has the lowermostinstabilityaround 12% for the period. Whereas,Mohandas and Renukadevi (2013) had studied the instability of BSE Sectoral Indices by considering data from 2001 to 2012 for 13 sectoral Indices from Bombay Stock Exchange. They used different models and found ARCH and GARCH is the best model to predict the volatility in the stock market.Similarly, Ansar et.al (2014), done the research to find out the risk and return of different portfolios and their impact on bullish and the bearish market. They found a significant performance in the portfolios return and risk. On the other hand, Patjoshi (2016) has done

the research in Indian stock market. He has taken Sensex and banking stocksindices to find the risk and return for the analysis. Similarly;Patjoshi and Tanty (2016) analysed the stock market volatility in BSE and NSE of India whilePatjoshi and Tanty (2017) scrutinizes the volatility of 30 companies of BSE SENSEX. They have taken daily return into consideration to find the volatility.

Alternatively Patjoshi (2016) investigated the issue and challenges faced by the Indian Stock Market while Patjoshi (2016), scrutinized suitable day in a week for investment, in the BSE.On the other hand Patjoshi and Nandini (2020) have done their research by taking the closing value of Sensex and different steel companies for the period from 2010 to 2019. They have used descriptive statistics, t test and correlation for the analysis. They found that Sensex average daily return is positive whereas all the sample companies return is negative. Also the volatility is more for the sample companies than Sensex. Similarly Patjoshi and Nandini (2020) analysed the day of the week effect in Indian stock market from the period 2000 to 2018 by taking the returns of Indices of BSE. They have used descriptive statistics and GARCH model for the study. They found a statistically significant return in the days of a week.

Objectives of the Study

i. The prime objective of this study is to analyze the risk and return of Sensex and selected sectoral indices from BSE.
ii. To determine the impact of sectoral indices returns on Sensex return.

Hypothesis of the Study

H_0 – there is no significant difference in the return of SENSEX and sectoral indices.
H_a - there is a significant difference in the return of SENSEX and sectoral indices.

METHODOLOGY

To find out the risk and return BSE 30 SENSEX and 15 different sectoral indices has been taken. Day wise closing value of SENSEX and sectoral indices from 2010 to 2019 has been taken into consideration for the analysis. All the secondary data were collected from BSE website. Daily closing value of BSE Sensex and fifteen Sectoral Indices of Bombay Stock Exchange, namely S&P BSE Bankex (Bank), S&P BSE Consumer Discretionary Goods & Services (Consumer Discretionary Goods & Services), S&P BSE Fast Moving Consumer Goods (Fast Moving Consumer Goods), S&P BSE Teck (Technology), S&P BSE Energy (Energy), S&P BSE Information Technology (Information Technology), S&P BSE OIL & GAS (Oil & Gas), S&P BSE Finance (Finance), S&P BSE Basic Materials (Basic Materials), S&P BSE Healthcare (Healthcare), S&P BSE Auto (Auto), S&P BSE Utilities (Utilities), S&P BSE Telecom (Telecom), S&P BSE Consumer Durables (Consumer Durables) and S&P BSE Realty (Realty) indices have considered for the study.

Methods of Investigation

The main objective for the research is to find out the risk and return tradeoff between SENSEX and 15 sectoral indices. Linear regression model is used to find the relationship between Sensex as the dependent variable and fifteen sectoral indices as an independent variable. Different statistical methods like descriptive statistics, correlation and regression is used for the analysis and to test the hypothesis.
The Daily returns of Sensex and fifteen sectoral indices have been calculated by using the below formula;

$$rt = \ln (It/It\text{-}1)*100$$

Where

RT is Return on index, ln is Natural logarithm, it is closing value of the index and it –1 is Closing value of previous dayindex

Standard Deviation and Variance

A standard Deviation may be an applied mathematics tool that measures the variability of returns from the arithmetic mean, or volatility. It's a live of the values of the variables around its mean or it's the root of the add of the square deviations from the mean divided by the amount of observations. It's denoted by sigma(s). Its calculated exploitation the formula mentioned below:

$$\sigma = \sqrt{[1/(N-1)] \sum (x_i - \bar{x})^2} \text{ over } i = 1 \text{ to } N$$

Where, $\bar{x}$is the sample mean, xi's are the observations (returns), and N is the total number of observations or the sample size.

Variance= σ^2

The variability in return includes both

Systematic and unsystematic risks

Correlation calculates the connection between two variables and is dignified by the correlation coefficient(r) with clarifications (x1, y1), (x2,y2),...(xn,yn), can be resulting by evaluating the correlation coefficient(r)

$$r = \frac{1}{n-1} \Sigma \left(\frac{x - \bar{x}}{s_x}\right)\left(\frac{y - \bar{y}}{s_y}\right)$$

Beta (β)

Market risk measure by Beta (β) and use to evaluate with the formula.

β= (Cov (ra, rm))/(Var (rm))

Where ra is the return of an index and rm is benchmark index return.

To calculate the enactment of Sensex with the help of sectoralindices data linear relationship accepted keeping Sensex as dependent variable and return of other sectoral indices as independent variableuse to calculated

R=a+ Σ(i=1)n⟦bi Ri ⟧

Where R = Return of Sensex Index

a = constant,

Ri = Return of banking stock indices

bi is the coefficient of particular banking stock index.

The paired t-test decides whether the difference from between two

P- Value

P-value is a yardstick to study the null hypothesis. The lesser the p-value, the further evidence we have. One may combine the p-value with the significance level to make the decision on a given test of the hypothesis. In such a case, if the p-value is less than some threshold (usually .05, sometimes a bit larger like 0.1 or a bit smaller like .01) then the null hypothesis will be rejected. In this study, the level of significance has been taken as a 5% confidence level.

DATA ANALYSIS AND INTERPRETATION

Comparative Analysis of Risk and Return of Sensex & Different Sectoral Indices

Table-1 elaborates the descriptive statistical analysis outcomes of Sensex and daily 15 sectoral indices returns from 1st January 2010 to 31st December 2019.

It has found from the table-1 that all indices shows positive means (average daily return) except Telecom sector and Realty sector, which shows negative returns during the study period i.e. from 1st January 2010 to 31st December 2019,.The average daily returns recorded highest for Consumer Durables sector (0.0960), whereas it found lowest for Telecom sector (-0.0148). By analyzing the mean returns of sample indices it has observed that top five sectoral sectors, which have recorded maximum returns and performed better during the study period, are Consumer Durables (0.0960), Auto (0.0863), Information Technology (0.0743), Fast Moving Consumer Goods (0.0723) and Bank (0.0687). On the other hand Telecom (-0.0148), Realty (-0.0112), Utilities (0.0131), Oil & Gas (0.0322), and Energy (0.0391) sectors have recorded minimum average daily returns. The average daily return of Sensex is found to be 0.0527, which is lesser than the average daily returns of Consumer Durables, Auto, Information Technology, Fast Moving Consumer Goods, Bank, Consumer Discretionary Goods & Services, Finance, and Healthcare sector.

In the case of standard deviation which is a measure of risk found to be lower for Healthcare (1.0522), Fast Moving Consumer Goods (1.0811), Consumer Discretionary Goods & Services (1.1500), Technology (1.2292) and Utilities (1.2846). In contrast, Finance (1.4756), Consumer Durables (1.5046), Bank (1.589), Telecom (1.7195) and Realty (2.3285) sectors are the higher risky sectors with higher standard deviation. Consequently, it shows that the Realty sector includes maximum risk than that of all other indices returns, while Healthcare return logged minimum risk. The daily returns distribution of all sample sectors returns are found to be positively skewed except Consumer Discretionary Goods & Services and Information Technology sector. All sectors returns are observed to be leptokurtic (peaked) by nature i.e. it is lowest in case of Fast Moving Consumer Goods and more peaked in case of Oil & Gas.

Analysis of Correlation between Sensex and Sectoral Indices Returns

Table-2 furnishes the correlation matrix for average daily returns of Sensex and average daily returns of sample sectoral indices over the extent of ten yearsfrom 1st January 2010 to 31st December 2019.From the table-2, it is found that the average daily returns of Sensex are positively correlated with that of all sectoral indices returns. The Sensex daily returns are highly correlated with that of the Bank sector (0.88), whereas it has recorded the lowest correlation with that of the Basic Telecom sector (0.12). The top five highly correlated sectors with Sensex are Bank, Oil & Gas, Auto, Technology and Realty. Less correlated sectors are Telecom, Utilities, Consumer Discretionary Goods & Services, Energy and Basic Materials.

Analysis of Beta of Sectoral Indices with Reference to Sensex

Beta measures the market risk. The beta of all sample sectoral indices with reference to Sensex has given below.The table-3 shows that Consumer Discretionary Goods & Services (0.1550), Utilities (0.1609), then Consumer Discretionary Goods & Services, Finance, Basic Materials, Energy and Telecom (0.1743), Basic Materials (0.1891) and Energy (0.1933) sectoral indices are the top five defensive indices by furnishing a lower value of Beta. On the other hand by accomplishing higher Beta value the more sensitive sectoral indices are Realty (1.4531), Bank (1.2253), Oil & Gas (0.9947), Auto (0.8904) and Technology (0.7741).

Analysis of Return per Volatility

Table 4 reveals the ranking of sample sectoral indices average daily returns rendering to return per volatility measured in terms of market risk beta. Sectors like Consumer Discretionary Goods & Services (0.4385), Finance (0.2900), Basic Materials (0.2745), Energy (0.2022) and Consumer Durables (0.1256) indices have ranked higher as

compare to other sectoral indices in the case of return per volatility. On the contrary, Telecom (-0.0850), Realty (-0.0077), Oil & Gas (0.0324), Bank (0.0560) and Technology (0.0670) indices returns have situated at backseat, which shows that if investors have to invest among different sectoral indices Consumer Durables sectorshave performed better than other sectoral indicesover the study period.

Analysis of Return per Standard Deviation

Table 5 reveals the position of different sectoral indicesaverage daily returns in association with standard deviation. From the table-5 it can observe that Fast Moving Consumer Goods (0.0669), Auto (0.0663), Consumer Durables (0.0638), Consumer Discretionary Goods & Services (0.0591) and Information Technology (0.0531) sectors have performed better (minimum risky), than other sectoral indices average daily returns throughout the study period.On the other hand, sectors likeEnergy (0.0274), Oil & Gas (0.0223), Utilities (0.0102), Realty (-0.0048) and Telecom (-0.0086) have to improve in the measure of return per standard deviation by means ofminimizing the risk for investment.

Regression Results for Sensex as Dependent Variable and Various Sectoral Indices as Predictors

Regression analysis explores the association between variables; characteristically, the association among a dependent variable and one or more independent variables. Regression analysis used for numerous purposes like forecasting, predicting and finding the causal effect of one variable on another. A regression method fundamentally comprises the gathering of data on the variables under study and assessing the quantitative result that they have on the other variables in addition to assess the significance of the relationship to the analysis being done.

The tables i.e., 6(a), (b) and (c) are resulting in the regression analysis amongst Sensex average daily returns as the dependent variable with the different Sectoral Indices average daily returns as independent variables. The goodness of fit significances of standard linear multiple regressions through Sensex return as the dependent variable and numerous determinants as forecasters are described in table 6(a) and the model result has elaborated in table 6(b). The model coefficients have revealed in table 6(c).

The adjusted R Square value of 0.9609 designate that around 96.09% of the association in Sensex average daily return is clarified by the sectoral indices average daily return included in the model. The complete significance of the model has estimated by ANOVA. The F-statistics value of 4016.9455 ($P<0.01$) displays that the sectoral indices return are jointly statistically significant at 1% level. As per table 6 (c) the coefficients of Bank (0.3017), Technology (0.2684), Oil & Gas (0.1790}, Fast Moving Consumer Goods (0.1542) and Auto (0.1200) sectors recorded high. However, the sectors like Consumer Discretionary Goods & Services (-0.0198), Information Technology (-0.0133), Consumer Durables (-0.0086), and Finance (-0.0030) and Telecom (0.0046) have lesser coefficients. Consequently, the average daily returns of Bank, Technology, Oil & Gas, Fast Moving Consumer Goods, and Auto sectors extremely influence on the Sensex average daily returns while Consumer Discretionary Goods & Services, Information Technology, Consumer Durables, Telecom, and Finance sectors have a lesser influence on Sensex average daily returns.

This regression model reveals that the Sensex average daily returns is a statistically significant association between average daily returns of Bank, Consumer Discretionary Goods & Service, Fast Moving Consumer Goods, Technology, Energy, Oil & Gas, Basic Materials, Healthcare, Auto and Consumer Durables indices (Sig. < 0.05). However, Sensex returns have a statistically insignificant association with the Information Technology, Utilities, Finance, Telecom and Realty sectors returns (Sig. > 0.05)

CONCLUSION

This research study found the risk-return analysis of Sensex returns and fifteen Sectoral Indices returns. It examined the correlation between Sensex return and fifteen Sectoral Indices return, during the period from 1st January 2010 to

31st December 2019. Consumer Durables, Auto, Information Technology, Fast Moving Consumer Goods and Bank sectors have performed better and Telecom, Realty, Utilities, Oil & Gas and Energy sectors have recorded minimum returns during the study period. The return of Sensex found lesser than the returns of Consumer Durables, Auto, Information Technology, Fast Moving Consumer Goods, Bank, Consumer Discretionary Goods & Services, Finance, and Healthcare sector. Subsequently, it found that Realty sector includes maximum risk than that of all other indices returns, while Healthcare return logged minimum risk. The returns of Sensex are positively correlated with that of all sectoral indices returns. The top five highly correlated sectors with Sensex are Bank, Oil & Gas, Auto, Technology and Realty. And lesser correlated sectors are Telecom, Utilities, Consumer Discretionary Goods & Services, Energy and Basic Materials. By analysing Beta it found that Consumer Discretionary Goods & Services (0.1550), Utilities (0.1609), Telecom (0.1743), Basic Materials (0.1891) and Energy (0.1933) sectoral indices are the top five defensive indices by furnishing a lower value of Beta. On the other hand by accomplishing higher Beta value the more sensitive sectoral indices are Realty (1.4531), Bank(1.2253), Oil & Gas (0.9947), Auto (0.8904) and Technology (0.7741). By means of rendering to return per volatility measured in terms of market risk beta. Sectors show that if investors have to invest among different sectoral indices then Consumer Discretionary Goods & Services, Finance, Basic Materials, Energy and Consumer Durables sectors have performed better than other sectoral indices over the study period. It is clear from the above that the Null Hypothesis (H_0), there is no significant difference between returns of Sensex and fifteen Sectoral Indices return is rejected. The regression model reveals that the Sensex average daily return has a statistically significant association between average daily returns of Bank, Consumer Discretionary Goods & Service, Fast Moving Consumer Goods, Technology, Energy, Oil & Gas, Basic Materials, Healthcare, Auto and Consumer Durables indices (Sig. < 0.05). However, Sensex returns have a statistically insignificant association with Information Technology, Utilities, Finance, Telecom and Realty sectors returns (Sig. > 0.05).

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Table 1.Descriptive Statistics of Sensex and Sectoral Indices

Particulars	Mean	Standard Deviation	Kurtosis	Skewness	Minimum	Maximum
Sensex	0.0527	1.1422	17.7734	0.9362	-7.5231	15.9900
Bank	0.0687	1.5890	8.3240	0.4529	-8.9758	17.5483
Consumer Discretionary Goods & Services	0.0680	1.1500	6.2517	-0.0027	-7.7155	11.3878
Fast Moving Consumer Goods	0.0723	1.0811	3.1665	0.0307	-6.3193	6.9608
Technology	0.0518	1.2292	8.9924	0.1292	-9.2932	13.1179
Energy	0.0391	1.4261	11.6522	0.3964	-9.5275	17.4737
Information Technology	0.0743	1.3984	8.8124	-0.2592	-11.7586	10.7833
Oil & Gas	0.0322	1.4433	13.8701	0.1157	-13.5610	17.4845
Finance	0.0678	1.4756	10.1252	0.4797	-8.3882	17.3459
Basic Materials	0.0519	1.4633	3.5077	0.0152	-7.8651	12.6160
Healthcare	0.0621	1.0522	3.3916	-0.1706	-6.9936	7.7494
Auto	0.0863	1.3014	3.2062	0.1979	-7.4623	10.6266
Utilities	0.0131	1.2846	10.6793	0.3606	-8.1134	15.3467
Telecom	-0.0148	1.7195	4.4956	0.2990	-9.4578	16.1846
Consumer Durables	0.0960	1.5046	4.8285	0.1532	-8.7565	12.4785
Realty	-0.0112	2.3285	6.2909	-0.1078	-18.5691	21.0645

Table 2. Correlation Matrixof Sensex and Sectoral Indices

Particulars	Sensex	Bank	Consumer Discretionary Goods & Services	Fast Moving Consumer Goods	Technology	Energy	Information Technology	Oil & Gas	Finance	Basic Materials	Healthcare	Auto	Utilities	Telecom	Consumer Durables	Realty
Sensex	1.00															
Bank	0.88	1.00														
Consumer Discretionary Goods & Services	0.15	0.17	1.00													
Fast Moving Consumer Goods	0.61	0.45	0.04	1.00												
Technology	0.72	0.49	0.08	0.38	1.00											
Energy	0.15	0.16	0.67	0.03	0.10	1.00										
Information Technology	0.60	0.38	0.04	0.31	0.95	0.06	1.00									
Oil & Gas	0.79	0.65	0.13	0.42	0.46	0.14	0.36	1.00								
Finance	0.18	0.22	0.81	0.04	0.09	0.69	0.06	0.14	1.00							
Basic Materials	0.15	0.16	0.84	0.03	0.07	0.69	0.03	0.13	0.78	1.00						
Healthcare	0.59	0.48	0.06	0.44	0.43	0.05	0.35	0.47	0.05	0.04	1.00					
Auto	0.78	0.69	0.16	0.48	0.48	0.09	0.37	0.60	0.14	0.11	0.52	1.00				
Utilities	0.14	0.15	0.78	0.04	0.07	0.70	0.03	0.13	0.75	0.79	0.03	0.12	1.00			
Telecom	0.12	0.12	0.55	0.02	0.09	0.48	0.03	0.11	0.52	0.53	0.04	0.09	0.52	1.00		
Consumer Durables	0.58	0.53	0.13	0.41	0.40	0.08	0.30	0.48	0.11	0.08	0.43	0.54	0.10	0.08	1.00	
Realty	0.71	0.70	0.19	0.39	0.45	0.14	0.32	0.60	0.18	0.16	0.48	0.63	0.15	0.12	0.56	1.00

Table 3.Beta of Sectoral Indices

Particulars	Beta	Rank
Realty	1.4531	1
Bank	1.2253	2
Oil & Gas	0.9947	3
Auto	0.8904	4
Technology	0.7741	5
Consumer Durables	0.7641	6
Information Technology	0.7394	7
Fast Moving Consumer Goods	0.5793	8
Healthcare	0.5430	9
Finance	0.2337	10
Energy	0.1933	11
Basic Materials	0.1891	12
Telecom	0.1743	13
Utilities	0.1609	14
Consumer Discretionary Goods & Services	0.1550	15

Table 4.Return per Volatility of Sectoral Indices

Particulars	Return	Beta	Return/Beta	Rank
Consumer Discretionary Goods & Services	0.0680	0.1550	0.4385	1
Finance	0.0678	0.2337	0.2900	2
Basic Materials	0.0519	0.1891	0.2745	3
Energy	0.0391	0.1933	0.2022	4
Consumer Durables	0.0960	0.7641	0.1256	5
Fast Moving Consumer Goods	0.0723	0.5793	0.1248	6
Healthcare	0.0621	0.5430	0.1145	7
Information Technology	0.0743	0.7394	0.1005	8
Auto	0.0863	0.8904	0.0969	9
Utilities	0.0131	0.1609	0.0816	10
Technology	0.0518	0.7741	0.0670	11
Bank	0.0687	1.2253	0.0560	12
Oil & Gas	0.0322	0.9947	0.0324	13
Realty	-0.0112	1.4531	-0.0077	14
Telecom	-0.0148	0.1743	-0.0850	15

Table 5.Return per Standard Deviationof Daily Sectoral Indices

Particulars	Return	Standard Deviation	Return/Standard Deviation	Rank
Fast MovingConsumer Goods	0.0723	1.0811	0.0669	1
Auto	0.0863	1.3014	0.0663	2
Consumer Durables	0.0960	1.5046	0.0638	3
Consumer DiscretionaryGoods & Services	0.0680	1.1500	0.0591	4
Healthcare	0.0621	1.0522	0.0591	5
Information Technology	0.0743	1.3984	0.0531	6
Finance	0.0678	1.4756	0.0459	7
Bank	0.0687	1.5890	0.0432	8
Technology	0.0518	1.2292	0.0422	9
Basic Materials	0.0519	1.4633	0.0355	10
Energy	0.0391	1.4261	0.0274	11
Oil & Gas	0.0322	1.4433	0.0223	12
Utilities	0.0131	1.2846	0.0102	13
Realty	-0.0112	2.3285	-0.0048	14
Telecom	-0.0148	1.7195	-0.0086	15

Table 6.Regression Results for Sensex as Dependent Variable and Various Factors as Predictors Model Summary

Multiple R	R Square	Adjusted R Square
0.9803	0.9609	0.9607

Goodness of Fit – ANOVA

Particulars	SS	MS	F	Significance F
Regression	3091.5303	206.1020	4016.9455	0.0000
Residual	125.7563	0.0513		
Total	3217.2866			

Regression Coefficients

Particulars	Coefficients	t Stat	P-value
Sensex	-0.0092	-1.9831	0.0475
Bank	0.3017	61.9211	0.0000
Consumer Discretionary Goods & Services	-0.0198	-2.2879	0.0222
Fast Moving Consumer Goods	0.1542	30.1330	0.0000
Technology	0.2684	19.5719	0.0000
Energy	0.0114	2.3329	0.0197
Information Technology	-0.0133	-1.2024	0.2293
Oil & Gas	0.1790	39.3095	0.0000
Finance	-0.0030	-0.5106	0.6097
Basic Materials	0.0140	2.1360	0.0328
Healthcare	0.0330	6.0071	0.0000
Auto	0.1200	21.7227	0.0000
Utilities	0.0067	1.0180	0.3088
Telecom	-0.0046	-1.3994	0.1618
Consumer Durables	-0.0086	-2.1819	0.0292
Realty	0.0044	1.4310	0.1526

Dependent Variable: Sensex

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RESEARCH ARTICLE

Morphology Prediction of Indanthrene (Pigment-Blue) using FORCITE

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ABSTRACT

The crystal bulk shape is highly significant for countless industrial applications. There are plentiful cases of procedures in the medicine industries where shape of the crystal is a vital aspect, namely handling, packaging, storage, filtration during processing, Milling and grinding.Hence, the connection between the internal atomic arrangement and morphology of the crystal is of excessive curiosity to especially chemists. We have used computational chemistry approaches using BIOVIA Material Studio to predict the morphology of a molecular crystal of Indanthrene.

Key words: crystal, Indanthrene, BIOVIA, morphology.

INTRODUCTION

Indanthrene,[1-3] an organic dye which mainly comprises of 2-aminoanthraquinone in reaction with potassium hydroxide when potassium salt is present in the environment. It is a pigment that has wide applications in various research areas, namely acrylic, pastel, and watercolour painting. It is used to dye cotton and also used as a food dye bearing E number E130. Here, we have illustrated regarding the prediction of morphology of the crystal from the atomic structure of a crystal of Indanthrene using BIOVIA Material Studio[4,5].

METHODOLOGY

We have optimized the crystal assembly of Pigment Indanthrene using Forcite and the COMPASS force field[6]. Forcite is a group of tools for molecular mechanics that allow us to examine an extensive variety of systems. The important approximation here is the potential energy surfaceis characterized by a classical forcefield. The forcefields are established by data parameterization from experiment and complex quantum mechanical calculations. Here, we have used COMPASS forcefield. Classically, Forcite is used to improve the geometry of a system precedinga quantum mechanical calculation or molecular dynamics simulation. Firstly,we have just minimized the molecules,

and the cells. We have parametrized with non-zero force field charges and used the bond increment approach. This is completed using an iterative procedure, in which the cell parameters and atomic coordinates are adjusted until the total energy of the structure is diminished. Forcite geometry optimization is based on dropping the magnitude of calculated forces and stresses until they become lesser than pre-defined convergence tolerances. The algorithm for growth morphology assumes the growth rate of a crystal face is reliant on the potential energy which is because of accumulation of a growth slice to aincreasing crystal surface. This techniquetrials to predict crystal habits initiated under nonequilibrium growth circumstances.We can calculate the amount of forces on an atom from the potential energy which depends on the selected force field.

RESULTS

For crystal structures, symmetry elements are necessarily taken into consideration from Forcite geometry optimization. After geometry optimization, the Forcite Energy task comes into picture thatallows us to compute the total energy of the definite system and reveals the energy gained from varied forcefield terms, such as van der Waals terms and bond. It can also specify if the structure has a rational geometry and if a geometry optimization should be done on this particular system.The summation method to be used for electrostatic interactions is taken as Ewald summation [7]. Here, we have only utilized the stable surfaces, which confirmed regarding the parameters defining reported surfaces. The Stable surfaces option informs regarding only for the utmost stable surface for each face.

The below table provides the each of the Miller indices characterizes one of the symmetry-related facets, the symmetry multiplicity of the facet, the distance, the area and percentage extent of a single facet, and the total area and total percentage extent of all symmetry connected facets. This table indicated the distance from the [011] plane is significantly higher than the nearest plane from center i.e. [200]. It is clearly noticed that the slowest growing (2 0 0) face covers almost more than 50 % of the crystal surface. The aspect ratio is obtained as 5.394. Inhibition of the growth of the fast growing (2 0 0) and (0 0 1) faces might lead to a more isometric crystal morphology.

The below table has shown the interplanar angles between facets.An important part of any classical simulation is the construction of a potential energy expression. For most forcefields, this is done by comparing the forcefield types of the atoms in a given interaction term with a list of combinations in the forcefield and assigning the parameters from the closest combination match. The Universal forcefield differs from this general approach in that it uses bond order information, as well as forcefield types, to generate the parameters for a given interaction. Thus, bond orders must be assigned before an energy expression can be constructed. Bond orders are determined from the bond type, thus, a single bond is assigned a bond order of 1.0, a double bond is assigned an order of 2.0, and so on. A bond that forms part of an aromatic system is assigned an order of 1.5. An important exception to this is the C_N bond in an amide link, which is assigned a value of 1.41 so as to give better agreement with the observed values for this bond length.Bond orders are usually assigned automatically by Forcite, but can be assigned manually if required.

CONCLUSION

We have utilised computational chemistry methods using BIOVIA Material Studio to forecast the morphology of a molecular crystal of Indanthrene. The growing (2 0 0) face which increases slowly that covers nearly more than 50 % of the crystal surface. Inhibition of the growth of the growing (2 0 0) and (0 0 1) faces which is moving very fast might lead to a more isometric crystal morphology.

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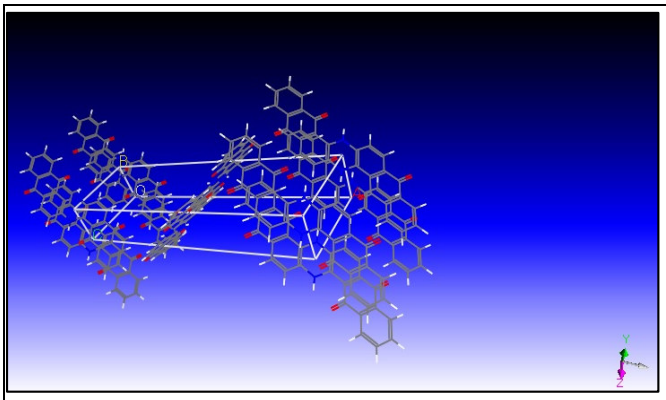

Fig . 1.Crystal structure of Indanthrene

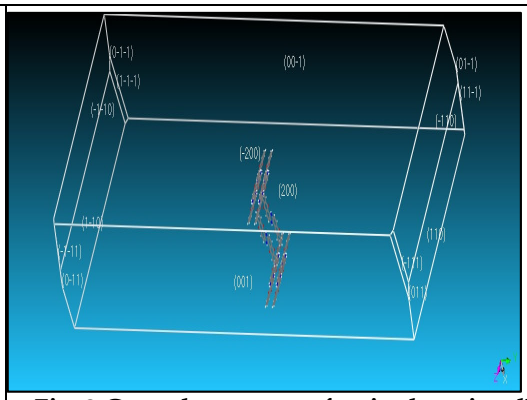

Fig .2.Crystal structure of a single unit cell of Indanthrene

Table 1. Symmetrically exclusive facets of the habit of Indanthrene

Hkl	Multiplicity	Center to Plane Distance	Area of a Single Facet	% Area	Total area	% Total area	Vertices
{ 2 0 0}	2	19.332	1.53E+04	29.648	3.06E+04	59.296	6
{ 0 0 1}	2	40.652	7.34E+03	14.199	1.47E+04	28.399	8
{ 1 1 0}	4	95.831	1.54E+03	2.983	6.17E+03	11.933	6
{ 1 1 -1}	4	103.256	47.573	0.092	190.292	0.368	5
{ 0 1 1}	4	104.061	0.548	0.001	2.192	0.004	3

Table 2.Interplanar angles between facets of Indanthrene

hkl	Angle
{ 2 0 0}	88.08
{ 0 0 1}	89.763
{ 1 1 0}	165.818
{ 1 1 -1}	126.834
{ 0 1 1}	52.105

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RESEARCH ARTICLE

Simulation of Dose Rates for Table Top Accelerator

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ABSTRACT

A Monte Carlo based simulation has been performed to study the dose rate of the existing TTA at IUAC and Manipal. The simulation result shows using a 3 mm thick MS sheet is good enough for shielding purpose.

Key words: Monte Carlo, simulation, MS sheet.

INTRODUCTION

Recently, a 50 kV table top accelerator (TTA) is setup at Manipal Centre for Natural Sciences (MCNS), Manipal Academy of Higher Education (MAHE) with the technical support of Inter University Accelerator Centre Delhi. A gamma survey is carried out around the TTA facility during the operation to ensure the radiation safety and to provide necessary shielding. The results are compared with the theoretical (Monte Carlo Simulation) values. The present work describe the details of the Monte Carlo Simulations of the dose estimation for the ion source assembly of TTA using the FLUKA [1] code & clearly showed that there are no any radiation hazard around the TTA to work.

MATERIALS AND METHODS

A cold plasma-based PIG ion source was fabricated and installed with MCNS 50 kV ion accelerator. With this, it has been possible to get a stable beam with 300 micro amps. The full ion source is assembled in nylon housing and connected to 50 kV power supply. Inside the nylon housing there is a small cylindrical Cathode body (37mm diameter made up of MS) and another small cylindrical Anode ring (22mm diameter made up of SS) are mounted in such way that they are in electrical insulation with each other and the High voltage has applied to anode ring keeping cathode at ground. A precaution has been taken in such a way that the required gas will flow from Cathode body via small opening without deteriorating the vacuum a lot. The above geometry has been used for simulations.

In order to simulate the experimental scenario, a simplified geometry of ion source assembly is considered for FLUKA simulation. In this simulation, a plane parallel beam of electrons having an energy of 50 keV incidents on a 6 mm thick mild steel plate kept at a distance of 2 cm from the source position. The EMFCUT card available in FLUKA is used to set the transport and production threshold for electrons and photons. The electrons and photons transport are scored using the USRBIN.

The photon energy distribution is scored at distance of 24 cm from the source position (marked as D1 and D2 in the figure 1) using the tracklength estimator USRTRACK.A total of 10^8 histories divided in 10 batches are used for the simulation. Later 1.5 mm thick Aluminum sheet as well as 1.5 mm mild steel sheet were placed at a distance of 22 cm one at a time and the same scoring were repeated.

RESULTS AND DISCUSSION

Fig 1 shows the electron distributions around the mild steel target. The scattered electrons are distributed within 8 cm from the mild steel. The electron interaction with material follow photon production. Figure 2 shows the photon distribution at in three different cases viz., (A) when there is no shield provided, (B) 1.5 mm Aluminum shield is provided and (C) 1.5 mm mild steel shield provided. It is clear from the figure 2 that the photons produced are spatially distributed with high intensity near the mild steel and the intensity decreases with distance. Figure 3 shows a comparison of simulated photon flux distribution at the detector D1 for the cases (A) and (B). The reduction in photon flux at D1 on the introduction of aluminum sheet is in accordance with the Fig 2. The estimated photon flux results with the aluminum shielding are then converted to dose rates with ICRP-74 [2] conversion factors and are compared with the dose rates measured with the ROTEM gamma survey meter. The measured dose rates are presented in Table 1, and it is clear that the measured dose rates are in good agreement with the estimated dose rates. On replacing the shielding with mild steel, the photon flux at D1 reduced considerably as it is clear from Fig 2(c). Hence the dose rates estimated with Mild steel are found to be well below the permissible dose level.

CONCLUSION

Preliminary simulation studies have been carried out for the estimation of dose rates around the ion source assembly of TTA. The simulated dose showed good agreement with the measured dose rates in the case of a 1.5 mm aluminum shielding. It is found that a 1.5 mm mild steel shield can prevent the photons coming out of the system and thus to reduce the dose below the permissible level. Presently we are using a 2mm thick MS cage over the ion source which ensure that there are no any radiation to the working environment making it safe & radiation free to work. Detail of the simulation and the data extraction will be presented.

ACKNOWLEDGEMENTS

We are very much thankful to MAHE manipal for financial support. One of the author PKR thanks to IUAC Delhi for their support . Specially Thanks to Dr. CPS and Dr..RK from IUAC delhi.

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Table 1.Dose Comparison

Position of measurement	Simulated dose rate using FLUKA [1]	Measured dose rates
D1	4.6 mR/hr	3.8 mR/hr
D2	1.5 mR/hr	0.9 mR/hr

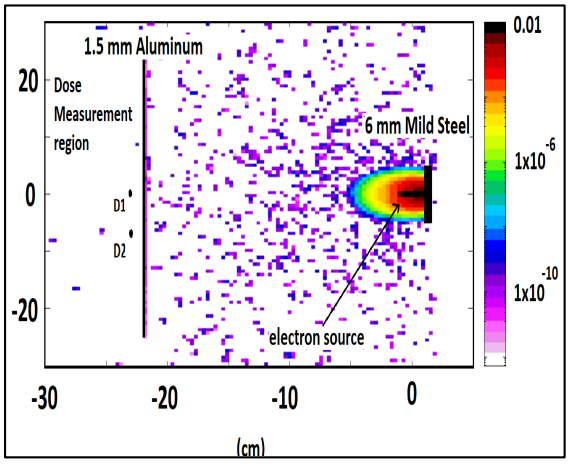

Fig.1. Secondary electron distribution due to mono energetic 50 keV p beam.

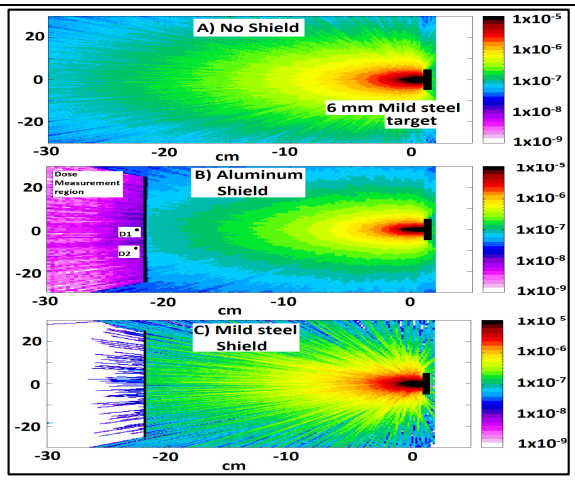

Fig 2. Photon distribution produced due to 50 keV electrons impinging on Mild steel target

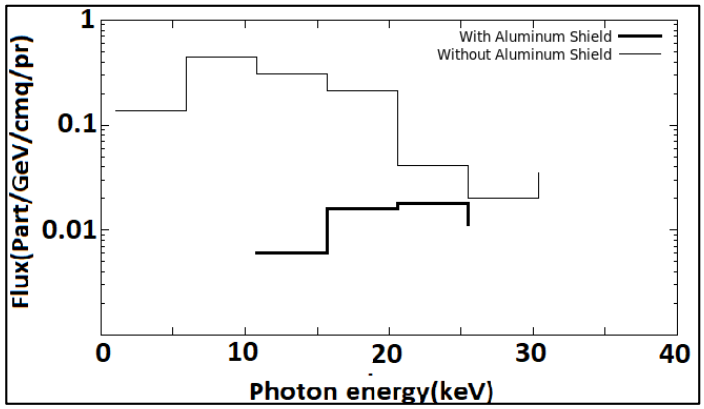

Fig .3. Secondary photon flux distribution at position D1

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REVIEW ARTICLE

Smart Irrigation for Food Security and Agricultural Sustainability

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ABSTRACT

Water shortage is a very common problem in the world as well as in India. Agriculture accounts for a considerable quantity of water in the form of irrigation. With continuous growth of the population, per capita availability of water is declining. Further, faulty agricultural practices are responsible for pollution of freshwater. The present irrigation system practiced in most of the developing countries is inefficient in terms of inferior water use efficiency and less water productivity. The target demand of food and agricultural commodities can be fulfilled by adopting latest and improved agro-techniques including efficient irrigation management. Technological development caused in agriculture can cope up with the future requirement of farm output with limited water. Hence, there is urgent need for adoption of smart irrigation technologies for food security. The paper focused on present context of water shortage and possible technologies of smart irrigation for agricultural sustainability.

Key words: Agriculture, water, irrigation, water use efficiency, smart irrigation, food security, sustainability.

INTRODUCTION

Water, the most precise liquid, is necessary for all fife forms. For successful raising of crops water is essential. Water also impacts industrial growth, socio-economic development and upkeep of healthy ecosystem. The fresh water content of world is about 45 thousand cubic km of which about 70 percent is used in agriculture. The ever-growing population of the world demands 60 percent more food by 2050 (FAO, 2017) and certainly enhanced agricultural production will consume more water than the present level.The world contains an estimated 1 400 million cubic km of water. But only 0.003% of this vast amount, about 45 000 cubic km, are fresh water resources that could be used for drinking, hygiene, agriculture and industry. But not all of this water is accessible because part of it flows into remote rivers during seasonal floods. As per an estimate, 2000-5000 litres of water are required to produce daily diet of one person. Thus agriculture consumes the lion share (about 70 per cent) of fresh water withdrawal and it may be more in some densely populated developing countries. Agriculture fulfills the basic need of food, fuel and fibre and raw

material of some industries and it is related to food, nutrition and livelihood security of the population which is the key indicator of development. Presently, agriculture is much more focused to meet the food and nutritional security, poverty alleviation, rural prosperity and sustainable management of ecosystem. Under the context of global warming and climate change, agriculture is facing further difficulty in achieving the target. Moreover, some faulty practices adopted in agriculture created problems like degradation of natural resources, loss of biodiversity and pest-disease problem which ultimately narrowed down the net return from the farming. Water, the key natural resource of agricultural production, is already polluted by non-judicious use of fertilizers, pesticides and other contaminants. Thus production of safe and healthy food on sustainable basis is a great challenge in agriculture based developing countries.

On the other hand, shortage of fresh water has already been noticed worldwide, which will be further stressed in many regions and in coming days severe water shortage may occur. The regions where per capita availability of water less than 1700m^3 are considered as stressed areas and if it comes down to 1000m3 the regions are called water-scarce regions. However, India is with 1544m^3 of per capita availability of water is moving towards water-scare country.

Irrigation in India

India is one of the agriculture-based developing countries with second largest farm output in the world only after China. The country has 17 percent of the world's human population with a large population of livestock, but only 4% of the fresh water resources of the world. The country has about 140 m ha of cultivated land of which irrigation accounts about 46 percent (64.6 ha) and remaining is rainfed area (Table 1). India receives a 4,000 billion cubic meters of annual rain.But rainfed agriculture in the country is facing tremendous variation, irregularity and shortage of seasonal rain with low agricultural productivity.In addition to that, depletion of groundwater, pollution of water, aquifers salinization due to rise of sea water table and wastage of freshwater by faulty irrigation practices are major issues in Indian agriculture which require urgent intervention for identification suitable methods of judicious water use in agriculture targeting sustainable farm productivityand food security of the country. The integrated management of water resources by efficient and optimum use of irrigation water is essential to maximize crop production (Zaman and Swaminathan, 2018).

The human population of India in 2050 is projected at 1.6 billion and at that time demand of food will also be increased proportionately. Interestingly, 15 percent of available freshwater was used for non-agricultural purposes in 1990, which will be 23.1 percent in 2050. That means the country needs to maximize agricultural production with less water and it will be a great challenge. In Indian context, groundwater is a major source of irrigation which accounts of more than half of irrigated land and supports about half of the population (Fishman *et al*., 2015). Over-dependence on groundwater caused into decline in the groundwater table and pollution of heavy metals. Under this situation enhancement of water use efficiency (WUE) is a prime concern by adopting improved agronomic management and precision water management.

Technologies for Higher Production with Less Water

There is no substitution to target more agricultural production in the country and so improved agronomic management is the only option to achieve higher yield with reducing water resources. Research and policy intervention are also required towards fulfilling the future demand and sustainable development. Rainwater harvesting and conservation agriculture are suitable options for intensification of agriculture (Zaman*et al*., 2017). Efficient use of low land eco-system through integrated farming system can ensure farm output for smallholders. Suitable technologies should be demonstrated and popularized among the farmers where ground water is polluted with heavy metals. Choice of crops is also important because in the water-scarce regions more water requiring crops like sugarcane and paddy should be avoided and ecologically hardy crops like pulses and millets can be raised (Maitra*et al*., 1998; Maitra, 2020).Rice can be cultivated by adopting alternative methods like system of rice intensification (SRI) and aerobic rice. Micro-irrigation (drip and sprinkler) can be adopted for maximizing water

productivity. Water pricing may be restructured and the practice of watershed development should be followed targeting groundwater recharge. Reclamation of saline soil and choice of suitable cropping system can enhance productivity.Utilization oftreated wastewater is another approach that can provide a feasible alternative source for irrigation water for enhancement of production. Overall good management practices (GAP) which includes integrated nutrient management, integrated pest management should be adopted for agricultural sustainability.

Irrigation Management

In India, three main irrigation methods are adopted, namely, surface, sprinkler and drip irrigation. For measuring WUE, the two methods are generally used.

1. Application Efficiency = volume of water stored in the root zone /total volume of water applied
2. Requirement Efficiency = volume of water stored in the root zone /water deficit prior to irrigation

At the field scale, these two efficiencies are measured, but different losses (conveyance and distribution) are not taken into account (Koech and Langat, 2018). For improving the WUE, it is essential to measure the quantity of water to be given to crops and for that purpose, scheduling irrigation is essential. Generally, farmers provide irrigation at field level on the basis of physiological stages of the crop, experience and availability of the water.But the application of more water than required reduces the irrigation WUE. Irrigation scheduling requires an understanding of the pattern of plant water use and different factors involved in water use by plants. These factors are weather conditions (sunshine, atmospheric temperature and soil temperature, relative humidity, wind speed), seasonal variation, and crop growth stage and canopy wetness. Evapotranspiration (ET) and soil moisture depletion are also scientific measures for scheduling irrigation.At present, technological advancement has changed the concept of irrigation and present day's agronomy is thinking of provision of smart irrigation, wherever it is possible (Figure 1). Remotely sensed data and sensor based network with or without Internet of Things (IoT) changed the concept of irrigation and made water management of crops more precise by adoption of smart irrigation techniques.

Smart Irrigation

In the era of worldwide water-shortage, it is better to use irrigation water judiciously and preciously. Smart irrigation systems can do that efficientlyby using real-time smart sensors for scheduling irrigation.The smart sensors used in the systemare for measuring soil moisture and irrigation in right quantity is scheduled as per the specific need of the crop. The effects of the quantity of irrigation water and frequency are important for successful raising of crop. The smart irrigation system works as a decision making tool for scheduling irrigation (on the basis of soil moisture depletion) and the system provides irrigation to crops precisely and thus WUE and water productivity are increased. Following are the two major types of smart irrigation system.

Arduino based smart irrigation system

In this method two components are there which are functional. First one is the sensor and second one is the motor. Controller here is the Arduino Uno board and it use IDE software. Moisture sensor detects the moister level of the required area and then the data is send to the Arduino board through the extension board. Arduino then makes the decision, based on programmed data, and gives a signal to the stepper motor or pump. Sprinklers are connected to the stepper motor or pump and they will sprinkle water at the desired area. Whole process is shown in the block diagram of figure 2.Once the soil will get its desired level of moisture, the sensor again sends a signal to the Arduino and it will send another signal to stepper motor or pump to stop. Thus the moisture level will be controlled automatically with the help of this system.

IOT based system

In recent smart irrigation system control is through Raspberry PI. Multiple sensors can be connected for multiple controls of things. Decision of the controller will control the stepper motor or pump and hence the sprinkler. Raspberry Pi is connected to the server through MQTT [Message Queuing Telemetry Transport]. MQTT is basically faster than older WSN protocol. Now in server if both sensor and weather forecasting cloud is implemented then the decision will be very precise and accurate in different weather condition also. They arrangement is all set to operate automatically. If there is any possibility of rain in weather cloud, then the current climatic conditions and upcoming possibilities of rain data log and also the current image of the environment will be sent to the user's mail. The whole block diagram is shown in figure 3. At that time sensor's data were sent to the MQTT client, whenever the client comes into the network, they will receive that data.

CONCLUSION

Presently, Indian agriculture is facing the problem of shortage and pollution of water. Agriculture, in future, will face tremendous pressure due to enhanced production target to supply food, feed and raw materials for industry with decreasing water resource.There is requirement of policy intervention and use of latest scientific technologies in irrigation water management and in this direction technology enabled smart-irrigation is one of the methods which can lead agricultural sustainability.

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Table 1. Irrigated area of India by different sources

Sources of irrigation	Area ('000 ha)
Canals	16908
Tanks	2248
Wells	11917
Tubewells	29165
Others	4329
Total	**64567**

Source: Government of India, 2018

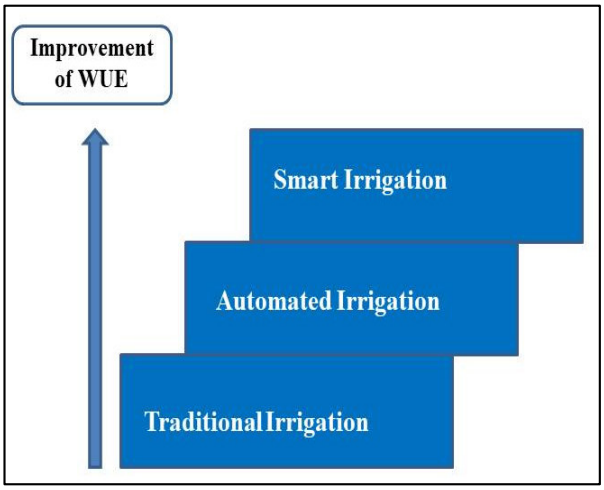

Figure 1.Advancement in irrigation technologies (adopted from Koech and Langat, 2018)

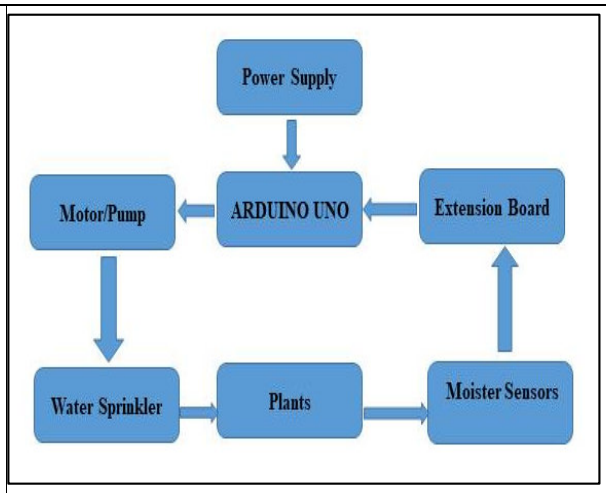

Figure 2.Arduino based smart irrigation system

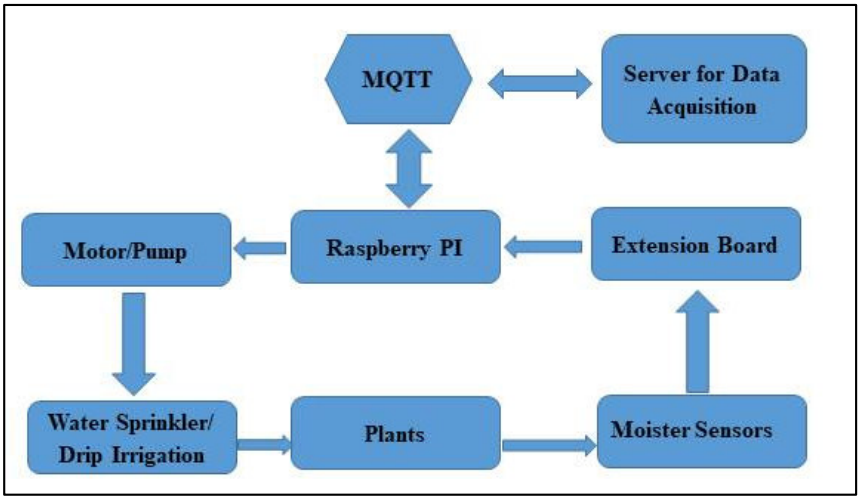

Figure 3: Raspberry Pi based smart irrigation system

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REVIEW ARTICLE

A Statistical Analysis of Pandemic COVID – 19, in Selected Europe Vs Asian Countries

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ABSTRACT

In modern era, the respiratory infection known as COVID-19, was reported as pandemic disease. The corona virus belongs to the family of coronaviridae.Members of the family Coronaviridae widely cause a broadrangeof spectrumdisease in both animal and human. In this family, uniquelyreplication of the RNA genome where absorbed for the generation of a deep seated, a set of amplifying viral mRNA molecules. Until 2003, coronaviruses alluring little intent beyond causing invasion of pathogens mainly in the upper mild upper respiratory tract infections. But near by a day this invase of pathogen changes dramatically in 2003 with the zoonotic SARS and the more recent diaster of MERS-CoV has confirmed the coronaviruses as significant causes of severe respiratory disease. Based on this, the present study focused on the survey of COVID -19, in India, China, United States and Italy from 31st December,2019 to 30th April. This study concludes that selected Europe and Asian different countries affected from COVID-19 the impact was very high in U.S. in all the aspects from number of confirmed cases, recoveries, and death when compared to other three countries. In Case of India the Percentages of confirmed cases were 78%, recovered cases were 19%, and death rate was 3% in India. Where as in China, origin of COVID-19, the percentage of confirmed cases was 50%, recovered cases were 47%, and death rate was 3%. In case of United states thePercentage of confirmed cases was 83%, recovered cases

were 12%, and death rate was 5% in United States. In Italy Percentage of confirmed cases was 66%, recovered cases were 25%, and death rate was 9% in Italy.

Key words: COVID-19, Europe country, Asian Country, Mobility rate.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is respiratory infection caused by virus corona2 (SARS-CoV-2), it have been first identified, December 2019 at the district of Wuhan, China. Then the domain spread world wideglobally, resulting in an ongoing pandemic [1].WHO declared that, Corona virus – COVID is an emergency prevalent pandemic on 30th January 2019 due to its vigorous epidemic spread.Most of the peoplevulnerableway infected with the COVID-19 virus will exploit it with mild to moderate respiratory disease and recover without requiring special treatment.[2] Which has common customary symptoms like fever, cough, fatigue, blown (shortness of breath), andHypogeusia(loss of smell and taste) as like anxiety with common respiratory infection. One of these days reach acute respiratory distress syndrome (ARDS), multi-organ failure, pyemia-septic shock, and severity of blood clots. The time from exposure to outbreak is typically around five days but may range from two to fourteen days[1].

Old-age pensioner, and those with underlying medical problems as well as geriatric problem such as , diabetes, Pulmonary fibrosis, asbestosis, pneumonitis, and other lung condition -chronic respiratory disease , and cancer are more likely to develop serious illness.[2] The virus will counterpane by spread droplet infection, between people by tending one, most recurrently via small droplets engender by coughing, sneezing, and talking. The droplets or smear usually fall to the bottom or onto surfaces instead of progress through air over long distances. Less frequently, people may also beinfected by touching a contaminated aspector with the gadget blight contamination via touching their face. It's most contagious during the pre incubation (first three days) after the onset of symptoms, although outspread is possible before symptoms meterialize, and from people who do not show primary symptoms.[1] The standard method of identification and confirmation methosis by real-time reverse transcription polymerase chain reaction (rRT-PCR) from a naso-pharyngeal swab. Chest CT imaging can also be accomdated for properlydiagnosing in individuals where there's a high-rise suspicion of infection based on symptoms and risk factors; however, guidelines do not recommend using CT imaging for routine screening.To control this, WHO endorse the preventive measures to terminate or prevent infection include repeated hand washing with soap or sanitizer, maintaining physical health and social distance from others (especially from those with symptoms), quarantine (especially for those with symptoms), covering coughs, and keeping unwashed hands faraway from the face. In addition, the utilization of a face covering by visor is also suggested for those that suspect they need the virus and their caregivers.

Recommendations for face covering use by the general public vary, with some authorities recommending for them, some recommending against them, and others requiring their use. There is limited evidence for or against the use of masks (medical or other) in healthy individuals within the wider community.[2] According to WHO there is no specific treatment or vaccine available for COVID-19, but many scientists and researchers are in a ongoing process to identify it. As of now, only symptomatic treatment is available for the patients with COVID-19 in all medicine systems.[1]This article provides a detailed overview of COVID-19 strategies among four different countries emphasizing on confirmed cases, death rate, and recovery until April 30 2020.

METHODOLOGY

The data's were collected from WHO and individual official countries website. The data's were compiled in MS Excel until April 30th 2020.

RESULTS AND DISCUSSION

This article provides the details of COVID-19 cases in different countries. Information on confirmed cases, death rate and recovered cases has been collected and compiled as a single data.

India

In India, the reported first case of COVID-19 was started on 30 January 2020 in Kerala. The Government of India mandate the direction nationalwide lockdown for first stage of 21 days from 25 March 2020 to 14th of April 2020. During this timing sequence, confirmed cases crossed 100 on 15th March, Slowly the cases esculatewith first victim of COVID-19 on 12th March 2020, 200 on 20th March after which lockdown was ordered by government of India. From the Epidemic period of lockdown, the cases history doubled due to lack of awareness,grasp, increased testing facility, and crossed 1000 on 29th of March 2020. On 1 April, the number of confirmed cases crossed 1500 with death of 41 people nationwide. On 5 April 275, people recovered from COVID-19 all across the nation. Until phase I lockdown barrel i.e. 14 April the number of confirmed cases were 10,815, 353 death were reported and 1190 recoveries across nationwide. Again, due to increasing cases the Government of India strictly ordered a nationwide lockdown from 15th of April to 2nd of May 2020. The fig1 explains the number of confirmed cases from 30 January to 30 April with an interval of 5 consecutive days interval. This graph represents the continuous increase in number of confirmed cases, which tells that people are not aware of the consequences in spite of lockdown and restrictions taken by the Government.

Fig 2 represents the number of death occurred due to COVID-19. Until 28th of March, the total number of deaths in India was 19. From March to April, the numbers of deaths are figured in graph with an interval of 5 days from 28th of March to 30th of April. The death rate also started increasing and was most common comparatively in those with co-morbities in the affected people than the healthy individual.As the cases started increasing, day-by-day the recoveries also increased from 7th of April with a number of 275 people across nationwide. Fig 3 provides information on recovered cases till 30th of April as the recovery started in April begining. Overall, until April 30 2020 the percentages of confirmed cases were 78%, recovered cases were 19%, and death rate was 3% in India which has been illustrated in Fig 4.

China

The COVID-19 pandemic was inceptive emerging in wuhan, china on 27th December 2019 as pneumonia. On 8thJanuary 2020 the new strain of Corona virus was pinpoint. By 29thjanuary the virus has almost broaden in full spread to all the provinces of mainland china. As of 31stdecember the total number of cases was 27. By 31stJanuary the WHO declared as Public Health Emergency of International Concern because of its wide spread globally. Till 11thfebruary both the cases including and excluding clinically diagnosed cases are shown in Fig 5. Clinically diagnosed cases are those, whichare not being tested but confirmed based on the medical imaging that shows signs of pneumonia.

From 16 February, both the cases were included as a single data, which has been listed below in Fig 6, in a different graph until 30 April. So, as of 30 April the total number of cases reached 82,874 which shows that there is a rapid increase in the number of cases which indicates that vigorous spread of the disease.

The Fig 7 represents number of death in china due to COVID-19. Until, 31 January the number of deaths was 248. By 5 February, the number of deaths crossed 500, and the death rate started doubling in each 5 consecutive days, 10 February the death rate crossed 1000, 20 February 2000. From 15 April to 20 April, the death rate crossed more than 1000 and then gradually decreased in the number of death comparatively reaching up to 4633 until 30th of April.

Fig 8 represents number of recovery until 2nd of February to 30th of April. We can see that there is increases in number of recovered cases gradually untill 5th of April and the graph begin constant till 30th of April. The recovery number started from 475 on 2thFebruary then crossed 2000 on 7th February and gradually the recovery started increasing day by day indicating some hope to the people across global.Overall, until April 30 2020 the percentage of confirmed cases was 50%, recovered cases were 47%, and death rate was 3% (Fig9) in China, which tells that though the cases, has been increased recovery rate has also been increased.

United States

The COVID-19 in U.S. reply the first reported on 21th January 2020. As the cases kick off, increasing U.S. declared a public health emergency on 31st January and on 2nd February had imposed restrictions on entry of Non-U.S. residents into the country. As the initial retaliation was very slow the cases started increasing to 3-fold of the initial case and national emergency was asserted on 13rd March and by that time, the cases exceeded 2000. By end of the March total cases reached 2,00,000 dying with a rapid increase in number of cases. Behind this, lockdown also the cases started increasing stupendously 30th April 2020 the total cases reached up to 1,062,675 as shown in Fig10.Fig 11 represents the number of death from starting from 6 of February reporting first death. The number of death increased day by day increased to 3-fold on 2 April 2020 to 1595. Thereafter, the number of death started increasing tremendously in U.S. despite of various efforts and treatment given to them and reached 57137 deaths by 30th of April. Fig12 represents total number of recovered cases. The recovery began in the mid of the March and by 31 March the recovered cases were 7251. Gradually the recovery also increased by initial of April and reached 155737 by end of 30 April.Overall, until April 30 2020 the percentage of confirmed cases was 83%, recovered cases were 12%, and death rate was 5% Fig 13 in U.S. which tells that the cases, has been increased much morecomparatively than other countries and more awareness to be created among U.S. citizens regarding COVID-19.

Italy

In Italy the first grave confirmed cases was conformed on 31st January 2020 by two tourists from china in Rome. On that day onwards the Italian government drapeall the flights to and from China. As the cases get going increasing in Italy, eleven municipalities in northern Italy were brought under quarantine. Still the cases were increasing so the quarantine and lockdown period was extended to almost everypart of Italy on 21st March. By the summing of Marchmonth the confirmed cases reached the peak with total number up to the rate105,792. Though the lock down was extended all over the country the cases were also increasing day by day and by the end of April the total number of cases reach up to 205463 as shown in Fig 14.Fig 15 represents the death numbers of COVID cases in Italy. The first death was confirmed on 21 February 2020 then rapidly increasing in number to 233 by 7 March and by end of 31 March the death number increased to 12428. After March the peak rose to 3-fold and by the end of 30 April the death number neared up to 30,000.

Fig 16 represents number of recovered cases from Italy till 30 April. The recovery started from mid of March and by 12 March the number crossed 1200 and by end of March to 15729. Then from April the recovery number increased rapidly and crossed 75000 by the end of April 2020.Overall, until April 30 2020 the percentage of confirmed cases was 66%, recovered cases were 25%, and death rate was9% as shown in Fig 17 in Italy, which tells that the cases, has been increased much less comparatively than U.S. and more awareness to be created among U.S. citizens regarding COVID-19.

CONCLUSION

This study concludes that out of four different countries affected from COVID-19 the impact was very high in U.S. in all the aspects from number of confirmed cases, recoveries, and death when compared to other three countries as shown in Fig 18. China being the motherland of COVID-19 the impact is comparatively less when compared to other countries. Though Government of these countries has taken various necessary actions, still the cases are not under control, which may be due to, lack of awareness among people or may be due to their economic status people are forced to come out in spite of knowing the consequences. Until some vaccines or medicines are not available for COVID-19, social distancing and personal hygiene is the only way to prevent this infection.

Limitations

Only four countries data's were reviewed in this study.

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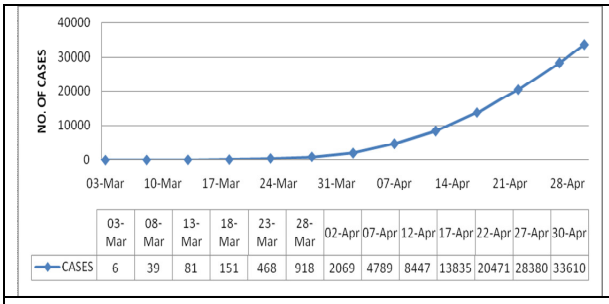


Figure 1: Graphical Representation of Number of confirmed cases from 30th January to 30th April with an interval of 5 consecutive days interval in India

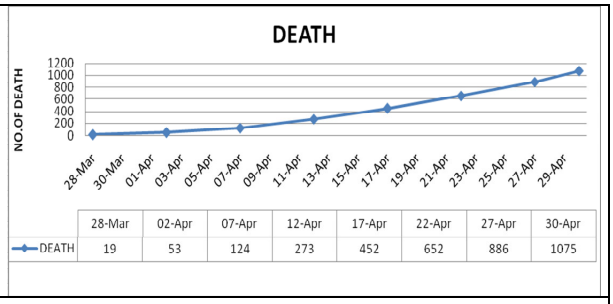


Figure 2: Graphical Representation of Number of Death cases from 30th January to 30th April with an interval of 5 consecutive days interval in India

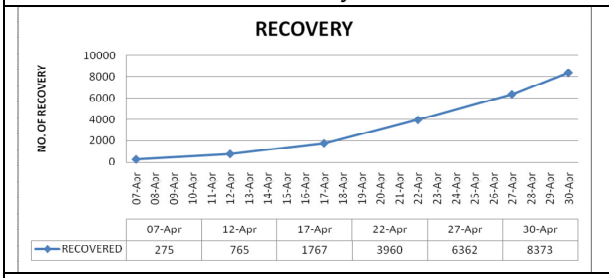


Figure 3: Graphical Representation of Recovery Rate from 30th January to 30th April with an interval of 5 consecutive days interval in India

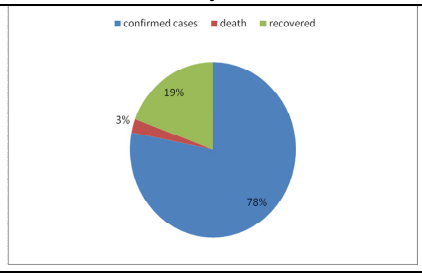


Figure 4: Representation of Percentages of confirmed cases were 78%, recovered cases were 19%, and death rate was 3% in India

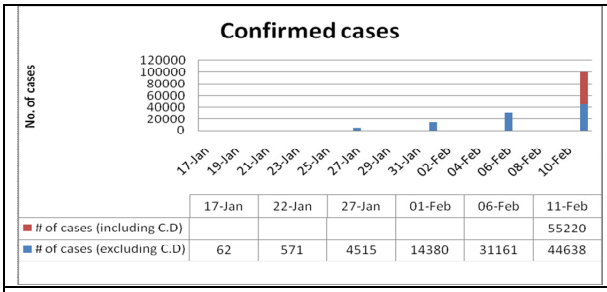


Figure 5:Graphical Representation of Clinically diagonosed cases from 30th January to 30th April with an interval of 5 consecutive days interval in China

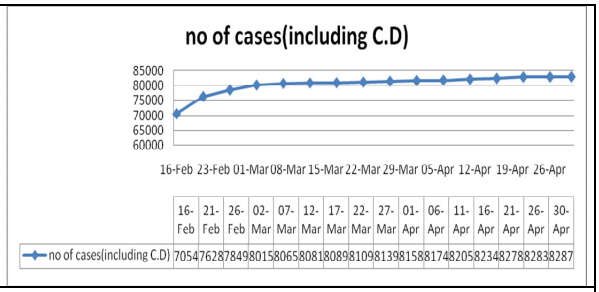


Figure 6:Graphical Representation of Number of confirmed cases including Clinically diagonosedfrom 30th January to 30th April with an interval of 5 consecutive days interval in China

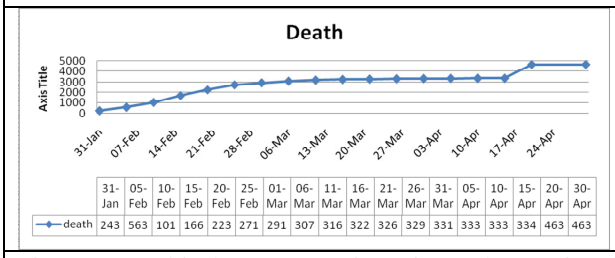


Figure 7:Graphical Representation of Deathcases from 30th January to 30th April with an interval of 5 consecutive days interval in China

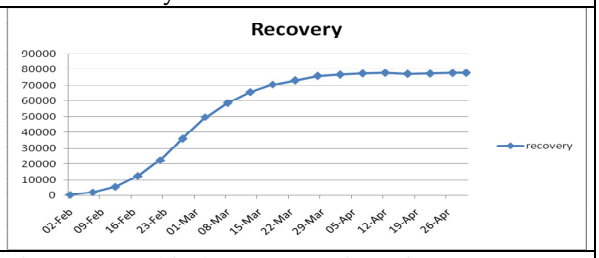


Figure 8:Graphical Representation of Recovery Rate from 30th January to 30th April with an interval of 5 consecutive days interval in India

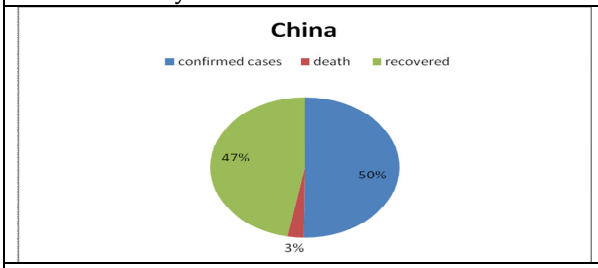


Figure 9: The percentage of confirmed cases was 50%, recovered cases were 47%, and death rate was 3% in China

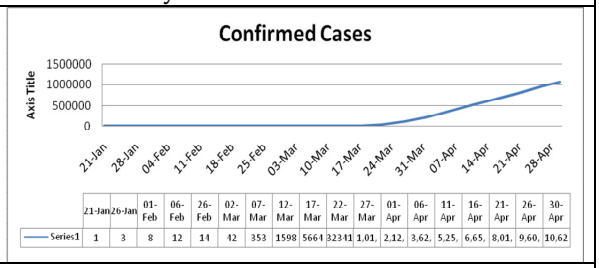


Figure 10: Graphical Representation of Number of confirmed cases including Clinically diagonosed from 30th January to 30th April with an interval of 5 consecutive days interval in United States

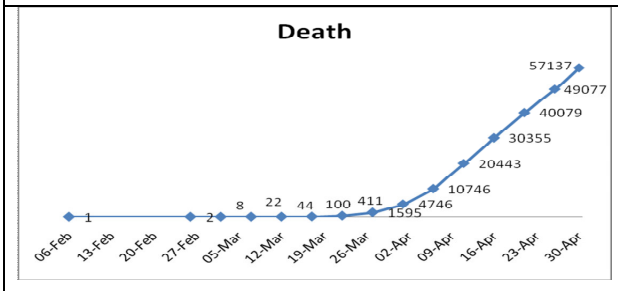


Figure 11: Graphical Representation of Number of Death cases from 30th January to 30th April with an interval of 5 consecutive days interval in United States

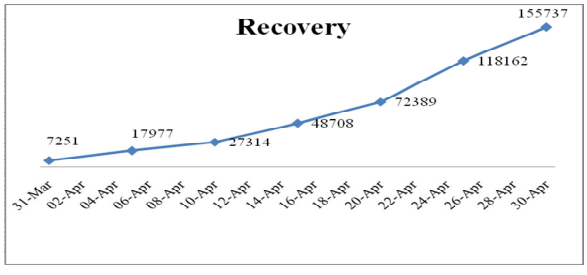
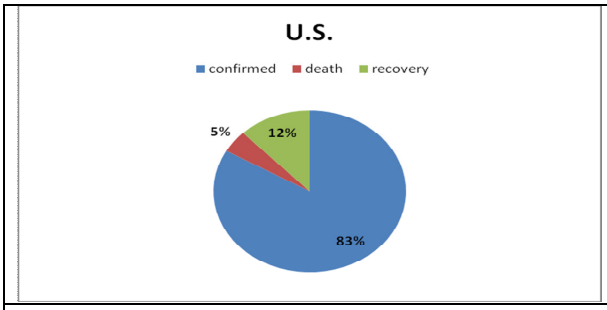


Figure 12:Graphical Representation of Recovery Rate from 30th January to 30th April with an interval of 5 consecutive days interval in United States



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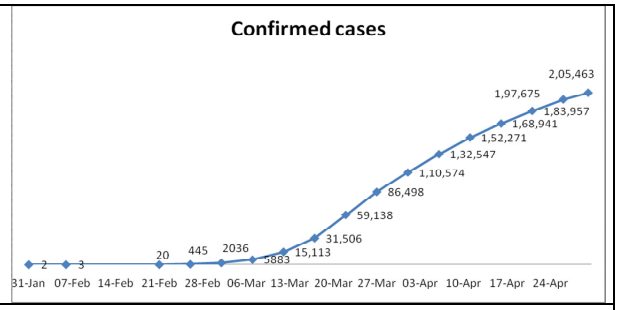


Figure 14:Graphical Representation of Number of confirmed cases including Clinically diagonosedfrom 30th January to 30th April with an interval of 5 consecutive days interval in Italy

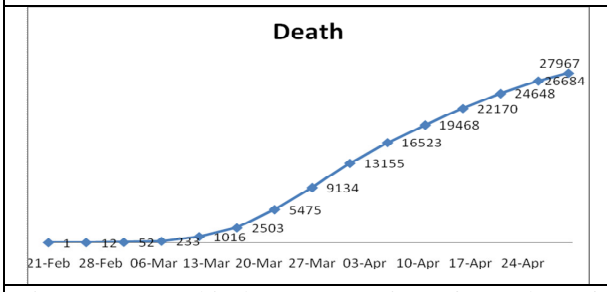


Figure 15: Graphical Representation of Number of Death cases from 30th January to 30th April with an interval of 5 consecutive days interval in Italy

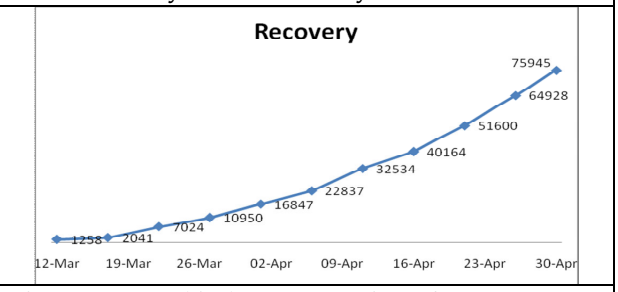
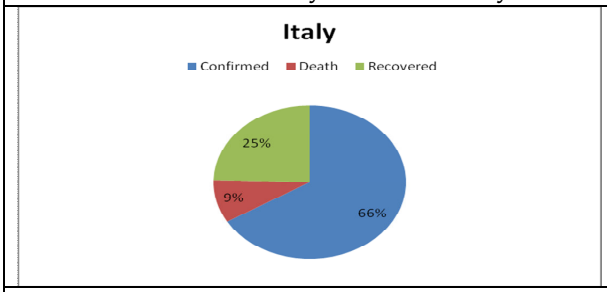


Figure 16: Graphical Representation of Recovery Rate from 30th January to 30th April with an interval of 5 consecutive days interval in Italy



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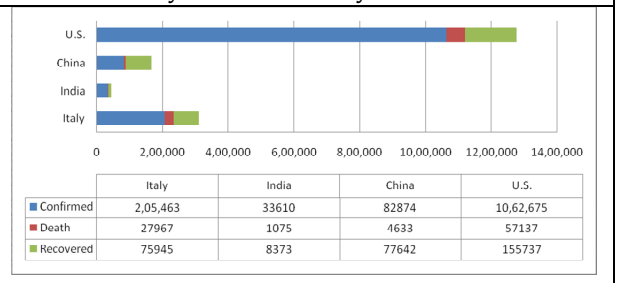

	Italy	India	China	U.S.
Confirmed	2,05,463	33610	82874	10,62,675
Death	27967	1075	4633	57137
Recovered	75945	8373	77642	155737

Figure 18- Comparison of Pandemic COVID-19 In selected Europe Vs Asian Countries

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RESEARCH ARTICLE

A Study on Language Acquisition and Empowering Vocabulary Skills through Watching Movies in Language Lab

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ABSTRACT

The present study aims to examine the responses of English language learners as well as teachers of English towards the integration of English movies in their classes as a tool to develop students' language skills. Fifty undergraduate students (Male and female) studying English in their B.Tech English language courses at Centurion University of Technology and Management, Odisha participated in the study. Questionnaires were distributed among the students to know their views and attitudes towards the language acquisition. The same was administered too. The researcher also conducted a review in the form of interviewing both students and teachers to explore their perceptions towards the use of movies in their classes. Moreover, teachers were required to write journals regarding the use of movies in their classes. The findings of the study indicate that both students and teachers had positive views and attitudes towards the use of movies in their classes to improve students' language skills. The study also offers pedagogical implications for the teachers of English with respect to the integration of films in their classrooms to improve students' language learning. A suitable and worth watching movie materials could enhance students' language learning process and increase their motivation to learn the target language.

Key words: Integration, Language Learning, Language Skills, Motivation, Movies, Technology.

INTRODUCTION

The language acquisition is undoubtedly one of the most cognitively challenging undertakings a student of a university may experience in his or her lifetime. In Centurion University, Students from different regions and backgrounds study here and opt different branches and most students have studied English as a foreign language for at least six years before they enter university. Nevertheless, most of them remain incompetent in their ability to use

the language. The reasons for this drawback are varied and complex. Teachers at Centurion University focus on vocabulary, grammar and skill drilling. At the same time it has been argued by the students that the materials used for teaching the language in most of the Language Labs are stereotyped to understand and some of them are task based. Recently, many language teachers, and scholars have been interested in investigating the effectiveness of a variety of strategies and methods that can be employed in the Language lab to facilitate the learners' mastery of language skills and optimize the teaching and the learning process in an effective way. A number of studies and records have revealed that watching movies can become an integral part of the curriculum and that can improve basic language skills: reading, listening, speaking, and writing .

In the recent years, the findings of several studies which have been conducted to investigate the impact of using movies in Language lab indicate their vital role in the teaching and the learning process. It's a known fact that films provide authentic language input and a stimulating framework for classroom discussions. They also focus a realistic view of the language and culture providing insights into the reality of life. Moreover, the integration of movies in the Language Lab can also improve the students' academic activities.

Literature Review:

Language is in terms of the four basic language skills: listening, reading, speaking and writing. In the oral mode, listening comprehension is that the receptive skill and speaking is that the productive skill, whereas within the written mode, reading is that the receptive skill, and writing is the productive skill (Four Skills within the English, 2013).The aim of learning English is to enhance the four language skills: reading, listening, speaking and writing of the Language learner, with support of an excellent number of English vocabularies and proper grammar, but this is not enough. The learners should be able to speak in English language. Furthermore, most of the Language learners have an honest reading and writing skill compared to listening and speaking skill. They can easily read and write, but it's difficult for them to talk in second language and mention themselves (Chun, 2006), because always the main focus has been on writing skill. Students do many writing activities from the primary year of their academic study until they write their research paper in last year and through time, they're going to have almost some courses associated with speaking and reading skills (Al-Muhtaseb, 2012). therefore, it's necessary for the instructors and learners to estimate the exertions and time given to pronunciation as an important a part of second learning , and that they have to decide which level of proficiency is required for effective communication (Gimson, 1980).

Varga stated a search question as follows: "Which skills are often developed with the assistance of feature movies?" (Varga, 2013, p. 343). The results demonstrate that each one the four skills of listening, reading, speaking, and writing are possible to develop with one single movie. Using movies in English Classes has beneficial effects on the learners' receptive and productive skills (Varga, 2013), since "much language production work grows out of texts that students see or hear" (Harmer, 2007, p. 267). Most of the instructors, experts and even learners believe that using movies in English Classes has many advantages as they're essential tools for developing listening skill (Varga, 2013).

The most dominant advantage of English movies in English Class is their authenticity (Varga, 2013). "Language is presented in everyday conversational settings, "in world contexts rather than artificial situations" (King, 2002:2)" (Varga, 2013, p. 344). Furthermore, movies pave they thanks to get conversant in the dialects of English (King, 2002). Another advantage of English movies is that in spite of demonstrating real materials associated with English . They offer learners with paralinguistic characteristics such as; facial expressions and motion of hands and body to express thoughts and feelings which they're going to have beneficial effects in communicative situations (King, 2002; Kusumarasdyati, 2004; Rammal, 2005). The way of presenting and selecting the films is important for developing the four language skills. The teacher must remember of the sort of the films because enjoying the movie is important to develop listening skills (RhinehartNeas, 2012). Therefore, documentary movies are one among the acceptable types which through it, people can experience something different and educate themselves. However, most of the scholars are becoming angry while they're studying history; whereas documentaries disclose history during a fascinating way for the scholars (Dunlop, 2015). The process of learning English through watching movies is learning by input. At the

start , many correct English statements will store within the head of Language learners, then the learners through the method of drilling can learn the statements and make their own sentences. While watching English movies, the learner are often conversant in informal speeches and slangs that He/She is unable to seek out them in English dictionaries (Szynalski, n.d).Movie production companies (Paramount, Universal, 20th century fox and etc.) are producing movies for native speakers, not for Language learners. Therefore,characters in the movie use the accent and the intonation which native speaker use in real life. So if Language learners watch English movies, they're going to learn their accent, words and statements they use to speak . English-language Learners learn many words that they never heard before, because while movie characters speak, they utter words and phrases that can't be found in books (Szynalski, n.d).Watching English movies in Langauge Lab may result during a "special experience of real feelings of accomplishment when students understand what's happening during a situation where native speakers use English" (Rammal, 2005, p. 5).

English movies improve Language learners' pronunciation and comprehension of speech , because if they can't comprehend the films , they're going to not have positive effects on the learners, and that they cannot learn anything from the movie, even they won't enjoy it. Furthermore, to grasp the films , the learner must know many English vocabulary with correct spelling and proper pronunciation (Szynalski, n.d). "English movies can motivate students to find out vocabularies and understand English better" (Budiana Putra, 2014, p. 1).Vocabulary, as a pillar of English , is believed to make a dominant a part of the method of learning English . Without enough vocabulary knowledge, an Language learner will face many problems in using the four language skills (reading, listening, speaking and writing (Gorjian, 2014). According to a study which was administered for Language learners, students announced that using movie may be a great way to reinforce English vocabulary and supply them more opportunities to use English language. Most of the scholars claimed that they might learn new words (approximately 3-5) while they watch a movie within the class, due to repetition of these words repeatedly throughout the movie (Ismaili, 2012).

METHODOLOGY

The researchers of this study have adopted a mixed-method approach in order to answer the research questions given below, which is an approach to research in which the researcher incorporates both quantitative and qualitative data, and then derives interpretations depending on the integrated strengths of both data to present a thorough comprehension of the research problem (Creswell, 2015). The study was made on a 5-point Likert Scale questionnaire to find out to what extent the students believed watching movies could help them improve their language skills in an English Communication class. The researchers also have conducted semi-structured interviews with few open-ended questions that examined both the students' and the teachers' ideas and opinions towards the integration of movies in theirLanguage Lab to improve students' language skills. In addition to thisthe teachers are required to write reflective journals about this experience and think critically of their classes when they use movies as a method of teaching

Participants

The participants in the study were 50 students from B.Tech., studying English language and Communication at Centurion University of Technology and Management, Odisha. The participants aged between 18 to 21 years. Four Languageteachers (2 male and 2 female)carried out the study. The language Lab and one E-Classroom of the University were utilised for the purpose of the study with 25 students in each class. The present study employed a convenience sampling method to select participants, which involves drawing samples that are both easily accessible and willing to participate in a study.

Follow Up

Students in the present study devoted one hour of their two hourLanguage Lab to conduct the movie activities over a period of three weeks. In this period, the students watched the following two movies

Week 1: *The Social Network (2001).* An award winning movie written by Aaron Sorkin. The natural dialogue and funny lines, make this movie really enjoyable to watch and of course it's easy to follow too. Everyone understands and knows Facebook and they will automatically be able to relate to the movie and they'll also be able to pick up a lot of good English vocabulary related to computers, technology and social networks.

Week 2: *The life of Pi(2012)*is a miraculous achievement of storytelling and a landmark of visual mastery. Inspired by a worldwide best-seller that many readers must have assumed was unfillable, it is a triumph over its difficulties. It is also a moving spiritual achievement, a movie whose title could have been shortened to "life."

Week 3: Review and presentation by the student and teachers viewers. Data Collection was done by the researchers.

The integration of movies in the classrooms was conducted following the steps for using feature films in language classes:

Previewing activities

At the beginning of the activity, students were allotted time for some warm-up previewing activities such as guessing the topic of the movie from its title and some images, some questions to activate their background knowledge. Students were also provided with some key vocabulary and few difficult expressions to facilitate their understanding of the movie scenes. It facilitates their learning of the new vocabulary and enhances their motivation to learn the target language.

Viewing movie segments

In this study, the short sequence approach or the fast track mode wasimplemented instead of viewing the full movie. The students watched the movie clips and bits in their classrooms which had a computer with a USB device connected along with headphones.

Viewing worksheets

Students were provided with worksheets that caught attention to particular details in the movie and required them to answer very short questions as well as comments.

Vocabulary and pronunciation sheet

For the period ofthree weeks, students were required to keep a *students' task* which was to filter through all the newly heard/learnt vocabulary and specify the details where they came across the word.

Movie Reviews

The students were asked to write one short review for the two movies they watched throughout the module. The same had to be presented on the third week. They were provided with some guidelines that helped them in the process of writing the review. Their reviews included a brief summary of the movie, their responses to the theme, the characters and the audio and visual imagery in the film, and how they were emotionally touched by the movie. Students were provided with some specific questions such as what is the learning outcome of the movie. Write a few sentences about your opinions on the movies and what you took away from watching the movie? What did you like about the movie? What did you like least about the movie? Why? Few more questions on Movie screen play, script and action of the movies were also provided.

Group work & a role- play

Students were given tasks for preparing a movie role-play in a group of four to six members; they had to select and memorise a scene of the movie to role-play in class. In the role-play, group members were required to work out in

collaboration and would ensure that each had an equal share. The instructors/teachers demonstrated one movie segment to the class in order to model the activity, and then the students started working in groups where they prepared scripts and acted out the movie scenes throughout thesethree weeks.

RESULTS

Questionnaire

A questionnaire was prepared with seven open minded questions and distributed among 50 selected students as mentioned before. Theteachers provided certain instructions before responding each question.The given analysis of the answers by the students revealed that on a broader level, they considered the integrating of movies in the classroom effective. The majority of the students found movies to be useful in developing their language skills as well as keep them interested and connected. Seventy five percent of the students strongly agreed that their English teachers should integrate more movie viewing activities in their classrooms to help them improve their language skills. Seventy percent of the participants agreed that they are more motivated and interested in learning English if their teachers use films in the classrooms. Seventy five percent of the students strongly agreed that it's easy to learn and understand English Language by watching movies in the classroom. More than half of the students strongly agreed that movies help them improving their vocabulary acquisition. Sixty three percent students agreed that movies decrease their anxiety and tension as well. Around sixty percent of students agreed that watching movies has a beneficial effect on them. Seventy seven percent students believe that they will learn English and participate in the classroom discussion if the teachers use .The majority of the participants appreciated the idea of the use of movies in their lessons. They discovered that movies are very useful for vocabulary and language acquisition.

An analysis of the interviews conducted with the teachers as well as the reflective journals submitted showed that using movies is a good resource for improving students' language skills.

Teachers' views/Feedback

The teachers agreed that it was not a waste of time to integrate movies in their respective classrooms. They believe that movies can largely help improve students' language skills, vocabulary, grammar, fluency and pronunciation in English. They used movies in the classrooms to conduct written tasks such as fill in the blanks, summary writing as well as oral activities such as Group Discussions, film presentations, or role-plays. Teachers in the current study believe that movies should be integrated in the syllabus design and used in the classroom. They also felt thatmovies helped the students learn about one's culture and mannerism and also the use of language in daily interaction. The one drawback that they mentioned was that finding suitable movies to be showcased is important but difficult to do. Choosing appropriate movies is important to achieve the set goals.

On the whole, the findings of the study show that integrating movies in the Language Lab is an effective tool which can help students improve their language skills in terms of their speaking skills, fluency, listening skills, vocabulary acquisition, pronunciation, and colloquial slang. Moreover, the findings also indicate that using movies in Language Lab can promote learning oriented interaction, engagement among students, and active learning environment.

DISCUSSION

The findings of the study indicated that the majority of the students agreed that the integration of movies in their Language Lab could help them improve their language skills. Besides improving listening and speaking skills, watching movies in English could provide a wealth of knowledge on slang, accents, informal interactional spoken English and cross-cultural information. The participants in the current study found that the integration of movies in

their classes has significantly improved their motivation to learn the English language. This can only be achieved when students are provided with a meaningful and authentic context, in which language proficiency can be improved and students feel less stressed and encouraged to use English as a tool for communication. The findings of the study indicated that movies are valuable and authentic materials for improving students' speaking skills.

The participants found themselves more interactive and engaged in the classrooms when the teacher used films more than when the teacher used the textbook or other learning materials. The participants also stated that movies are beneficial for enhancing their interactional skills.Students in the present study responded that through films they were able to learn how native speakers initiate and sustain a conversational exchange, negotiate meaning, and nonverbal communication. The participants in the current study highly delighted at the exposure to the real English used by native speakers in the movie, which as they mentioned helped them become more confident to speak in English. They also appreciated the exposure to informal and conversational use of English, which helped them learn the slang and informal phrases used by native speakers. It is observed from the results that the students found the pre viewing introduction to the movie of great help in understanding and comprehending the movie. The teachers who carried out also agree that it is important to have activities related to the movie in order to fulfil its pedagogical use. Movies can be invaluable pedagogical tools if accompanied with perfect learning activities. The audio-visual aids provided in the movies helped create a meaningful learning experience for the students.

The results of the study indicate that movies can be effective pedagogical tools when used appropriately in Language lab. Language teachers should be careful while selecting films for their lessons. Their choice should be based on the interests and the proficiency levels of the students.

CONCLUSION

The results of the study conclude that movies are powerful pedagogical tools that can help in developing students' language skills. The participants in the study have shown their positive attitudes towards the integration of movies in their Language Lab to improve their English. The study also indicates that using movies as a tool in the foreign language classroom could enhance the students' motivation to learn the language and they take more interest towards it. Teachers in the current study stated that movies increased students' participation and engagement in the classroom. The students also believed that movies could help improve their vocabulary acquisition more as they provide them with a wealth of information about a variety of vocabulary, phrases, and colloquial expressions. However, in order to fulfil its pedagogical purpose, movies should be strategically selected based on the course curriculum, students' interests, and their proficiency level. While preparing the tasks and the materials that incorporate the movies into classes and labs, the main goal of using this authentic material and the objectives of the specific lesson should always be kept in mind. Moreover, language teachers should not ignore the importance of planning useful and meaningful tasks for students before and after viewing in order to make the teaching focus more explicit, therefore students want treat it as an absolute source of enjoyment and entertainment.

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Table 1.

S.No.	Question	Strongly Agree	Agree	No idea	Disagree	Strongly Disagree
1	Do you think your English teachersshould use more movie viewing activities in the classroom to help you improve your language skills?	75%	15%	4%	6%	0%
2	Do you agree that watching movies motivate you to learn English language?	70%	15%	6%	9%	0%
3	Do you think watching movies in the classroom makes it easier for you to learn and understand English?	75%	10%	7%	8%	0%
4	Do you agree that movies can help you in improving your vocabulary?	55%	31%	10%	4%	0%
5	Does the viewing of movies in the Language Lab decrease your anxiety and tension in language learning?	63%	17%	12%	8%	0%
6	Do you think watching movies in English has a beneficial effect on improving your English Language skills?	58%	20%	10%	12%	0%

7	Are you interested in learning English and participating in classroom discussions if the teacher uses movies as teaching materials?	77%	10%	3%	10%	0%

S = Student

Table 2 **6.2. *Students Interview***

S1	*Watching movies make learning English in a more fun way. Discussing with others can allow us to share ideas of the movie, so we can learn from each other.*
S2	*I would like to learn English in this way…I hope we can have the opportunity to watch movies and discuss them in the classroom in future."*
S3	*The activities and the students' task note helped me remember the meanings and usages of words better."*
S4	*The movie The Social Network helped me to write my assignment easily as it .It can also help me in the Speaking Assessment as I will be able to pick up a lot of good English vocabulary related to computers, technology and social networks.*
S5	*I like The Life of Pi, and after watching it I learned some new vocabulary and phrases that I can use in daily conversations."*
S6	*This is a great way to enrich our vocabulary through the dialogue in the movie. Movies make me remember the new words so quickly than the reading circles and textbooks; we can use this vocabulary in writing and speaking*
S7	*Movies are a very good resource in the English language classroom. It is interesting for the students and also can raise their awareness how people interact in naturally occurring conversations"*
S8	*I am really impressed with this method and that is very useful too, and the activities helped me a lot to understand the movie easily*
S9	*In my opinion using movies in class is a good way to learn English, it helps us to concentrate more and be interested in the lesson*
S10	*watching movies in the classroom can develop our speaking skills…..we heard the native speakers' accent and may be this can help us to pronounce and communicate in a better way"*

Table 3

T1	*Using movies in the classroom can significantly promote and foster learning as they cater for diverse learning styles and intelligences… movies offer great authentic materials, they expose students to real language*
T2	*I use movies to engage them in class discussions, to help them learn new words, as well as to get them to do written and oral activities… students are more motivated when the assignments are based on movies*
T3	*They were so interactive and willing to express their opinions, they also learned a wide range of vocabulary and phrases… practiced using some grammatical rules*
T4	*They were actively involved in meaningful discussions… stimulated their thinking and imaginations… movies helped the students learn about one's culture and mannerism and also the target language and learnt how they interact in daily life.*
T2	*The primary objective of using movies was to reinforce specific units in their textbook… active in class and responded very well to the activities.*

T = Teacher

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RESEARCH ARTICLE

Argemone mexicana: A Wonder Weed of Sustainable Bio-additive for Diesel Engines

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ABSTRACT

Bio additives from edible oils increases the volume of low-carbon fuels, but detriments the food chain security in developing countries by rising global food prices. The present work was an investigation to develop an economic fuel additive to mineral diesel from *Argemone mexicana* for fuelling diesel engines and evaluating the performance and emission studies. The esterification followed by transesterification improved combustible properties, engine performances and declined hazardous emissions to well below than that of petroleum diesel.GCMS study was conducted to characterise the developed additive. Fuelling of bio-additive in absolute and 10 to 20% package was conducted by rigorous engine trial. The engine trial inferred that 10 to 20% blend with mineral diesel can be fuelled to commercial diesel engines with better fuel economy without any adulteration or engine modification in engine hardware system.

Key words: Bio additives, *Argemone Mexicana*, transesterification, engine hardware system,

INTRODUCTION

Argemone mexicana is a rarefied wonder prickly leafage weed belongs to pappaveraceae family, grows widely in many parts of the globe.*Argemone mexicana*, commonly called prickly poppy, it is an annual weed mainly known in India among herbalists for its several medicinal properties. *Argemone mexicana* oil has recently been reported as a unique source for biodiesel because of several favourable characteristics [1]. *Argemone Mexicana* thrives on any type of soil, can endure long periods of draught and needs minimum nourishment. It has no serious production problems caused due to insects, pests or browsing by cattle and sheep. Propagation is by seed and the crop is harvested in the same season in just four and half months. The yields expected from *Argemone mexicana* would be close to 2.5 ton/ha, oil content varies from 35 to 40%. The present work investigated the possibility of an economic absolute and additive

fuel package by a novel fuel synthesis from *Argemone Mexicana.* Fig.1 shows *Argemone mexicana* leafageat different stages of maturity.

MATERIALS AND METHODS

Economic fuel development

The present process of producing bio-diesel from *Argemone mexicana* involves extraction of oil from the seeds, removal of alkaloids and gums and esterification followed by transesterification using dilute H_2SO_4 and KOH as catalyst. The degummed oil and transesterified oil were characterized in terms of fatty acid composition by gas chromatography. The engine trial was conducted by fuelling the absolute and additive fuel package to assess the increase in run time versus load in comparison to mineral diesel. The degummed oil was esterified with methanol mediating H_2SO_4 as catalyst. Acidic nature of oil thus formed was neutralized by methanolic KOH solution. The reaction was carried out with stirring intensity 200 to 250rpm, 4h duration and 50OC. After completion of the reaction, the bio-additive (transesterified oil) formed a separate layer above un-reacted oil which was separated by a separating funnel. Glycerol, un-reacted methanol and KOH were removed from the oil by partitioning with water. The bio-additive was centrifuged to separate adsorbed moisture from oil. The oil was kept in a desiccator under vacuum for GC-MS study, physico-chemical properties and engine performance analysis as bio-additive to petro diesel.

Extraction of Argemone oil

The different samples of *Argemone mexicana* seeds were sun dried for two weeks, cleaned and weighed. After cleaning the seed samples were cooked in an oven for 1.5 hour and then pressed in a screw expeller with five times at 130 rpm. The residual cake was collected and pressed in the expeller ones again. Now the cake and oil was collected and weighed and oil yield was calculated.

$$\text{Oil Yield} = \frac{AOW}{ASW} \times 100\%$$

Where *AOW* =Weight of *Argemone* oil extracted (g), *ASW*=Weight of *Argemone* seeds (g)
The oil content was found to be 35% to 40%.

Removal of alkaloids and gums

Argemone oil thus extracted contains gums and alkaloids such as phosphates, proteins carbohydrates, water residue and resins. The removal of alkaloids and gums ameliorates the oxidation stability of biodiesel from *Argemone mexicana*. The extracted oil of 100ml was mixed with 25ml of phosphoric acid, stirred at 1000 rpm, 60C, for 30 minutes in a centrifuge machine. The alkaloids and gums resided at the bottom were separated by a separating funnel. The oil thus obtained is washed with distilled water at 100^0C several times to remove suspended gums. After washing the water content in oil was evaporated by heating the oil at 100^0C.The oil thus obtained is termed as alkaloid and gum free crude *Argemone oil* (CAO).

Esterification followed by transesterification

A liquid mixture was formed by mixing degummed oil with methanol and H2SO4 in the ratio (50:1:0.1), stirred by magnetic stirrer. The stirring parameters chosen were 200rpm at 60oC for 3h. Acidic nature of oil thus formed was neutralized by methanolic KOH solution. The apportion chosen was oil: Alkali: MeOH (25:0.2:05), stirred with intensity 200 to 250rpm, 4h duration and 50OC. The oil was passed through anhydrous Na2SO3. After completion of the reaction, the bio-additive (transesterified oil) formed a separate layer above un-reacted oil which was separated by a separating funnel. Glycerol, un-reacted methanol and KOH were removed from the oil by partitioning with water. The bio-additive was centrifuged to separate adsorbed moisture from oil. The oil was kept in a desiccator

under vacuum for GC-MS study, physico-chemical properties and engine performance analysis as bio-additive to petro diesel.

Characterization of degummed oil and bio-additive

Physical properties of crude *Argemone* oil (CAO), its different blends with petroleum diesel (PD), such as AME-10, AME-20(*Argemone* methyl ester 10% & 20% with PD), and transesterified oil of *Argemone* (TEO) was measured as per IS & ASTM specifications and compared with that of petroleum diesel as base line fuel, shown in Table-1

Gas chromatography–mass spectroscopy (GC-MS)

Fatty acid composition of crude *Argemone* oil (CAO), and the corresponding ester composition after transesterification(TEO) was investigated employing gas chromatography–mass spectrometry (Varian, gas chromatography 4000 Ion Trap mass spectroscopy) equipped with Column: VF 5-MS (30m x 0.25mm ID x 0.25um df).Helium being the carrier gas at flow rate of 1 ml min^{-1} . The temperatures of both injector and detector were set to 350^0C. The temperature programme used was: initial retained temperature was at 45^0C for 1 min., raised from 45^0C to 55^0C at 1^0C min^{-1} increment then raised from 55^0 C to 290^0C at 15^0C min^{-1} increments and finally kept for 5 min. at 290^0C. Total runtime for each sample was 35 min. Gas chromatograms of CAO and TEO were presented in Figs. 4 and 5 respectively.

Engine test

Engine testing was investigated by fuelling petroleum diesel (PD), crude *Argemone* oil (CAO), transesterified oil (TEO) and its blends with petroleum diesel at 10% and 20% proportions in a commercial diesel engine having specification given in table-2.Engine runtime (seconds), fuel consumption (ml/sec), percentage increase in run time (%) with increase in load(BHP) were compared with reference to petroleum diesel being baseline fuel as shown in Fig.2(a),2(b) and Fig.3 respectively. The engine performance test was done according to BIS: 5994-11 [2]. Hazardous emissions of the engine like carbon monoxide (CO), carbon dioxide (CO_2), nitrogen oxides (NOx) and hydrocarbons (HC) were measured using AVL make gas analyser as shown in Fig.6(Table-3). Fuel consumption was measured by U-tube manometer.

RESULTS AND DISCUSSION

Properties of oil

Successive esterification and transesterification of crude *Argemone* oil (CAO) with methanol lowered specific gravity of CAO. Transesterification dropped specific gravity of TEO (transesterified oil) to a comparable value with that of PD (petroleum diesel) as displayed in Table 1.

The temperature at which a cloud of wax crystal first appears in a liquid when cooled under controlled conditions during a standard test is called cloud point.The novel synthesis lowered the cloud point from 8^0c (CAO) to -1^0c (TEO) as shown in table-1. Lower cloud point comparable to that of petroleum diesel improves the low temperature operability quotient of the TEO both in absolute and additive package when fuelled to commercial diesel engines.

The acid value, also called neutralization number or acid number is milligrams of potassium hydroxide (KOH) that is required to neutralize the acidic constituents in one gram of bio diesel sample. The present investigation dropped the acid value of TEO (Table 1) which indicates low free fatty acid content, less corrosive fuel, less probability in fuel filter clogging and the presence of water in biodiesel is less. Too much amount of free fatty acid can cause functioning problems at low temperatures and fuel filter clogging. This parameter can also be used to measure the

freshness of the biodiesel. Fuel that has oxidized after long-term storage will probably have a higher acid value.The iodine value (IV) or iodine number is a quality standard for evaluating biodiesel stability to oxidation and a measurement of total instauration of fatty acids measured in grams of iodine/100 grams of biodiesel sample, when formally adding iodine to the double bonds. Biodiesel with high IV is easily oxidized in contact with air. The present fuel synthesis dropped the IV to an acceptable value close to that of petroleum diesel (Table 1). However TEO with a slightly higher IV than that of petroleum diesel tends to polymerize and form deposits on injector nozzles, piston rings and piston ring grooves but AME10 and AME20 have IV proximal to PD and have no adulteration or engine hardware modification problem.

Viscosity of fuel is a specified standard for diesel engines within a fairly narrow range. In order to develop the high pressures needed in modern injection systems, the clearances between the plunger and barrel is approximately ten-thousandth of an inch. In spite of this small clearance, a substantial fraction of the fuel leaks past the plunger during compression. Low viscosity causes leakage and a significant power loss. High viscosity results insufficient supply of fuel to fill the pumping chamber and thereby loss in power. Acceptable higher limit of viscosity for a biodiesel is 6.0 centi-poise. The present fuel synthesis lowered the viscosity of TEO to 4.981cst.However AME10 and AME20 have viscosity which is very close to that of petroleum diesel (Table 1) tending to negligible power loss.

The flash point is the lowest temperature at which a combustible mixture can be formed above the liquid fuel. The flash point is determined by heating a sample of the fuel in a stirred container and passing a flame over the surface of the fuel. The present fuel synthesis dropped the flash point of TEO to an acceptable range close to that of petroleum diesel (Table 1).However AME10 and AME 20 have flashpoint comparable to PD, thus no combustion problem.
The quality of the fuel to auto-ignite at the temperatures and pressures present in the cylinder when the fuel is injected is measured by a dimensionless number called cetane number. It implicates the ignition delay time a fuel experiences from injection to combustion. Generally, higher the cetane number, shorter the ignition delays time, and higher the tendency of the fuel to ignite. The novel fuel synthesis brought the cetane number close to that of petroleum diesel (Table 1).However AME10 and AME20 have cetane number slightly higher than that of PD tends to have no ignition delay problem.

GC–MS analysis of oil

Fatty acid(FFA) composition of crude *Argemone* oil (CAO), and the corresponding fatty acid methyl ester(FAME) composition of TEO after transesterification was analysed by GC–MS. Analysis inferred that both FFA and FAME were present in both the oil samples, but in different proportions. After the retention time, the concentration of FAME (Fatty acid methyl ester) was augmented and the concentration of corresponding FFA in oil is lowered. Substantially higher concentrations of FAMEs were responsible for lowering viscosity of transesterified oil as compared to CAO. Several additional FAMEs, named methyl esters of palmitic acid (RT: 23.181), linoleic acid (RT: 24.25) and arachidonic acid (RT: 27.877) etc. were detected in TEO of *Argemone* oil. CAO contains palmitic acid, linoleic acid and arachidonic acid as free fatty acids and two-step transesterification converted those fatty acids to their methyl esters.

Engine test analysis

At different loads(BHP) the engine runtime(seconds),fuel consumption(ml/sec),and increase in run time(%) for 20 ml oil were noted and plotted as shown in Fig.2(a),Fig.2(b) and Fig.3 respectively. Outcome revealed that engine runtime per unit amount of oil was lowered with increasing load on engine, which in turn increased fuel consumption of the engine. Reportedly parallel observations were found by Meng et al [3].Initially at low load, runtime difference between PD and methyl ester blended PD was comparatively less, but with increasing load that disparity becomes more. It infers that both CAO and TEO were effective to increase diesel engine fuel efficiency, especially in presence of high load. Percentage increase in runtime for PD, CAO, TEO, AME10 and AME20 oils (Fig.

3) also indicated that fuel efficiency of TEO added PD (AME10 &AME20) over neat PD increased with increasing load on the engine. Data revealed that maximum 50% increment in runtime was recorded when 20% TEO was mixed with 80% PD.

Exhaust emission analysis

Hazardous emissions of carbon monoxide, carbon dioxide, unburned hydrocarbons, nitrogen oxide and free oxygen in the exhausted smoke were investigated by AVL gas analyser and the results for all the tested fuels were presented in a bar chart as shown in Fig 6(Table-3).These emissions were reduced due to TEO blending with PD. Additive package of 10% and 20% TEO lowered the smoke percent and concentration of unburned hydrocarbon (HC), CO, CO_2 and NO_x in emitted smoke as compared to neat PD. Gas chromatography infers the presence of comparatively higher concentration of several unsaturated FAMEs in TEO than CAO and possibly responsible for more energy generation. Reportedly Schumacher et al. [4] and Sheetan et al [5] investigated that additive package of biodiesel has propensity to lower the formation of combustible mixture and possibly be addressed to comparatively higher carbon monoxide and unburned hydrocarbon concentrations in emissions.

CONCLUSION

The present investigationunveiled that crude *Argemone* oil (CAO) was alkaloid and gum free after degumming.Degummed oil was treated with two-steps successive esterification and transesterification processes in presence of acid and alkali catalyst respectively to obtain transesterified argemone oil (TEO). Investigation of several physical, chemical properties and engine fuel efficiency testing inferred that 10% to 20% additive blend of TEO with PD resulted close performance to PD, with higher fuel economy and negligible power loss. Except for very high load, the engine fuel efficiency after 20% TEO adulteration was also similar to that of 10% blended PD. The present development of biodiesel in laboratory scale would promote innovative thinking to produce it in industrial scale. To summarise, the additive package of 10% to 20% TEO with PD was economically more viable than neat PD and fuelling TEO or CAO in absolute package would lead to low temperature operability problem.

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Fig.1 ***Argemone mexicana*** **leafage; at different stages of maturity.**

Table 1. Physical properties of oils

Property	Unit	IS:15607 specification	CAO	AME10	AME 20	TEO	PD	Test methods
Specific gravity	---------	0.87-0.90	0.928	0.86	0.84	0.88	0.831	IS:1448
Cloud point	^{0}C	---------	8	-3.7	-2.6	-1	-4	ASTM D2500
Acid value	mgKOH/gm	≤ 0.5	19.517	0.45	0.47	1.251	0.367	ASTM D 974
Iodine value	gmI_2 /100gm	---------	325.92	84.5	86.3	92.61	70.50	ASTM D 1510
Viscosity @ 40^{0}C	cst	3.5-5.0	38.85	3.51	3.89	4.981	3.64	ASTM D445
Flash point	^{0}C	≥ 120	220	68	70	128	65	ASTM D 93
Cetane number	----------	≥ 51	40	55.6	56.4	42-48	45	ASTM D 613

Table 2. Engine specifications

Description	HA57L165
Type	Diesel four stroke,6cylinder water cooled, direct injection, inline overhead valve
Aspiration	Turbo charged with inter cooler
Maximum output	165KW@ 2500rpm
Maximum torque	800Nm @1400-1900rpm
Bore and stroke	104x113mm
Piston displacement	5.759 litres
Compression ratio	17.5 :1
Firing order	1-4-2-6-3-5
Fuel injection type	Common rail system CPN2.2(CRS)

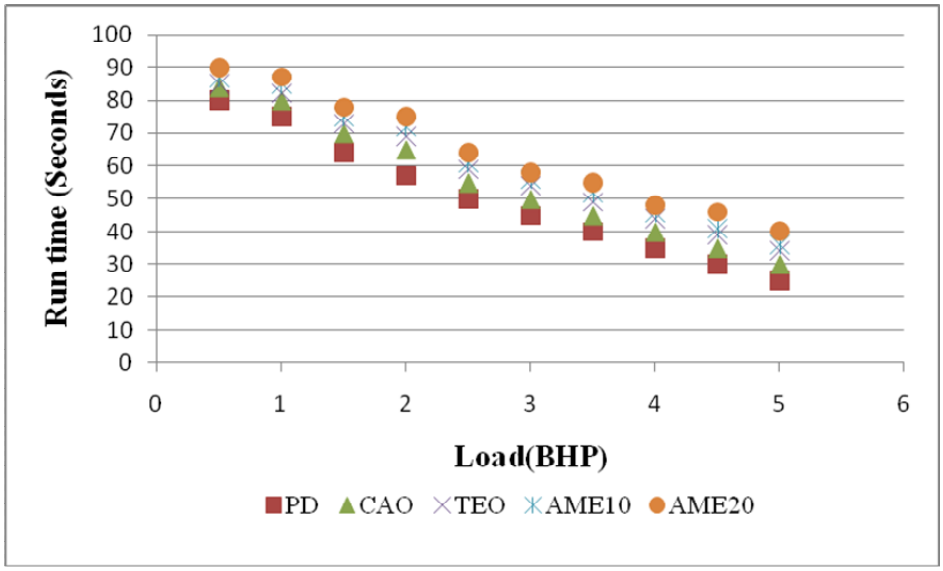

Fig. 2(a). Engine run-times for 20 ml oil at different load factor

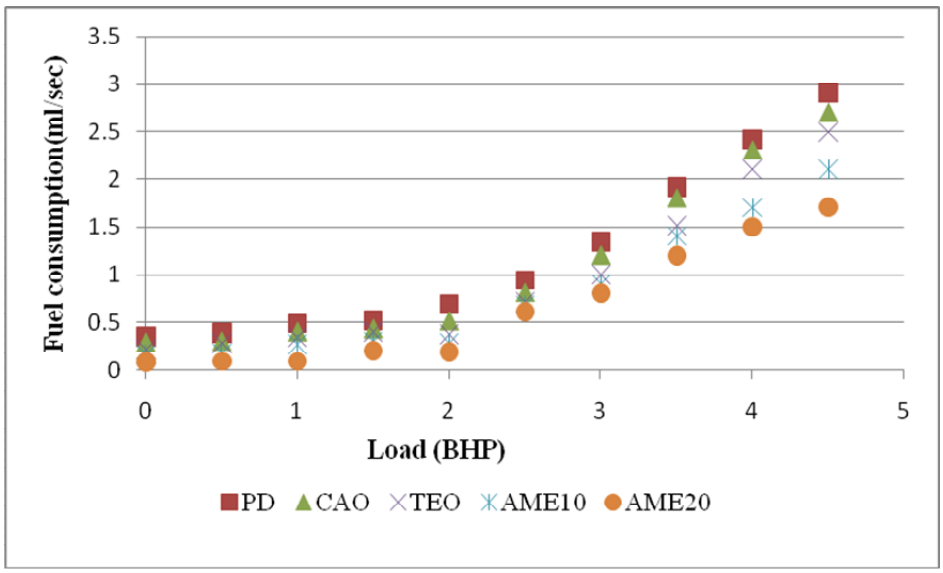

Fig. 2(b). Fuel consumption per second at different load factor

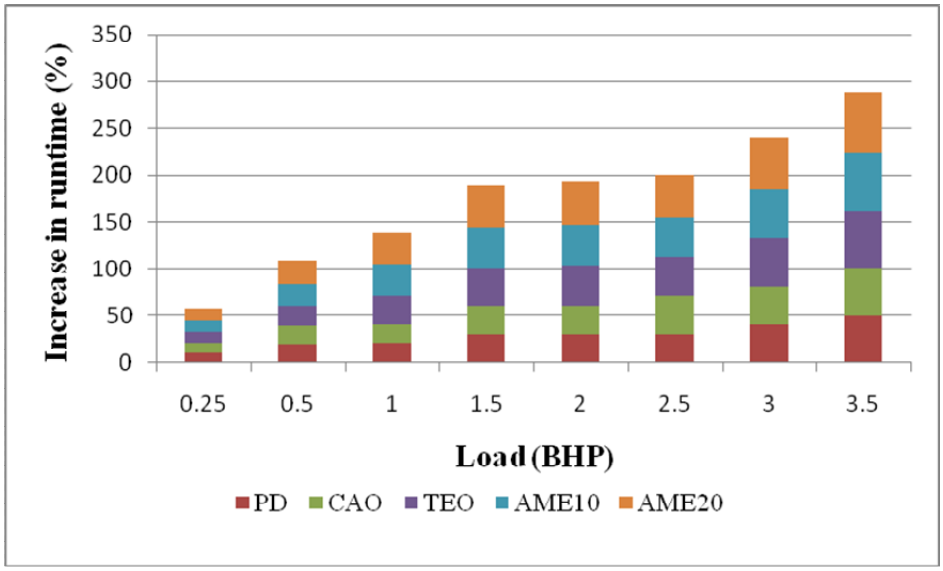

Fig. 3.Percent increase in run-time for different oils at variable load.

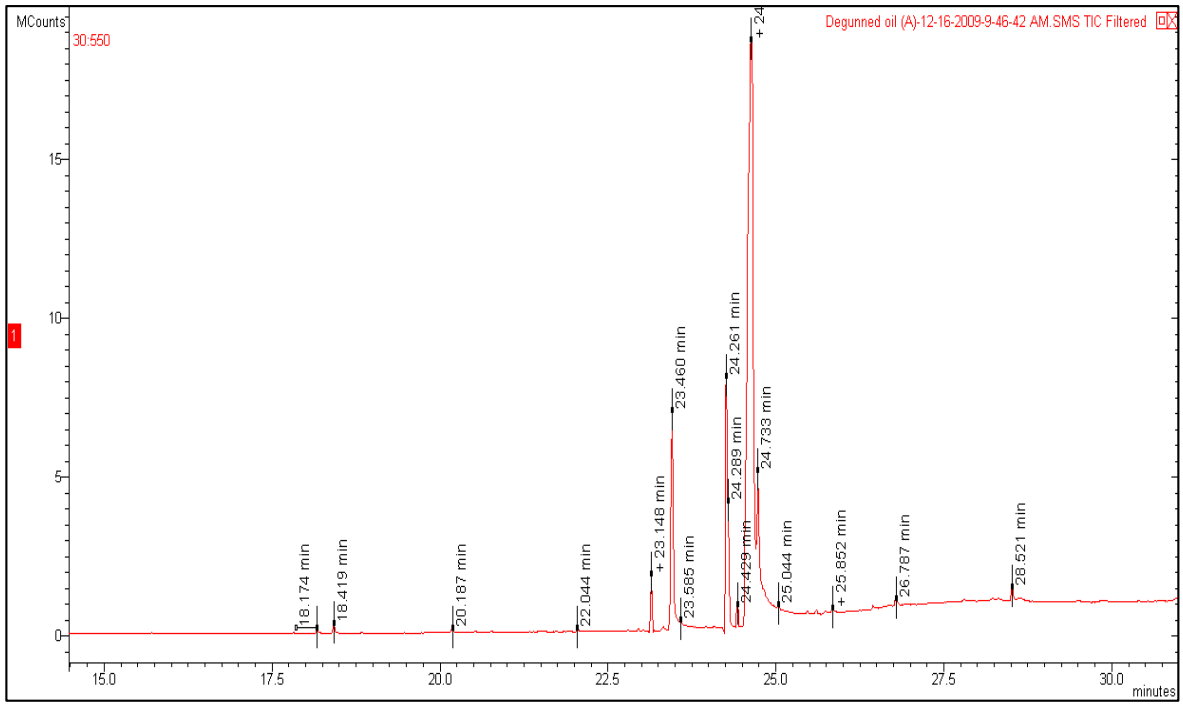

Fig. 4.Gas chromatography diagram of CAO

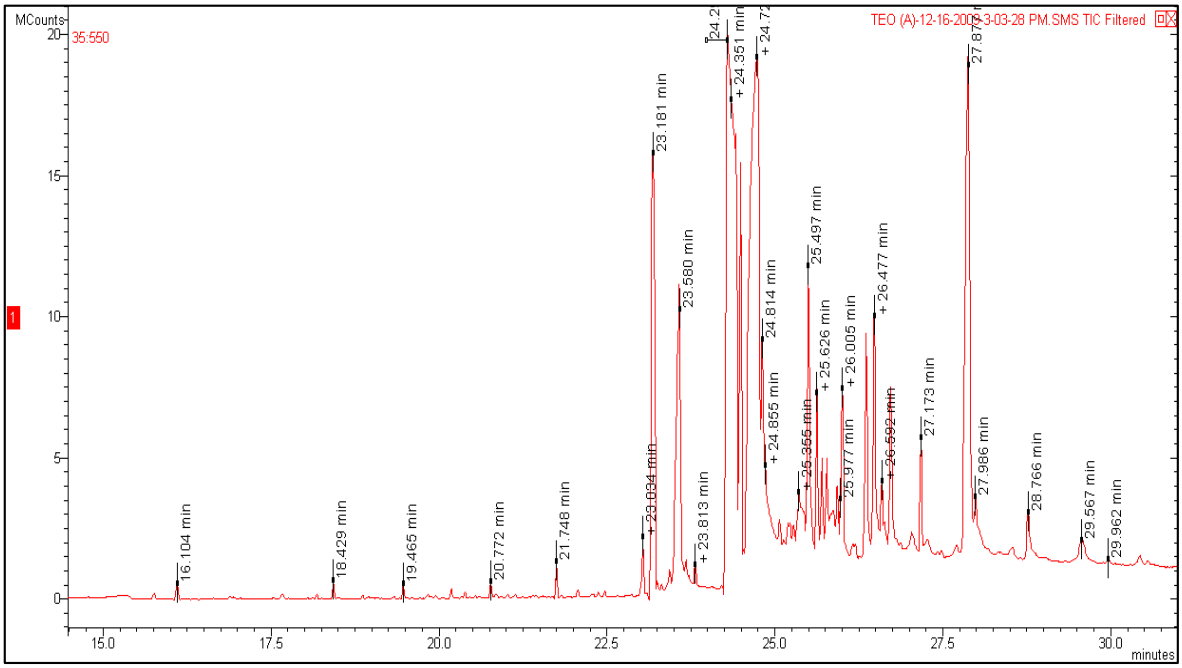

Fig. 5.Gas chromatography diagram of TEO

Table 3.Hazardous emissions

Emissions	PD	CAO	TEO	AME-10	AME-20
CO in%	0.30	0.31	0.06	0.49	0.65
HC in ppm	40	19	17	18	19
CO_2 in %	3.10	2.81	3	3.20	3.30
O_2 in %	15.20	15.41	16.52	15.90	16.18
NO_x in ppm	198	146	142	108	105

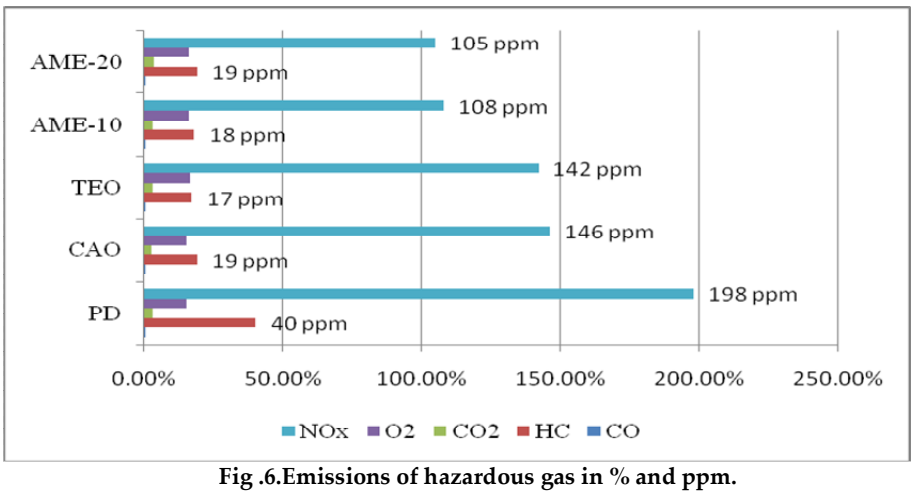

Fig .6.Emissions of hazardous gas in % and ppm.

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REVIEW ARTICLE

A Review on Ethnobotanical Survey of Medicinal Plants used against Urinary Tract Infections

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ABSTRACT

Urinary tract disease (UTI) is one of the most serious general medical issues influencing both genders however females are increasingly susceptible because of the distinctions in urogenital and conceptive life structures, physiology, and way of life. As in UTI, various pieces of the urinary tract are influenced and grimness due to UTI is progressively regular in ladies all things considered and more established men. Due to multi-drug safe strains and high repeat rates, UTI has become a significant financial weight. The present review article was planned to describe the ethnobotanical study which focused on the conventional medicinal plants used by the local circlet treat human diseases and the antimicrobial analysis against Urinary Tract Infections which is a very common disease mainly affects the tribal community.

Key words: Ethnobotanical, Medicinal plants, Tribal, Urinary tract infections

INTRODUCTION

Ethnobotany is the study of relationship between people of ancient society and their plant environment. Ethnobotany is also defined as anthropological viewpoint to botany as it integrates techniques from anthropology and also botany, ecology, medicine, cultural, religious and other disciplines (Martin, 1995). Ethnobotany term was first suggested by John Harshburger to delimitate a specific field of botany and describe plant uses in 1896 (cited in Cotton, 1996). Researches focuses on the ecological knowledge of the aboriginal people and traditional culture and agriculturalists(Martin, 1995). The work of ethnoecological research is not limited to pure science only; it also can help to understand the kinetic relation between biodiversity and social and cultural system (Hamilton et al, 2003). The prospective of higher plants as source in the field of new drugs is still not explored.

Urinary tract infections are most common bacterial inflectional diseases of significant morbidity and extreme medical costs. Nearly about 95% of UTIs are caused by bacteria included Escherichia, klebsiella, Enterobacter and proteus. Also gram positive sp. plays a role in the infection. Most UTIs are caused by specific E.coli strains denoted as uropathogenic E.coli (UPEC).UPEC possess a variety of techniques of aboriginal and local communities provide worthy information world- wide and can be effective model for biodiversity policies.

Man has used plants to treat common infectious diseases and some of these traditional medicine are still included to treat various diseases. Medicinal plants are abundant sources of antimicrobial factor. According to World health organization (WHO) about or more than 80% of the world population relies on traditional medicine for their primary health care necessity. In Early civilization of china, India and the north east, medicinal plants uses as a source torelief sickness traced back virulence factors(VFs),which the organism uses to attach, invade and injure the host.UTI pathogenesis is an intricate process regulated by different host and behavioural factor, holding properties of infecting pathogens, including VFs. In most cases the host faecal matter is the source ofthe infecting E.coli strain, and spread the lower urinary tract via the perineal, vaginal, and periurethral areas where they may establish colonization.

C.albicans is the most common cause of nosocomial fungal UTIs worldwide. Candida albicans and non-candida species are considered important parts of microbial normal flora in the oral cavity, alimentary canal and vagina in a wide range of healthy peoples. They colonize on the external side of urethral opening in premenopausal and healthy females.The presence of c.albicans and NACA species in urine is known as candiduria. UTI is asolemn condition which infect one or more parts of the urinary system. UTI is one of the most commonly occuring bacterial infection ,which occur at any time in anyhumanbeing. UTIs are caused by bacteria which travel to the urinary bladder via the opening of urethra by multiplying; it may spread from bloodstream to the kidney.

Role of two potential medicinal plants used against UTIs

Zingeeber officinale (Dhanik, 2017),Methanol extract from rhizome of Zingiber officinale posses strong antibacterial activity against E.coli. Essential oil from zinger has strong antimicrobial activity against the disease causingfungus. Gingerol and shagelol are identified as more active factors. Ethanolic extract of zinger powder have strong repressing activities against *Candida albicans.*Phytoconstituents of Z. officinale are: Sesquiterpenes,Steroids,Paradol,Gingerol,Gingerones,Shogaols,Diarylheptanoids,Meso-3,5-diacetoxy-1,7-bis(4'-hydroxy-3'-methoxyphenyl) heptanes,Hexahydrocurcumin,Tetrahydrocurcumin.

Vetiveria zizanioides (Pareek et al., 2013), Vetiveria zizanioides usually known as khuskhus or Khus grass. The adventitious fibrous root are aromatic in nature and so worthy. UTIs cure by the stem decoction of Vetiveria zizanioides. The crude root extract of V.zizanioides have the strong antimicrobial activities against E. coli, S. aureus. The polar ethanolic extract show fine antibacterial activity against E. coli. The root extract posses a large zone of supression than leaf extract against E. coli.The root and shoot extract of vetiver posses antifungal activities against *Candida albicans.*Phytoconstituents of V. zizanioides are: Phlobatannins, Saponins, Flavonoids, Steroids, Alkaloids, Carbohydrates, Proteins, Anthroquinonine, Oil and resin, Terpenoids, Glycosides.

Ethnomedicinal work in Abroad

Ethnobotany focuses on the relation between indigenous plant and local inhabitants. The Bulgarian flora is important for its diversity (Kultur and Sami, 2009) and 741 taxa of them are known as medicinal plant. Plants like Calendula officinalis L., Tiliasp, Rosa sp., Cratageous monogyna Jacq., Mentha sp., Chamomilla reticulata are some of thefrequently reported plants in Bulgaria are used for disease treatment and prophylaxis (Ploetz,2000; Kultur and Sami,2009; Kozuharova et al., 2013)

Indonesia ranked second in terms of mega biodiversity containing up to 30000 plant species (Bappenas, 1993). 7000 among the species recognised as medicinal plant (Eisai, 1986) with 950 have known medicinal properties;283 species are registered being cultivated and used in medicinal industry traditionally and 250 species are harvested as raw material in industries (Zuhud et al., 2001).The tropical forest about 74% of 121 active compound such as digitoxin, reserpine, tobocucorin and ephendrin are used to develop important modern medicine in the united states which are derived from the medicinal plant collected from tropical forest (Farnsworth et al.1985). Lao PDR is a country located in the heart of the Indochinese peninsula in Southeast Asia. About 1400 medicinal plants found from 10000 species of plants and animals of Lao PDR. In USA about 25% of prescriptions allotted by pharmacies contain drug mainly come from plant, with at least one or two main ingredient derived from plant (Fernado, 2001; Laird and Kate, 2002).

Malaysia is one of the 12th mega diversity centres of the world. About 1200 species reported have medicinal properties Out of 12000 species of vascular plant species reported in Malaysia (Mohamad Setefarzi, 2001). Agathis borneensis, Erigeron linifolius, Sceleria sumatrensis are some medicinal plant traditionally used as Malay medicine in Kuala, Nerang, Kedah (Zainon et al., 2000).An ethnobotanical research was conducted on the basis of traditional use of wild plant among the Lega slash-and-burn agriculturalist of eastern Zaire. 287 plants were collected and the report is the first step to survey and cover several research sites in Legaland. More than 300 specimens were collected with their ethnomedicinal information through the study. Miah and Rahman reported the cultural, religious and ceremonial uses of Curcuma longa L. and leaves of O.sanctum, T.indicain forest of Bangladesh. Half or more than half of the medicinal plant are planted by the local individuals purposively for their medicinal purposes (Miah and Rahman, 2006). L. inermis leaf paste used as adornment for marriage ceremony and other celebration in South Asia, the middle east and Africa which is proposed by Cartwright-Jones. Sheng-Nongs herbal book suggested the aboriginal sources of folk knowledge on uses of herbals in China. It comprises 365 plants, animal and minerals which is useful as medication from time of Sheng-Nongs (Sheng, 2001).

Long, et al. (2009), showed investigation of ethnomedicine from 1999-2002 in Chuxiong, central Yuann Province, South China. The Yi medicine give an important contribution to the field of ethnomedicine in China. About 116 species of 58 families of medicinal plant used by the Yi people traditionally were documented through the study. Jaradat et.al, (2017), documented 57 plant species of 30 families were used by indigenous traditional healer of Palestine in treatment of various urinary tract diseases. Apiaceae was found the most prevalent family under the study.Ammivisnaga and Ammimajus were widely used species to treat urinary tract infection in this study.

Ethnomedicinal work in India

Jain, (1994) reported that India has about 45000 plant species, From them some several thousand posses medicinal properties. Well known ethnomedicines have been identified which used to treat skin, liver, joint and intestinal diseases. the species like Curcuma, Bacopa, Asclepias reported to the recent drug development work. Singh , et al., (2009) reported 40 medicinal plant of 27 families in the tribal area of Chandauli district of UP, which is the less studied regions for its ethnomedicinal value. Namsa ND, et al., 2009 reviewed the herbal medicine to treat anti-inflammation related disorder such as muscle swelling, cut wound, rheumatism, insect bite, burn by fire and hot water by the Lohit community of Arunachal Pradesh,India. About 34 species of 22 families were recorded through survey. B. ceiba, X. indicum, L. clavatum, M.palmata are some plants reported to treat anti-inflammation related disease.

The ethnomedicinal plant against worms and insect in Aravalli hill range of India. 49 plant species of 29 family with 67 remedies were identified and reported through the study. Mitragyna parvifolia (Roxb.) Korth is reported first time in ethnomedicinal claim (Bhardwaj, et al., 2011). Indigenous knowledge of anti-diarrhoeal medicinal plant proposed by the traditional healer of Parinche in Pune district, Maharastra. During the study, about 28 flowering plants were documented which act against Diarrhoea. Some of them are C. sepiaria, D. pentaphylla, L. pinnatifida, Z. jujube (Tetali, et al. 2009).

Saikia, et al. (2006) proposed the medicinal plant used to cure skin ailments and for cosmetics in Assam. About 85 plants of 49 families were reported for their therapeutic uses to treat skin ailments about 14 plants are used to cure multiple skin diseases. C.longa and M.azaderach are the major plants among them. Through this study 18 skin problem remedies were also documented. Pulipati,et al., (2017) give effective natural remedies to cure UTIs instead of antibiotics. The study included 25 natural remedies and Some of them are V.macrocarpon, M.alternifolia, C.paradisi, A.sativum, A.comosus which posses great therapeutic significance to treat UTIs.

Ethnomedicinal work in Odisha

Ethnobotanical survey were carried out in tribal residing in Bonsai, Sundargarh and Panposh Forest Division of Sundargarh District. Plant that are used for pesticide, diseases, foods, industrial, stupefiers were documented through the study. Second author documented 83 plant sp. of 78 genera belonging to 42 families from which interesting and new species were found. Some plants reported from the study were H.antidysenterica, which is used to cure snake bite, S.polyandrum, used to cure cardiac ailment (Prusti and Behera, 2007).Panda, (2018) documented 68 ethnomedicinal plants from Jajpur district of Odisha. These plants were used to cure various diseases. Some plant parts like seed, leaf, bark, stem, whole plant and oil are used in raw or cooked form to treat cough cold, inflammation, jaundice, epilepsy, malaria, skin disorder etc. some documented plants are A.squamosa, A.paniculata, T.petula etc.Pattanaik, et al. (2008) documented ethnobotanical survey of tribal area in Malkangiri district. About 34 plants of 33genera and 25 families and their therapeutic uses in 17 ailments such as headache, toothache were recorded.

Sahu, et al., (2013) carried out ethnobotanical study in Boudh district of Odisha. A total 20 traditional agricultural crop species, about 150 forest species, 8 traditional vegetables species were collected through the study. Some of the species are E.coracana, P.pinnata, C.urens. During the survey 31 plant species of 29 genera belonging to 20 families have an etnomedicinal uses for dental care by the tribal community of Mayurbhanj, Sundargarh, Angul, Balangir districts of Odisha. Some of the plant species are C.procera, F.chappar, J.curcas, P.reticulatus are found to cure dental care like tooth decay, pyorrhea, foul smell etc (Singh et al., 2013).Kumar et al., (2016) studied anti snake venom activity of plant used by tribes of Koraput district. About 38 plants of 36 genera belonging to 29 families were identified to treat snakebite. Raulvolfia serpentine is most commonly used species in treatment of snank bite. The maximum number of plants to treat snake bite is belongs to Apocyanaceae family.

Dhal, et.al (2014) give an ethnobotanical survey of Nawarangpur district. A total 69 plant species of 43 families were reported under this study with reorganization of several plant species to treat different disease. Some plant species are T.terrestris act against ringworm, M.ferrea act against constipation, B.ceiba act against dysentery etc.Mahalik et al. (2015) found 315 plant species of 295 genera of 75 families during the field survey out of which 26 species have ethnomedicinal data related to utis. Some of the plant species collected from the survey is *Zingiber officinale*, *Withania somnifera, Vetiveria zizanioids, Solanum virginianum* etc from Dhenkanal district, Odisha.

CONCLUSION

All the access identified in the review are reported as herbal medicine has long been establishedancient and useful forms of remedial source used by humans. Developing countries trust on medicinal plant and traditional therapeutic practices for health care necessity. Thus the proper identification and documentation of traditional medicine plant should be conserved in a good order. Urinary tract infections are distributed all over the world or are cosmopolitan. The under developed countries are used traditional plant in a traditional wayas a source to cure UTIs. The above literature review presents a brief account for uses of medicinal plant which posses good resistance as compared to antibiotics.

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RESEARCH ARTICLE

Study of Iris Flower Classification using Logistic Regression and Principal Component Analysis

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ABSTRACT

Machine learning becomes most trending area for doing research to develop autonomous system. It involves wide application like regression, classification and clustering in different field of research. In this paper Iris flower classification has been done with the help of multi class logistic regression. A statistical technique called Principle Component Analysis has been used for dimensionality reduction and feature extraction method which make the classification accurate and faster. Some case studies has been performed which reveals that the accuracy level increases with the increase of number of principal component as well as increase in the percentage of training set data. The best result achieved with 80% of training data set and three principal components taken during training of the regression model.

Key words: Machine Learning, Classification, Iris Flower, Principal Component Analysis, Regression.

INTRODUCTION

In recent scenario, most of the systems get automated with the help of Machine Learning [1]. The research and development in the field of Machine Learning and artificial intelligence has been growing faster, where almost all the machine learning algorithm are now a day's leaning towards data science [1, 2]. Data science is the field of study which analyzes big data and performs data filtering, preparation for relevant data extraction. The data scientist are gathering data from different multiple sources and applies machine learning and other analysis to extract most relevant information from the collected data sets [3, 4].

The machine learning is the methods which use different algorithms to extract data, learn from the extracted data, and then predict future trends for the corresponding study. It is the concept of making a machine to take decision with the help of learning process by the help of computer algorithm which in turn helps the machine to learn from their experience and predict the output based on the experience called as learning. Machine Learning algorithm is

trained using a set of training data which create a model. After training the model it will feed with a test data set and the model makes prediction base on learning stage. The prediction result is then evaluated and performs the accuracy measure which leads the algorithm to ready for deployment to the machine [5].The phases of machine learning classified to two parts one is training/learning and other is testing. The learning phase is again categorized in to three types: Supervised, Unsupervised Learning and Reinforcement Learning [6].

Supervised Learning is the one, where the target output is known during training, where as in case of unsupervised learning the model learns through its own experience and observation, then able to create any pattern in the data set. In contrast to both of these two the reinforcement learning has the ability of an agent to interact with the environment and find out what is the best outcome [5]. Basically for regression and classification problems the supervised learning is best suitable where as for clustering type problem which involves finding groups in data uses unsupervised learning algorithm [7]'.

METHODOLOGY

Principle Components Analysis

Principal Component Analysis (PCA) [8] is a statistical method that uses an orthogonal transformation to convert a set correlated data set to a set of linearly uncorrelated dataset. These uncorrelated data sets are called as the principal components [9, 10]. This method mainly used as a pre-processing technique for dimensionality reduction or feature extraction method for different problem. Because for classification problem with a large correlated data set, it takes more time for execution , even it may leads to less accurate output, that reduce the efficiency of the system. PCA extract the relevant features data and express it as a set of new orthogonal data [11].The number of the principal components is lesser than or equal to the number of original data set. Out of the principal components the first principle components have more variance and the variance level is decreasing with the higher order of principal components. The Principal component analysis (PCA) was developed in 1901 by Karl Pearson [12]. Now it is mostly used as a tool in data analysis and for making prediction. The normalization of data set is required before determining the principal components. The normalization of perform by subtracting each data from its mean of the data series.

The Steps for PCA

Step 1: Collect the data set and standardize it:

Compute the mean vector of the dataset and subtract the mean from each data vector, $\Psi = \frac{1}{M}\sum_{i=1}^{M}\Gamma_i$, Where Γ_i represent each column of the data matrix. $\Phi_i = \Gamma_i - \Psi$, Thus the zero mean matrix will be A= [Φ_1 Φ_2 Φ_3 Φ_4 Φ_M].

Step 2: Calculate the covariance matrix

From matrix 'A' calculate the Covariance matrix C by using the following formulae
$C = \frac{1}{M}\sum_{n=1}^{M}\Phi_n^T\Phi_n$

Step 3: Calculate the eigen values and corresponding eigenvectors of the covariance matrix

Computing Eigenvectors and Eigen values, Sort the Eigen pairs and compute the best *M* best eigenvectors and form a new space

Step 4: Projection and Transform Matrix

Construction of the projection matrix that will be used to transform the data set onto the new feature subspace. Transform the samples data onto new space with Y=X.W where X=data samples, W=new feature subset, Y=Principal Components which are projected on to the feature subspace.

Regression Analysis

Regression analysis is a type of statistical processes for estimation of the relationships between different variables. It is a predictive modeling technique. It estimates relationship between a dependent variable (target) and one or more independent variables (predictors or features) [13, 14]. In case of Logistic regression it assigns observations to a discrete set of classes during classification. But in case of linear regression, the outputs maps to continuous number values, where as in case of logistic it maps output using the logistic sigmoid function which return a probability measure that can then be mapped to two or more different classes [15].

There are basically three types of logistic regression: Binary (Pass/Fail), Multi (three or more categories without ordering), Ordinal (three or more categories with order). Binary logistic regression is the classification algorithm which classify into two classes. It uses a sigmoid function and the decision boundary is either 1 or 0. In case of multi classes logistic regression instead of output map to either 0 or 1, it map to 0,1,2,…n. Logistic Regression uses the logistic function to find a model that fits with the data points and the function restricted between 0 and 1[16].Logistic Regression uses a logistic function, which defined as y = 1 / (1 + e^-x). This logistic function is a sigmoid function (Figure 1).

The binary logistic regression model takes real-valued inputs and makes a prediction to a class for probability <=0.5, where as it predict to another class if the probability is >0.5.For multi class logistic regression, it divides the problem into n binary classification problems. For each class, predict the probability the observations are in that single class. For each sub-problem, we select one class (YES) is selected and all the others into a second class (NO). Then we take the class with the highest predicted value [13, 14].

SIMULATION RESULT

The experimental study has been performed using Python 3.6 with installed package scikit-learn, Pandas Library and the data set of Iris flower has been collected from machine Learning IRIS Dataset [17]. This dataset contain 150 data set for three class of iris flower namely Iris-Setosa, Iris-Versicolor, Iris-Verginica, where each class or species of flower having 50 set data set. The data set contain four features of the Iris flower i.e. Sepal Length, Sepal Width, Petal length, Petal Width. The sample of data set has been shown below in Table 1.The study based on classification of Iris flower with the help of Logistic Regression based machine learning technique and some cases studies. The entire data set has been randomly dived into two category training set and test set. Then both the train and test set have been standardize by making mean value 0 and standard deviation of 1. Generally PCA is used for feature extraction as well as dimensionality reduction when there is a large set of data. But in the case of IRIS flower the data set is not so large but it has been process through the dimensionality reduction and feature extraction to have a study of application of PCA.

After feature extraction from of 4 sets of feature set through dimensionality reduction, PCA has been calculated and the first two principal components has been taken as features set (Figure 13). These two principle components have been taken into consideration for training and testing purpose.The training set data which include the features set and target output class has been fit to the logistic Regression Model for training the system. In this case the logistic regression model used for Multiclass classification, so the model needs to enable for multiclass.

After successful training of the data set the test set features has been given as test data to the trained Model for the prediction. Predicted results have shown below in table 2.

In the test set the target are known but only the features set data have been given and predict the class and compare the predicted value with the known class type. In the first case 80 % of data set has been used for training and 20% used of total data set for testing purpose. In the predicted result, it was predicting 26 dataset correctly from 30 dataset. The accuracy level was computed to be 86%.In the further different case study has been taken to study the effect of percentage of training and test number of dataset as well as the number of principal components to the accuracy level of prediction.

Case 1: Accuracy Level Vs Principal Components

The graph (Figure. 4) express that with increase of the principal components selected for training the data then the accuracy level of prediction will also increase. For a large set of data the accuracy will increase for certain number of principal components, but if it increases more a specific then there may chances of decreasing of accuracy. Here the 80% data set has been taken as training data and 20% has been taken as testing data set.

Case 2: Accuracy Level Vs Percentage of Training and Testing Set

The prediction has been done for the testing set and the accuracy level has been calculated. In this case study, the prediction has achieved to 100 percentages with 80 % of training set data and 20% of training data. It can be seen that when the number of training data set decrease correspondingly the accuracy percentage is also getting decrease. The accuracy percentage reduced to 97, 93 and 92 percent corresponding to 70-30, 60-40 and 50-50 training and the comparison of accuracy percentage with principal components and percentage of training data set and testing data set combination shown in figure 5.

Case 3: Accuracy Level Vs Number of Principal Components Vs Percentage of Training

In the third scenario(Figure.6) , it has been compare all the cases which show that for every case if the number of principal component taken are increased then the accuracy level also increasing , even for all the cases with a fixed number of principal components, the accuracy level increases then the accuracy level also increases.

CONCLUSION

In this paper the iris flower has been classified using the multiclass based logistic regression. The dataset for the classification include petal, sepal length and width. Though it was not a large data set, still for the study of dimensional reduction technique, PCA has been implemented. The selected features have been used for training the regression model and test data set has been used for classification. Three scenario has been studied here that reveals that the accuracy level for prediction get increase if more number of principal components taken for classification and the other is that the accuracy level for prediction get decrease if the percentage of training data taken are reduced. But ultimately, it was giving best result for three selected principal components and 80% of total data as training set and rest 20% taken as testing set. In future Linear Discriminant Analysis will be implemented for feature extraction and the result will be compare with PCA.

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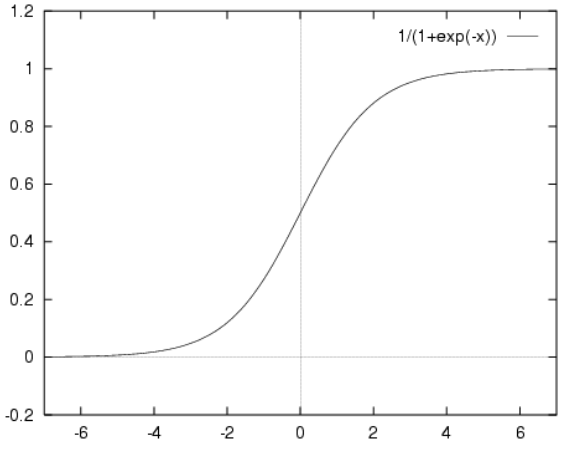


Figure 1: Sigmoid Function

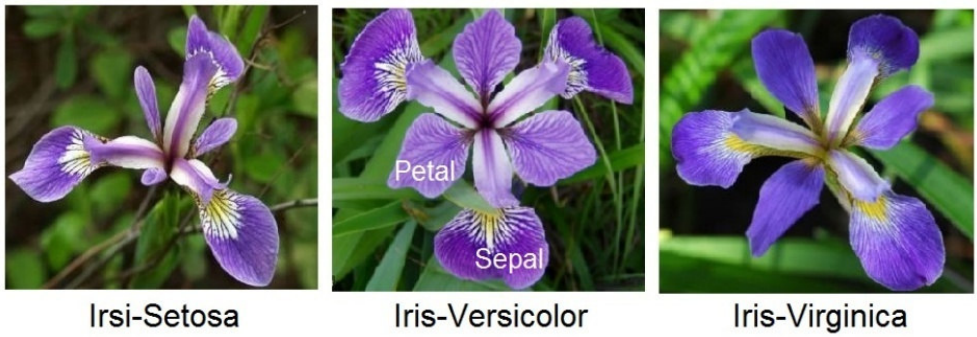


Figure 2: Types of Iris Flower

SN	Sepal Length	Sepal Width	Petal Length	Petal Width	Target
1	5.1	3.5	1.4	0.2	Iris-setosa
2	4.9	3	1.4	0.2	Iris-setosa
3	4.7	3.2	1.3	0.2	Iris-setosa
4	4.6	3.1	1.5	0.2	Iris-setosa
5	5	3.6	1.4	0.2	Iris-setosa
6	5.4	3.9	1.7	0.4	Iris-setosa

(a)

SN	Sepal Length	Sepal Width	Petal Length	Petal Width	Target
51	7	3.2	4.7	1.4	Iris-versicolor
52	6.4	3.2	4.5	1.5	Iris-versicolor
53	6.9	3.1	4.9	1.5	Iris-versicolor
54	5.5	2.3	4	1.3	Iris-versicolor
55	6.5	2.8	4.6	1.5	Iris-versicolor
56	5.7	2.8	4.5	1.3	Iris-versicolor

(b)

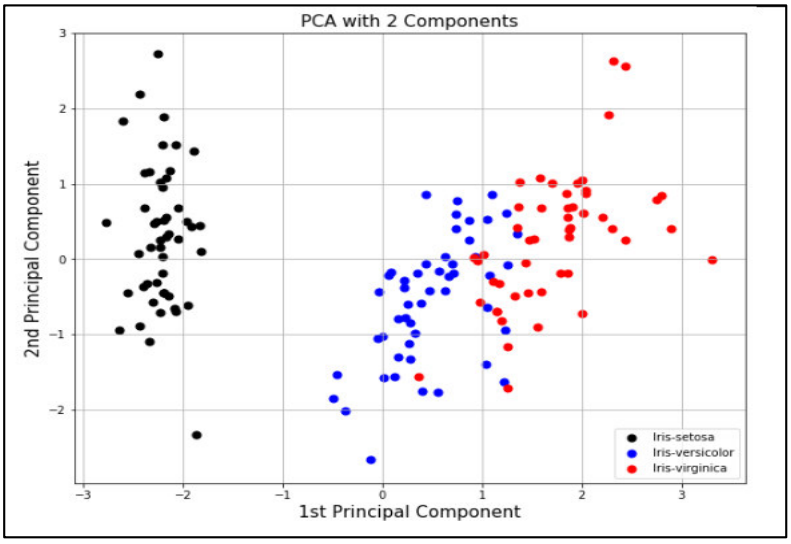
SN	Sepal Length	Sepal Width	Petal Length	Petal Width	Target
101	6.3	3.3	6	2.5	Iris-virginica
102	5.8	2.7	5.1	1.9	Iris-virginica
103	7.1	3	5.9	2.1	Iris-virginica
104	6.3	2.9	5.6	1.8	Iris-virginica
105	6.5	3	5.8	2.2	Iris-virginica
106	7.6	3	6.6	2.1	Iris-virginica

(c)

Table 1.Feature data for all three class of iris flower (a) iris-setosa, (b) iris-versicolor, (c) iris virginica

	1st Principal Component	2nd Principal Component
0	-2.264542	0.505704
1	-2.086426	-0.655405
2	-2.367950	-0.318477
3	-2.304197	-0.575368
4	-2.388777	0.674767
..	...	...

(a)



(b)

Figure 3. The principal component analysis (a) The first two principal components (b) first two principal components represented as a scattered plot

Testset Target Class					
Iris-virginica	Iris-versicolor	Iris-setosa	Iris-virginica	Iris-setosa	Iris-virginica
Iris-setosa	Iris-versicolor	Iris-versicolor	Iris-versicolor	Iris-virginica	Iris-versicolor
Iris-versicolor	Iris-versicolor	Iris-versicolor	Iris-setosa	Iris-versicolor	Iris-versicolor
Iris-setosa	Iris-setosa	Iris-virginica	Iris-versicolor	Iris-setosa	Iris-setosa
Iris-virginica	Iris-setosa	Iris-setosa	Iris-versicolor	Iris-versicolor	Iris-setosa
Predicted Class					
Iris-virginica	Iris-versicolor	Iris-setosa	Iris-virginica	Iris-setosa	Iris-virginica
Iris-setosa	Iris-virginica	Iris-virginica	Iris-versicolor	Iris-virginica	Iris-versicolor
Iris-versicolor	Iris-virginica	Iris-versicolor	Iris-setosa	Iris-versicolor	Iris-versicolor
Iris-setosa	Iris-setosa	Iris-versicolor	Iris-versicolor	Iris-setosa	Iris-setosa
Iris-virginica	Iris-setosa	Iris-setosa	Iris-versicolor	Iris-versicolor	Iris-setosa

Table 2.The known target output for the test class and the predicted output for same data

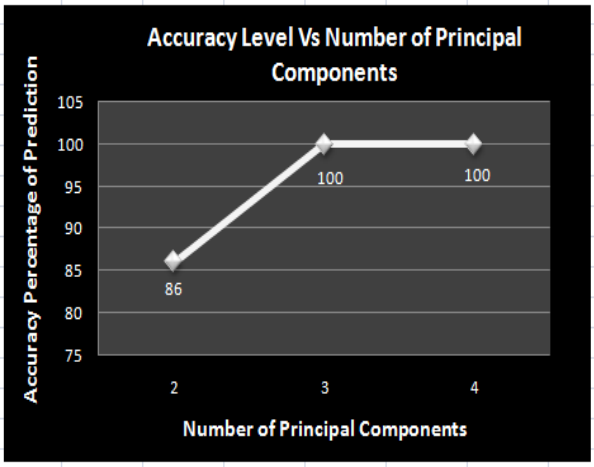


Figure 4: Comparison of Accuracy level and Number of principal components

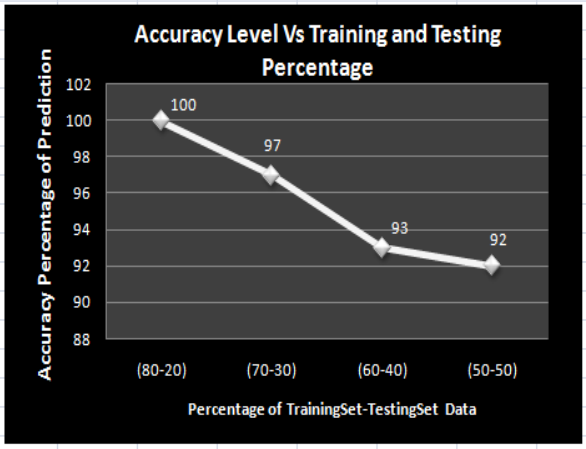


Figure 5: Comparison of Accuracy Level Vs Percentage of Training and Testing Set

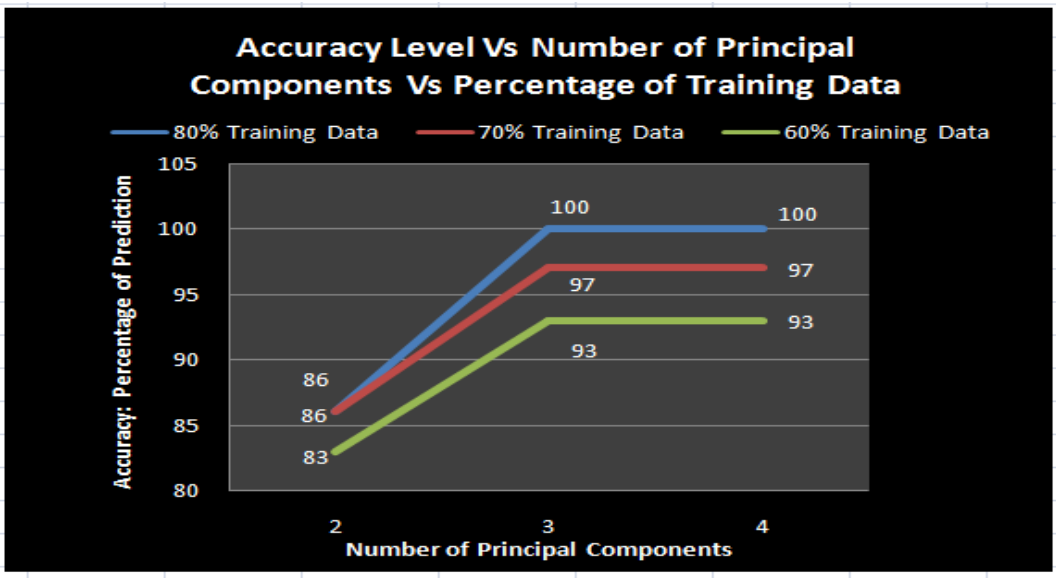


Figure 6: The comparison of Accuracy level, Number of principal components and percentage of training data

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RESEARCH ARTICLE

Nutrient Management with and without Gibberellic Acid on Yield Components and Production Efficiency of Winter Sweet Corn (*Zea mays* L. *saccharata*).

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ABSTRACT

A field experiment was conducted at Campus Farm, M.S. Swaminathan School of Agriculture, Centurion University of Technology and Management, Paralakhemundi, Odisha, India during winter in 2018-2019. The soil was clay loam in texture and acidic in reaction (pH 6.24) with low in available nitrogen and medium in available phosphorus, potassium and sulphur. The four nutrient management treatments containing 100 % recommended dose of NPK (120 kg nitrogen, 26.19 kg phosphorus and 49.81 kg potassium /ha), 125 % recommended dose of NPK (150 kg N, 32.74 kg phosphorus and 62.26 kg potassium /ha), 100 % recommended dose of NPK + 30 kg S/ha and 125 % recommended dose of NPK + 30 kg S/ha were tested with foliar application of gibberellic acid @ 100 g/ ha and without gibberellic acid adopting factorial randomized block design with eight treatments combination and three replications. Experimental results revealed that nutrient management treatments exerted remarkable influence on the yield attributes like cob length, cob girth and cob weight and production efficiency . Application of 125% recommended dose of NPK + 30kg S/ha recorded the highest number of cobs/ plant (1.78), cob length (22.78 cm), cob girth (21.62 cm), green cob weight (477 g) and production efficiency (159.79 kg/ day /ha). The foliar application of gibberellic acid @100 g/ ha had positive effect on cob length and cob weight along with production efficiency while number of cobs/ plant and cob girth were non significant. Application of gibberellic acid @ 100 g/ha increased cob length (22.69 cm), cob girth (21.44 cm), green cob weight (460.50 g) and production efficiency (156.72 kg/ha/day) over no gibberellic acid spray. The interaction effect between NPK levels and gibberrelic acid was significant for cob length, cob weight and production efficiency but no positive interaction effect was noticed for number of cobs / plant and girth

of cob. The use of 125 % recommended dose of NPK and 30 Kg S/ ha with foliar spraying of gibbberellic @ 100 g /ha recorded the maximum number of cobs /plant (1.87), cob length (23.23 cm), cob girth (21.83 cm) and cob weight (495.33 g) along with production efficiency (164.93 kg/day/ha) over all other treatments combination.

Key words: Nutrient management, gibberellic acid, yield attributes, production efficiency, winter sweet corn.

INTRODUCTION

Sweet corn is grown for diverse purpose for human consumption, green fodder to fed livestock animals and raw material to meet the industry requirement. The sweet corn is highly prized compared to other types of corn because of its delicious taste and soft and sugary endosperm. So it is having greater contribution in diet diversification and improvement in the nutrition of the people. After harvest of green cob, the green plants are used for quality fodders as a source of additional income for the farmers. Sweet corn is capturing sound market in most of the urban and semi urban areas of the country. Sweet corn increases the income of growers as it ranks second in farm value and fourth in commercial crops (Rathod *et al*., 2018).

Due to non-availability of suitable production technology, the farmers are not growing sweet corn in commercial scale. Just like maize, sweet corn depletes the soil fertility as heavy feeder crop. Therefore, the soil will be replenished with requisite quantities of nutrients to sustain crop production at optimum level. Hence, nutrient management is quite indispensible to boost the production and productivity of sweet corn. It is ascertained that application of NPK favorably increases the yield attributes and fresh cob yield in sweet corn (Bharud *et al*., 2014 and Muhumed *et al*., 2014). After N, P and K, the secondary nutrient sulphur is essential for synthesis of chlorophyll that increases the efficiency of photosynthesis which directly promotes carbohydrate metabolism to reflect the yield (Sutar *et al*., 2017). The use of high analysis sulphur free fertilizers, no use or less use of organic manures, adaption of multiple cropping system and cultivation of high yielding varieties and hybrids of crops are leading to mining of sulphur in Indian soils (Sutar *et al*., 2017). The yield attributes and grain yield of corn are enhanced favorably with application of sulphur up to the level of 45.0 kg/ha (Sutar *et al*., 2017). Plant growth regulators influence the various vital activities and found essential at all the crop developmental stages. The phytohormone gibberellin influences the crop growth and development throughout the crop growing period resulted in increasing the production and productivity of crops (Hedden and Sponsel, 2015).. Gibberellic acid has specific role in enzymatic activity to facilitate the metabolic processes, flowering and carbohydrate synthesis (Davies, 2004). Singh et al. (2018) observed the positive effect of gibberellic acid sprayed @ 40 t0 60 g/ ha in enhancing the growth, yield attributes and yield of maize. Keeping all those facts in view, the field experiment was undertaken to find out the influence of NPK levels and sulphur along with gibberellic acid on yield attributes and production efficiency of winter sweet corn in order to devise a suitable production technology.

MATERIALS AND METHODS

Experimental soil and it's analysis

The soil was collected by auger to the depth of 20 cm in various location of experimental field before conduction of experiment. The representative soil sample was air dried and analyzed for physical and chemical properties. The mechanical analysis of soil was done by Bouyoucous hydrometer method as per the procedure suggested by Piper (1966). The content of sand, silt and clay fraction of soil was 25.2, 35.3 and 39.5 (%), respectively. The textural triangle diagram out lined by Black (1965) was referred and the texture of soil was clay loam. The soil was acidic in reaction with pH of 6.24. The soil pH was measured with digital pH meter with glass electrode after mixing the soil

and water in the ratio of 1: 2.5 as per the procedure suggested by Jackson (1973). The initial fertility status of soil was low in organic carbon (0.47 %) and available N (171.6 kg /ha) and medium in available P_2O_5, K_2O and S containing 29.4, 276.7 and 27.48 kg/ha, respectively. The soil organic carbon (Dichromate oxidation of organic matter) and available nitrogen by alkaline potassium permanganate method, phosphorus by sodium bicarbonate method, potassium by ammonium acetate method and sulphur by turbidimetry method were determined as per the procedure suggested by Walkley and Black (1947), (Subbiah and Asija (1956) , Olsen *et a*l., (1954) , Jackson (1973) and Massoumi and Cornfield (1963), respectively.

Experimental design and treatment details

The four nutrient management treatments (100 % recommended dose of (120 kg nitrogen, 26.19 kg phosphorus and 49.81 kg potassium /ha), 125 % recommended dose of NPK (150 kg N, 32.74 kg phosphorus and 62.26 kg potassium /ha), 100% recommended dose of NPK + 30 kg S/ha and 125 % recommended dose of NPK + 30 kg S/ha) in factor A and two levels of gbbberellin (gibberellic acid @ 100 g/ha and no gibberellic acid) in Factor B comprising of eight treatments combination were tested. The field experiment was laid out in factorial randomized block design with three replications in the plot size of 4.8m x 4.2m comprising of 24 plots.

Sources of fertilizer and cytokinn

In the fertility levels of 100 % and 125 % recommended dose of NPK treatments without sulphur, the sources of fertilizers were diammonium phosphate (18% N and 46 % P_2O_5), urea (46 % N) and muriate of potash (60 % K_2O). In treatments receiving 100 % recommended dose of NPK + 30 Kg S/ha and 125 % recommended dose of NPK + 30 Kg S/ha, the complex fertilizer grade 20: 20: 0:13 containing 20 % N, 20 % P_2O_5, 0% K_2O and 13 % S as source of N, P, K and S, respectively, diammonium phosphate, urea and muriate of potash were chosen as sources of fertilizer. The source of sulphur was provided through complex fertilizer 20: 20: 0:13 grade was used in the treatments containing the combination of NPK and sulphur. The commercial grade gibberellic acid (GA 94) was chosen as source of gibberellin for the experimental purpose.

Cultural operations performed

The primary tillage was done by ploughing two times through tractor attached with cultivator followed by single ploughng with rotavator in order to obtain the desired seed bed. After final land preparation, the field was made to twenty four plots in size of 5.0 m x 4.2m with bund width of 30 cm and replication gap of 1 m. The sweet corn hybrid golden cob F1 of East West seed international company was sown on 26 th December, 2018 with spacing of 50 cm between rows and 30 cm within plants. Just before sowing, full dose of phosphorus and sulphur along with 50 % nitrogen and potassium were applied in crop rows as basal. The hoeing followed by weeding operation was carried out manually at 15 and 35 days after sowing. The remaining quantities of 50 % nitrogen and potassium were top dressed at 35 days after sowing (DAS) followed by earthing-up operation. The commercial grade gibberellic acid (GA 94) @ 100 g/ha was sprayed in two equal splits of 50 g/ha at 6 and 8 weeks after sowing with hand operated knapsack sprayer in spray volume of 500 litres /ha. The crop was irrigated as and when necessary with help of sprinklers fitted with sensors. The insecticide acephate @ 0.02 % was sprayed at 35 days after sowing by knapsack sprayer with spray volume of 500 l/ha to control the stem borer infestation. The green cobs at soft dough stage were harvested by plucking manually on 21 st March, 2019.

Recording of data at harvest

At harvest, ten plants from each plot were selected randomly for taking observations on number of cobs/plant, cob length, cob girth and cob weight. The mean values were taken for data interpretation. The weight of green cob was taken from each plot and converted to yields in kg/ha. The production efficiency was calculated by dividing the yield in kg /ha with duration of crop. The formula of production efficiency is depicted below as suggested by Singh *et al*., 2018..

$$\text{Production efficiency (kg/day/ha)} = \frac{\text{Grain yield (kg/ha)}}{\text{Duration of crop in days}}$$

Statistical analysis

The data collected from various yield components and production efficiency were analyzed by the method of analysis of variance as described by Gomez and Gomez, 1984. Statistical significance was tested by computing F value at 0.05 level of probability and critical difference was calculated if the effect is found significant for treatment comarison.

RESULTS AND DISCUSSION

Effect of nutrient management treatment on yield attributes

The fertility levels had no significant effect on number of cobs/ plant (Table 1). The number of cobs/ plant was increased with 125 % recommended dose of NPK + 30 kg S (1.78) followed by 125 % recommended dose of NPK (1.77) and 100 % recommended dose of NPK + 30 kg S (1.68). The data on cob length showed that application of nutrient management treatments significantly influenced the cob length (Table 2). The combined application of 125 % recommended dose of NPK + 30 kg S/ha recorded the maximum cob length (22.78 cm) being at par with 100 % recommended dose of NPK + 30 kg S/ha (22.60 cm) and 125 % recommended dose of NPK (22.47 cm). The lowest cob length was observed in 100 % recommended dose of NPK (21.77 cm).

Application of fertility levels exerted the remarkable effect on cob girth (Table 3). The highest cob girth was observed in 125 % recommended dose of NPK + 30 kg S/ha (21.62 cm) that did not differ significantly from 125 % recommended dose of NPK (21.48 cm) and 100 % recommended dose of NPK + 30 kg S/ha (21.23 cm). The use of full recommended NPK dose gave the lowest cob girth (20.37 cm). An introspection of data from Table 4 pointed out the positive effect of fertility levels on single cob weight. The cob weight was the highest with 125 % recommended dose of NPK + 30 kg S/ha (477.00 g) being statistically at par with 125 % recommended dose of NPK (464.17g) and 100 % NPK + 30 kg S/ha (448.50 g). The former two treatments were significantly higher than 100 % NPK (414.67 g). There was no significant difference between 100 % recommended dose of NPK and 100 % NPK + 30 kg S/ha with respect to cob weight. Increase in yield attributes by application of 125% recommended dose of NPK + 30 kg S/ha was resulted in owing to adequate supply of plant nutrients to enhance the availability and absorption of it that reflected the vegetative growth. It facilitated the better translocation of photosynthates from source to sink thus, enhanced the yield attributes. Similar favourable effect of higher levels of NPK in augmenting the yield attributes in sweet corn is supported by earlier research works performed by Bharud *et al*., 2014. The positive impact of sulphur fertilization up to dose of 45 kg /ha in improving the yield attributes of maize was reported by Sutar *et al*., (2017) .

Effect of gibberellin on yield attributes

The spraying of gibberllic acid failed to exhibit the significant effect on number of cobs/plant (Table 1). The number of cobs/plant was observed more with application of gibberellic acid @ 100 g/ha (1.78) than no gibberllic acid (1.64). Data depicted in Table 2 indicated that gibberellic acid @ 100 g/ha significantly increased the cob length (22.69 cm) over no gibberellic acid application (22.12 cm). Application of gibberellic acid had no remarkable effect on cob girth (Table 3). The cob girth was higher with gibberellic acid @ 100 g/ha (21.44 cm) than that of no gibberellic acid spray (20.91 cm). Significant difference was observed due to gibberllic acid application with respect to cob weight (Table 4). The cob weight was favourablly increased with application of gibberellic acid @ 100 g/ ha (460.50 g) over no gibberellic acid (411. 57 g). Application of growth hormone gibberellin largely affected the strength of physiological source that influenced the crop growth which was leading to the accumulation of photo assimilates during the crop growing period. Hence, it favourably influenced the yield attributes like cob length and cob girth thereby increased

the cob weight. It mostly depended on the way they were partitioned between desired storage organs of crop. The plant growth regulator is responsible for increasing the hydrolyzing and oxidizing enzyme activities thereby improve the mobilization of reserve food materials from source to the developing sink. The favorable effect of gibberellins in improvement in yield attributes of maize is corroborated with the findings of Singh et al., 2018 .

Interaction effect of nutrient management treatment and gibberellic acid on yield attributes

A close examination of data presented in Table 1, Table 2, Table 3 and Table 4 showed that the interaction effect berween fertility levels and gibberellins was found significant for cob length and cob weight while number of cobs/plant and cob girth was not significantly affected by interaction effect. The number of cobs/plant was maximum with 125% recommended dose of NPK + 30 kg S/ha with gibberellic @ 100 g/ ha (1.87) and 100% recommended dose of NPK + 30 kg S/ha with gibberellic @ 100 g/ ha (1.83). Application of 125% recommended dose of NPK + 30 kg S/ha with gibberellic @ 100 g/ ha recorded the highest cob length (23.23 cm) and followed by 100% RFD + 30 kg S/ha with gibberellic @ 100 g/ha (22.93 cm). The cob girth was maximum with 125% recommended dose of NPK + 30 kg S/ha with gibberellic acid @ 100 g/ ha (21.83 cm) closely followed by 125% recommended dose of NPK with gibberellic acid @ 100 g/ ha (21.77 cm). The use of 125 % NPK + 30 kg S/ha with spraying of gibberellic acid @100 g /ha recorded the highest cob weight (495.33 g) which was at par with 125 % recommended dose of NPK+30 kg S/ha along with spraying of gibberellic acid @100g /ha. This is achieved due to favourable interaction effect of 125 % NPK + 30 Kg/ ha with gibberellic acid in increasing the growth and expansion of plant canopy thus, facilitated better absorption of solar radiation thereby increased the photosynthetic efficiency which consequently improved the dry matter production. It reflected the better translocation of photosynhates from source to sink that resulted in augmenting the yield attributes.

Effect of nutrient management treatment treatments on production efficiency

The data on production efficiency depicted in Table 5 revealed that application of fertility levels significantly influenced the production efficiency of sweet corn. The highest production efficiency was recorded with 125 % recommended dose of NPK + 30 kg S/ha (159.79 kg/day/ha). It was followed by 125 % recommended dose of NPK (152.64 kg/day/ha) and 100 % recommended dose of NPK + 30 Kg S/ha (147.31 kg/day/ha) which remained at par with 125 % recommended dose of NPK + 30 kg S/ha. Application of 100 % recommended dose of NPK gave the lowest production efficiency (144.56 kg/day /ha). The favourable effect of 125 % recommended dose of NPK in conjunction with sulphur in enhancement of the production efficiency is ascribed to adequate nutrient supply that reflected the yield attributes which directly governs the cob yield. Moreover, application of 125% recommended dose of NPK + 30 kg S/ha is resulted in effective translocation of photosynthates from source to sink thus, increased the yield attributes and consequently the production efficiency. The positive response of of sweet corn to higher doses of NPK in augmenting the yield is in corroboration with findings of Bharud *et al.*, 2014 and Muhumed *et al.*, 2014 . Sutar et al. 2018 reported the beneficial effect sulphur fertilization with the economic dose of 45.0 kg/ha.

Effect of gibberellins on production efficiency

Data depicted in Table 5 indicated the significant increase in production efficiency due to application of gibberellic acid @ 100 g/ha (156.72 kg/day/ha) over no spray of gibberellic acid (145.53 kg/day/ha). The accumulation of photo assimilates during the crop developmental stages depend on the way they are partitioned between desired storage organs of crop which enormously affects the crop yield. The plant growth regulators helps to increase the hydrolyzing and oxidizing enzyme activities thereby improves the mobilization of reserve food materials from source to the developing sink and reflects the enhancement in yield. The favorable effect of gibberellic acid on improvement of yield attributes reflected the production efficiency of sweet corn. These results are in conformity with the findings of Singh et al., 2018 .

Interaction effect of nutrient management treatments and gibberellins on production efficiency

The data on production efficiency presented in Table 5 indicated that the interaction effect between nutrient management treatments with gibberellin was found significant. Application of 125 % recommended NPK + 30 kg S/ha sprayed with gibberellic acid @ 100g /ha registered the highest production efficiency of 164.93 kg /day/ha) closely followed by 125% recommended dose of NPK with gibberellic acid @ 100g /ha (160.73 kg /day/ha) which were statistically at par with each other. This is resulted in owing to favourable effect of nutrient management treatments with gibberrellic acid on enhancement of yield contributing components like number of cobs/plant, cob length, cob girth, and individual cob weight which ultimately lead to increase in production efficiency.

CONCLUSION

It is inferred from the present investigation that application of 125 % recommended dose of NPK with 30 kg S/ ha in conjunction with foliar application of gibberellic acid @ 100 g /ha is found suitable to augment the yield parameters and production efficiency of sweet corn grown during winter season.

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Table1. Effect of nutrient management treatments and gibberellic acid and their interaction effect on number of cobs /plant in sweet corn

Fertility levels	Gibberellins		Mean
	No gibberellic acid	Gibberellic acid@100 g/ha	
100% Recommended dose of NPK	1.60	1.63	1.62
125% Recommended dose of NPK	1.73	1.80	1.77
100% Recommended dose of NPK + 30 kg S/ha	1.53	1.83	1.68
125% Recommended dose of NPK + 30kg S/ha	1.70	1.87	1.78
Mean	1.64	1.78	-
Significance test	Fertility levels	Gibberellin	Interaction
CD (P=0.05)	NS	NS	NS

Table 2. Effect of nutrient management treatments and gibberellic acid and their interaction effect on green cob length (cm) in sweet corn

Fertility levels	Gibberellins		Mean
	No gibberellic acid	Gibberellic acid @100 g/ha	
100% Recommended dose of NPK	21.73	21.80	21.77
125% Recommended dose of NPK	22.13	22.80	22.47
100% Recommended dose of NPK + 30 kg S/ha	22.27	22.93	22.60
125% Recommended dose of NPK + 30kg S/ha	22.33	23.23	22.78
Mean	22.12	22.69	-
Significance test	Fertility levels	Gibberellin	Interaction
CD (P=0.05)	0.63	0.52	1.03

Table 3. Influence of nutrient management treatments and gibberellic acid and their interaction effect on green cob girth (cm) in sweet corn

Fertility levels	Gibberellins		Mean
	No gibberellic acid	Gibberellic acid @100 g/ha	
100% Recommended dose of NPK	20.10	20.63	20.37
125% Recommended dose of NPK	21.20	21.77	21.48
100% Recommended dose of NPK + 30 kg S/ha	20.93	21.53	21.23
125% Recommended dose of NPK + 30kg S/ha	21.40	21.83	21.62
Mean	20.91	21.44	-
Significance test	Fertility levels	Gibberellin	Interaction
CD (P=0.05)	0.93	NS	NS

Table 4. Effect of nutrient management treatments and gibberellic acid and their interaction effect on single green cob weight (g) in sweet corn.

Fertility levels	Gibberellins		Mean
	No gibberellic acid	Gibberellic acid @100 g/ha	
100% Recommended dose of NPK	408.33	421.00	414.67
125% Recommended dose of NPK	458.33	470.00	464.17
100% Recommended dose of NPK + 30 kg S/ha	441.33	455.67	448.50
125% Recommended dose of NPK + 30kg S/ha	458.67	495.33	477.00
Mean	441.67	460.50	--
Significance test	Fertility levels	Gibberellin	Interaction
CD (P=0.05)	25.23	17.84	35.68

Table 5. Production efficiency (kg/ha/day) of sweet corn as influenced by nutrient management treatments and gibberellic acid and their interaction effect

Fertility levels	Gibberellins		Mean
	No gibberellic acid	Gibberellic acid @100 g/ha	
100% Recommended dose of NPK	138.02	151.10	144.56
125% Recommended dose of NPK	144.55	160.73	152.64
100% Recommended dose of NPK + 30 kg S/ha	144.51	150.11	147.31
125% Recommended dose of NPK + 30kg S/ha	154.65	164.93	159.79
Mean	145.43	156.72	---
Significance test	Fertility levels	Gibberellin	Interaction
CD (P=0.05)	10.05	7.10	14.21

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RESEARCH ARTICLE

Development and Validation of D-Penicillamine in Rat Plasma using Liquid Chromatography coupled with Mass Spectroscopy (LC-MS/MS): Application to Pharmacokinetic Study

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ABSTRACT

Penicillamine is a chelating agent its recommended for the elimination of excess copper in patients with Wilson's disease and it reduces excess cysteine excretion in cystinuria. In this work, a simple, high sensitive and reproducible liquid chromatography coupled with mass spectroscopy (LC-MS/MS) method was developed and validated for the determination of D-Penicillamine in rat plasma. Both D-Penicillamine and Penicillamine D3 (internal standard, IS) were separated by using Hypersil-BDS column through isocratic elution mode, of Acetonitrile / water containing 0.1% formic acid (55:45, v/v), at a flow rate of 0.8 mL/min. The MS/MS system was operated in a positive ion mode followed by ESI multiple reaction monitoring (MRM) mode, and the MRM transition was optimized as m/z150.0 →114.9 for D-Penicillamine and 153.0 →118.0 for IS. The method showed good linearity in the range of 10 to 3500 ng/mL (R^2=0.99) and sensitivity for D-Penicillamine with the Lower limit of quantification (LLOQ) of 10 ng/mL. The intra-and inter-day accuracy ranged from 96.2-106.7%, 98.4-104.0%, respectively. The intra-and inter-day precision was less than 10.3% and 8.0%, respectively. The extraction efficiency and absolute recovery were more than 66.5% and 71.3%, respectively. In addition, a good matrix effect of less than 10% was obtained. The valiated LC-MS/MS method was successfully applied to the pharmacokinetic study of D-Penicillamine in rat plasma.

Keywords: D-penicillamine; LC-MS/MS; pharmacokinetics; rat plasma.

INTRODUCTION

Penicillamine is a tri-functional organic compound consisting of an amine, carboxylic acid and a thiol. A gem dimethyl group is also present in the same carbon (beta to carboxylic acid) where the thiol group is present. Penicillamine is a thiol which was identified from hydrolysis of pencillin in the 1940s (Joyce *et al.,* 1989). A decade later it enters the clinical use of chelating agent and found in urine in the treatment of penicillin (Langlois *et al.,* 2013) and It exists two stereoisomers but D-isomer was medicinally active and its opposite enantiomer L-Penicilamine is highly toxic and harmful to health. D-Penicillamine is listed on the World Health Organizations (WHO) list of essential medicines, the safest medicine needed to treat few diseases in human health system. It's primarily used to treat Wilson disease; a rare genetic disorder of copper metabolism, D-Penicillamine treatment relies on its binding to accumulated copper and elimination through urine. It is also used in the treatment of heavy metal poisoning, rheumatoid arthritis and kidney stone due to high cysteine levels and can be measured in plasma by derivatization methods (Netter *et al.,* 1987 and McCabe *et al.*, 2019) Apart from the medicinal properties, it has been observed with few patients with common side effect such as rashes, loss of appetite, nausea, diarrhoea and reduction of white blood cells level. It is mainly metabolised through liver and some patient's liver problem also noticed. Use of this medicine in pregnancy may affect the embryo or baby.

Thiol containing compounds are mostly used in the treatment of rheumatoid Arthritis and Wilson's disease. In literature there are many High Performance Liquid Chromatography (HPLC) methods reported with Electro chemical Detector (Abounassif *et al.,* 1983; Rolf *et al.,* 1978), Fluorescence detection (Mozow *et al.,* 2000) and luminescence detection (Zhang *al.,* 1997) were reported to detect and quantify the D-pencillamine. Several methods reported by Spectrophotometer (Amir *et al.,* 1987; Abdalla *et al.,* 2013), Spectroflurimetric (Raza *et al.,* 2010), Colorimetric (Racci *et al.,*1982),1, 2-naphthoquine-4-sulfonate(NQS) Reagent (Abdalla *et al.,* 2013). LC-MS/MS method was reported in dog plasma for quantify the D-Penicillamine and the LOQ was found to be 1.0 µg/mL (Langlois DK *et al., 2013*). None of the method was reported for the determination of D-Pencillamine in rat plasma by LC-MS/MS.

In this study, we develop and validate high sensitive and reproducible novel LC-MS/MS method for determination of D-Pencillamine in rat plasma samples. We have optimised time gaining and a cost effective method of regular estimation D-Pencillamine in rat plasma samples. In addition, one more objectives of this study is to estimate the pharmacokinetic parameters of D-Pencillamine in rat plasma after oral administration of 25 mg/kg of Pencillamine.

MATERIALS AND METHODS

Chemicals and reagents

Standard Penicillamine (purity >99%) was purchased from Vivan Life science, India. Penicillamine D3 (IS) was purchased from Bioorganics, India. Acetonitrile, methanol and Formic acid of HPLC grade were purchased from Sigma-Aldrich, India. Ultra-pure water of 18 MΩ/cm was obtained from Milli-Q purification system, Millipore, MA, USA. The animal study was conducted at Radiant Research Services Pvt Ltd, #99/A, 8th Main, III Phase Peenya Industrial Area, Bangalore-560058. All applicable national and international ethical guidelines for maintenance and experimental studies with Wistar rats were followed.

Instrumentation and conditions

A Shimadzu Nexera X2 HPLC system consisting of a SIL-30 ACMP autosampler, SIL-30 AD pump, CTO-10 ASVP column oven and DGU-20A3R degasser was employed. The analytes separation was carried out on a Thermo scientific BDS HYPERSIL C8 column (100 mm × 4.6 mm, 3 µm) at 40°C. The 0.1% Formic acid in Acetonitrile (55%, v/v) and 0.1% Formic acid in water (45%, v/v) were used as the mobile phase, at flow rate of 0.800 mL/min were

employed. The temperature of autosampler was maintained at 4°C, the injection volume was 5 µL for each sample, and the chromatographic run time was within 4.5 min. An API 4500 triple quadrupole instrument (Applied Biosystems, Toronto, Canada) was used for targets' detection in a positive ion mode followed by ESI multiple reaction monitoring (MRM) mode. Protonated precursor→ product ion transitions optimized were 150.00→114.90 for D-Penicillamine and 153.00→118.00 for IS, as shown in Fig.1 and Fig.2. Turbo spray voltage was set at 5500 V. Source temperature remained at 500°C. Entrance potential was 10 V Nitrogen was applied as nebulizing gas (45 psi) curtain gas (50 psi), and collision gas (6 psi). The three compound-dependent parameters, including the declustering potential, collision energy and cell exit potential, were optimized at 36, 16 and 22 V for D-Penicillamine and IS. Quadrupoles 1 and 3 were maintained at unit resolution. Data processing was performed with Analyst 1.6.3 software package (Sciex, USA).

Preparation of calibration standards and quality control (QC) samples

The standard stock solution of 1 mg/mL D-Penicillamine was prepared by dissolving in 1% Formic acid in methanol and stored at ambient temperature. The standard stock solution of 1 mg/mL IS was prepared by dissolving in methanol and stored at 4°C before use. The stock solution of D-Penicillamine was further diluted with 20% methanol to prepare working solutions at several concentration levels. The calibration curves were constructed by spiking proper volumes of D-Penicillamine standard solution into blank plasma with corresponding volumes to obtain the desired concentrations at 10, 20, 50, 100, 300, 750, 1500, 2800 and 3500 ng/mL, and 4000 ng/mL IS was prepared through diluting the standard stock solution with methanol. The same procedure was also employed for the preparation of quality control (QC) samples at four concentration levels, denoted as 5 ng/mL (LLOQ, lower limit of quantitation), 30 ng/mL (LQC, Low-quality control), 1375 ng/mL (MQC, Middle-quality control), and 2750 ng/mL (HQC, High-quality control). All calibration standards and QC samples were prepared freshly in the dark room.

Extraction of plasma samples

The samples stored in the freezer at -20°C were thawed at room temperature prior to pretreatment. 50 µL plasma for each sample was pipetted to a 1.5 mL polypropylene tube, and 200 µL acetonitrile with IS (Penicillamine D3 solution, 4000 ng/mL) was added in order to extract analytes and precipitate proteins, then the mixture was vortexed for 1 min. Then this was centrifuged at 10,000 rpm for 5 min at 4ºC on an eppendorf 5810R centrifuge (Eppendrof AG, Hamburg, Germany). The clear supernatant organic layer (180 µL) was transferred into 2 mL glass tubes and evaporated to dryness at 30ºC using nitrogen evaporator (Turbovap®, Biotage, USA). The residue was reconstituted in 100 µL of the 50% methanol in water, vortex mixed for 1.0 min and centrifuged at 10,000 rpm for 5 min. Finally, 90 µL of the clear supernatant were transferred into glass micro-vials and 5µL were injected onto the LC-MS/MS system for analysis.

Method validation

The method was validated for selectivity, specificity, recovery, linearity, accuracy, precision and stability using US Food and Drug Administration (USFDA) guidelines [US DHHS *et al.*, 2001] for the assay in rat plasma.

Carry-over

It is carried out by injecting mobile phase solution followed by extracted blank, extracted LLOQ, extracted upper limit of quantification (ULOQ), and then once again extracted blank. It is considered to be having no carryover if the interference peak obtained at the retention time (RT) of D-Penicillamine is not more than or equal to 20% of extracted LLOQ or interference at the RT of ISTD is less than or equal to 5% of internal standard response of extracted LLOQ in reinjected blank sample.

Specificity

The selectivity of the present method was established by checking the blank plasma (without spiking with D-Penicillamine) obtained from different batches of rat plasma samples including blank plasma made of six independent rat plasma. All the blank matrices along with their respective LLOQ samples were processed and analysed as per method. The blank matrices were considered to be free of interference if the responses for measured peak at the retention times (RT) of analyte were less than 20% of extracted LLOQ response and that at the RT of ISTD was less than 5% of extracted ISTD. All the batches were found to have no endogenous interference with analyte peak and ISTD peak. The sample preparation was the same as the protocol described above.

Linearity and sensitivity

To evaluate the linearity of the method, the analysis of calibration standards at 9 non-zero concentrations was carried out through preparing three replicates for each concentration level. The calibration curves were made by using the peak area ratios of D-Penicillamine to IS versus the D-Penicillamine concentrations with a least-squares linear regression analysis, and fitted to the $y=bx+c$ using the weighing factor ($1/x^2$). The lowest concentration level on the calibration curve was to be considered as the lower limit of quantitation (LLOQ) if the target response was at least 5 times more than that of noise (Signal/Noise)≥10). Moreover, the peak of LLOQ sample should be identifiable, clearly separated, and reproducible with the accuracy and precision less than ±20.0%. The accuracy and precision of calibration standards for the nominal concentration levels except for LLOQ should be less than ±15.0%.

Accuracy and precision

For calculating accuracy and precision of the method, QC samples at four concentration levels (10, 30, 1375, 2750 ng/mL) were determined. Six replicates of each QC level were analyzed each day for the determination of intra-day accuracy and precision. This process was repeated three times over three consecutive days for the measurement of inter-day accuracy and precision. The accuracy was calculated and expressed in terms of %Accuracy = [(detected concentration)/(theoretical concentration)]×100%, and the precision was expressed as relative standard deviation (RSD) at each level. The deviation of accuracy and precision at each level for nominal concentration should be less than ±15% except for LLOQ for which it should not be more than ±20%.

Recovery and matrix effects

The absolute recovery, extract efficiency, and matrix effects of the analytes were measured by using D-Penicillamine -spiked rat plasma samples (n=6) at three different concentration levels of 30, 1375, 2750 ng/mL. Three groups of samples were prepared: group 1 represented the rat plasma sample spiked before extraction; group 2 represented the rat plasma sample spiked after extraction at equal concentration level; group 3 represented the standard solution of corresponding concentration prepared with the mobile phase. The absolute recovery was calculated as the peak area of group 1 divided by the peak area of group 3. The extract efficiency was calculated as the peak area of group 1 divided by the peak area of group 2. The matrix effects were calculated as the peak area of group 2 divided by the peak area of group 3, and the inter-subject variability of matrix effects at each concentration level should be less than ±15%

Stability

To ensure the reliability of the results, the stability of D-Penicillamine was evaluated by using QC samples under several conditions, including autosampler stability, freeze-thaw stability, short- and long- term stability. The

autosampler stability was determined at 4°C for 48 h. During the freeze-thaw stability assay, the stability was evaluated after three complete freeze-thaw cycles (-20°C to 25°C) on the consecutive days. The short and long-term stability was tested by analyzing QC samples stored at ambient temperature for 24 h, and at -20°C for 15 days, respectively. The results for these assays were evaluated by calculating the peak area ratio (analyte/IS) of stability samples against freshly prepared calibration curve samples. To meet the acceptance criteria, the deviation should be within ±15%.

Pharmacokinetic study

Six male wister rats (180 ± 30 g) were fasted 12 h but allowed water ad libitum before the day of administration. Oral formulations were prepared in suspension form by triturating an accurately weighed amount of powdered compound with 10% polysorbate 80 in containing 0.5% methyl cellusoe (cP 4000) make up the volume with in methyl cellulose (0.5%, w/v water). Oral doses of 25 mg/kg were administered using a gavage needle at 5 mL/kg to rats after an overnight fast (12 hr). Feed was offered 4 h after dosing. Blood samples (0.20 mL) were collected from retro-orbital sinus at Pre-dose, 0.25, 0.5, 1, 2, 4, 6, 8, 12 and 24 h post dose in K_2-EDTA (di-potassium ethylene diamine tetra acetic acid) tubes and were kept on ice till further processing. Plasma was separated by centrifugation at 4°C for 10 min at 4500 rpm and stored at -20°C till further analysis. Pharmacokinetic parameters such as the maximum plasma concentration (C_{max}), area under the concentration-time curve (AUC), time to reach the maximum concentration (T_{max}), half-life (t1/2) and elimination constant (Kel) were estimated by means of a non-compartmental analysis using SAS® version 9.4.

RESULTS AND DISCUSSION

Bio-analytical method establishment

Protein precipitation method was used for the preparation of different plasma samples. Methanol was chosen as the precipitation solvent at a 3:1 optimal ratio. The Prepared samples were used for HPLC-MS/MS analysis. The tuning of MS parameters was performed in positive as well as negative ionization modes for D-Penicillamine and IS by using 100 ng/mL tuning solution. A comparison showed that the positive ionization mode displayed a higher response than that of the negative ionization mode for D-Penicillamine and IS. Therefore, the positive ionization mode was selected to determine the targets. The protonated precursor ions [M+H]+ were appeared at m/z 150.0 corresponding to D-Penicillamine and 153.0 corresponding to IS in the Q1 MS full scan mass spectra, Subsequently, the mass spectrometer was set up in multiple reaction monitoring mode to monitor the transitions from the precursor ion to product ion. As shown in Fig. 1 and Fig. 2, the precursor ions were fragmented into several fragments, while those appeared at m/z 114.9 and 118.0 were the major fragments. Thus, the MRM transition for D-Penicillamine and IS was selected as m/z 150.0→114.9 and 153.0→118.0, respectively. Furthermore, to establish an accurate and effective separation method, the liquid chromatographic conditions including the constitution of mobile phase, the flow rate, the category of column, and column temperature were also optimized. After careful comparison of various parameters, we established the reliable conditions for determining the concentration of D-Penicillamine in treated plasma, that is, the concentration of D-Penicillamine was measured by using the BDS Hypersil C8 column (100 mm×4.6 mm, 3 μm) with the mobile phase of 55% 0.1% Formic acid in Acetonitrile and 45% 0.1% Formic acid in water (v/v) at 40°C under the flow rate of 0.8 mL/min.

Method validation

Specificity

The specificity of the developed method was verified by using different batches of rat plasma samples. Displayed the specificity of the method with the chromatograms of blank plasma (Fig. 3B), blank plasma spiked with 4000 ng/mL

Penicillamine and IS (Fig. 3A), and real plasma at 0.5h after an oral administration of 25 mg/kg Penicillamine (Fig. 3C). The retention times for Penicillamine and IS under the optimized conditions were at 2.05 and 2.05 min, respectively, within a whole run time of 4.5 min suitable for routine analysis. It was found that no interferences in the chromatograms of the detected samples were around the retention times of D-Penicillamine (2.05 min) and IS (2.05 min). The results indicated that the developed method possessed good specificity for D-Penicillamine and IS in rat plasma. Moreover, the chromatograms of the detected samples showed good peak shapes for D-Penicillamine and IS.

Linearity and sensitivity

The calibration curves of D-Penicillamine exhibited good linear response over the concentration range of 10.0-3500 ng/mL spiked with 4000 ng/mL IS. Atypical calibration plot equation deduced from three calibration curves was $y=0.000757x+0.0003$, $R^2 = 0.9959$ (y represented the peak area ratio of D-Penicillamine to IS, x represented the spiked concentration of D-Penicillamine in blank plasma). The mean accuracy ranged from 97.6 to 105.0%, and the precision was lower than 3.8% (Table 1). In addition, the lower limit of quantification (Signal/Noise ≥10) for D-Penicillamine reached down to 10.0 ng/mL, which was indicative of the high sensitivity of the method.

Accuracy and precision

The accuracy and precision of the method were assessed by measuring the QC samples spiked with D-Penicillamine at the concentrations of 10, 30, 1375, 2750 ng/mL and IS of 4000 ng/mL in blank plasma. As shown in Table 2, the intra-day precision value (RSD, n=6) was less than 10.3%, and the intra-day accuracy value (%, n=6) ranged from 96.2 to 106.%. Moreover, the inter-day precision value (RSD, n=18) was less than 8.0%, and the inter-day accuracy value (%, n=18) ranged from 98.4 to 104.0%. The results were adequately in consistent with the acceptable criteria depicted in the corresponding experiment section.

Recovery and matrix effect

As depicted in Table 3, the absolute recovery rate of D-Penicillamine at three different concentrations of 30, 1375, 2750 ng/mL (n=6) ranged from 69.2% to 72.2%, and the extraction efficiency of the employed protein precipitation method varied between 65.5% and 69.5%. Calculated matrix effect values were less than ±15% (2.4%, 3.5%, 1.2 %), therefore, it could be inferred that the disturbing errors from plasma matrix was negligible for the reliability of the results. Besides, the results revealed that the sample preparation procedure provided relatively clean extracts. of course, for the low matrix effects, the optimal conditions of HPLC-MS/MS couldn't be ruled out.

Stability

Shown in Table 4, the results of stability experiments indicated that D-Penicillamine was stable in the autosampler setting at 4°C for 2 days with mean bias within ±2.9%. The deviations were from -4.5% to 0.96% after five freeze-thaw cycles at -20°C to 25°C on consecutive days, which showed D-Penicillamine was still stable in the process of freezing-thawing. During the short-term (at ambient temperature, 24 h) and long-term (at - 20°C, 15 days) stability assay, it was found that the bias values were from -5.8% to 1.1%, -4.5% to 0.3%, respectively. All these results above met the acceptance criteria of the deviation within ±15%, and indicated that D-Penicillamine was stable enough in rat plasma to be accurately analyzed throughout the experiment.

Application in a pharmacokinetic study of D-Penicillamine

Finally, the method was successfully applied for the determination of D-Penicillamine concentration in Wister rat plasma after an oral administration at a dosage of 25 mg/kg. Fig.4 showed the mean concentration of D-Penicillamine-

time profile in rat plasma. The results revealed that D-Penicillamine concentration in rat plasma could be measured up to 24 h for all rats by using the developed method. Moreover, it was found that the LLOQ of the method was enough to meet the determination of D-Penicillamine plasma concentration for 24 h. Thus, the data obtained from 0.25 to 24 h were employed to investigate the pharmacokinetic behaviour of D-Penicillamine in rat plasma. The main pharmacokinetic parameters were shown in Table 5. It was found that D-Penicillamine flowed into the circulation system and reached its peak concentration (C_{max}=2407.287±579.1245ng/mL) at T_{max}=2 h after an oral administration.

CONCLUSION

In this study, a simple, rapid, high sensitive and reproducible LC-MS/MS method has been developed and validated for quantification of D-Penicillamine in rat plasma. This LC-MS/MS method has significant advantages with good sensitivity (LLOQ-10 ng/mL) and adequate extraction recovery with shorter chromatographic run time. Then, simple and rapid protein precipitation method used exhibited acceptable extraction efficiency for D-Penicillamine and IS, and the matrix effects of the whole analyzing method were low enough to be negligible. The validated method has been successfully adopted to evaluate the pharmacokinetics parameters of D-Penicillamine in rat plasma.

Abbreviations

AUC : Area under the concentration-time curve; C_{max}: Maximum plasma concentration; HPLC : High Performance Liquid Chromatography; HQC: High-quality control; IS: Internal standard; K_2-EDTA : Di-potassium ethylene diamine tetra acetic acid; Kel: Elimination constant ; LC-MS/MS : Liquid chromatography coupled with mass spectroscopy; LLOQ : Lower limit of quantification; LQC : Low-quality control; MQC : Middle-quality control; MRM : Multiple reaction monitoring; QC : Quality control; RT : Retention time; RSD : Relative standard deviation; $T_{1/2}$: Half-life; T_{max}: Time to reach the maximum concentration; USFDA : US Food and Drug Administration; ULOQ : Upper limit of quantification; WHO : World Health Organizations.

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Authors' contributions
All the authors have contributed equally to this research work. All authors read and approved the final manuscript.

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Availability of data and materials
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Table 1. Precision (expressed as %RSD) and accuracy (%) of calibration curve of D-Penicillamine in rat plasma (n=3)

Penicillamine concentration(ng/mL)	Precision (%)	Accuracy (%)
10	3.8	103.9
20	0.5	99.8
50	2.5	98.2
100	1.3	97.6
300	0.7	98.8
750	2.7	101.5
1500	3.0	100.4
2800	1.7	105.0
3500	1.3	100.6

Table 2. Precision (expressed as %RSD) and accuracy (%) for D-Penicillamine in rat plasma

	Intra-day (n=6)		Inter-day (n=18)	
Added concentration	**Accuracy**	**Precision**	**Accuracy**	**Precision**
(ng/mL)	%	%	%	%
10	97.8	5.3	98.5	4.6
30	101.7	4.8	103.5	5.9
1375	103.9	10.3	104	8.0
2750	98.0	3.5	102.2	4.4

Table 3. Absolute recovery, extract efficiency, and matrix effects of D-Penicillamine in rat plasma (n=6)

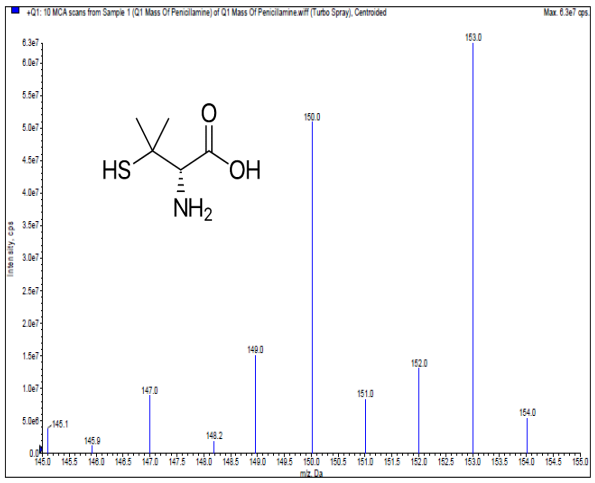
Added concentration	**Absolute recovery**	**Extract efficiency**	**Matrix effects**	**Type of effect**
ng/mL	**%**	**%**	**%**	
30	70.7	67.2	102.4	2.4% enhancement
1375	72.1	69.5	103.5	3.5% enhancement
2750	69.2	65.5	101.2	1.2% enhancement

Table 4. Stability of D-Penicillamine under various conditions (n=6)

Stability	**Storage condition**	**Level**	**RSD**	**Bias**
		ng/mL	**%**	**%**
Autosampler stability	at 4°C, 2 days	30	3.1	-1.1
		2750	3.4	-2.9
Short-term stability	at ambient temperature,	30	5.9	-5.8
	24 h	2750	2.6	1.1
Freeze-thaw stability	after 5th cycles	30	3.6	-4.5
	at -20°C to 25°C	2750	4.3	0.96
Long-term stability	at -20°C , 15 days	30	2.7	-4.5
		2750	4.6	0.3

Table 5. Pharmacokinetic parameters of D-Penicillamine after a single oral administration of 25 mg/kg in rats (n=6)

Parameters	**Unit**	**Value**
C_{max}	ng/mL	2407.287 ± 579.1245
AUC_{0-t}	ng.hr/mL	23462.637 ± 8250.8761
AUC_{0-inf}	ng.hr/mL	24757.059 ± 8846.7029
T_{max}	hr	2.0
$t_{1/2}$	hr	5.372
K_{el}	1/hr	0.131



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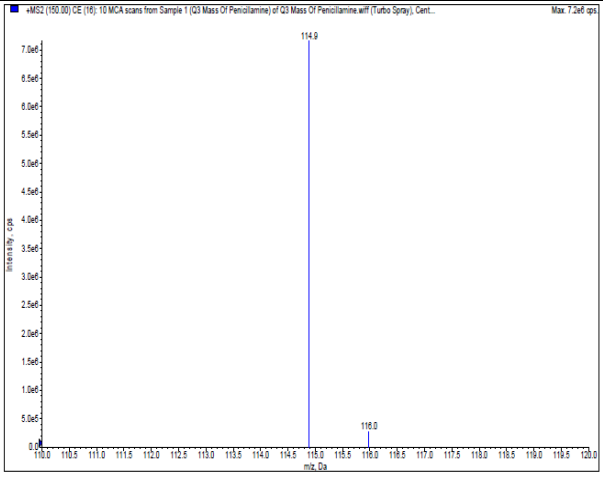
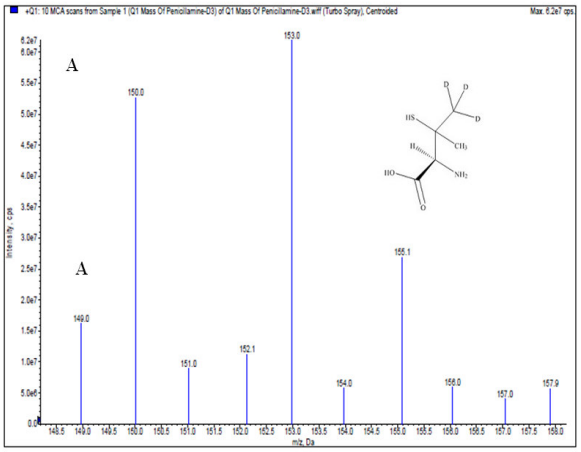


B

Fig.1.Parent ion spectra and structure of (A) D-Penicillamine (150.0) and (B) Product ion spectra of D-Penicillamine (114.9)



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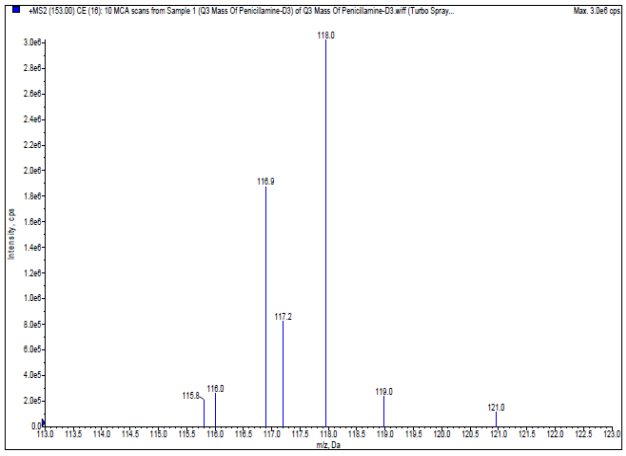

B

Fig. 2.Parent ion spectra and structure of (A) D-Penicillamine D3 (153.0) and (B) Product ion spectra of D-Penicillamine D3 (118.0).

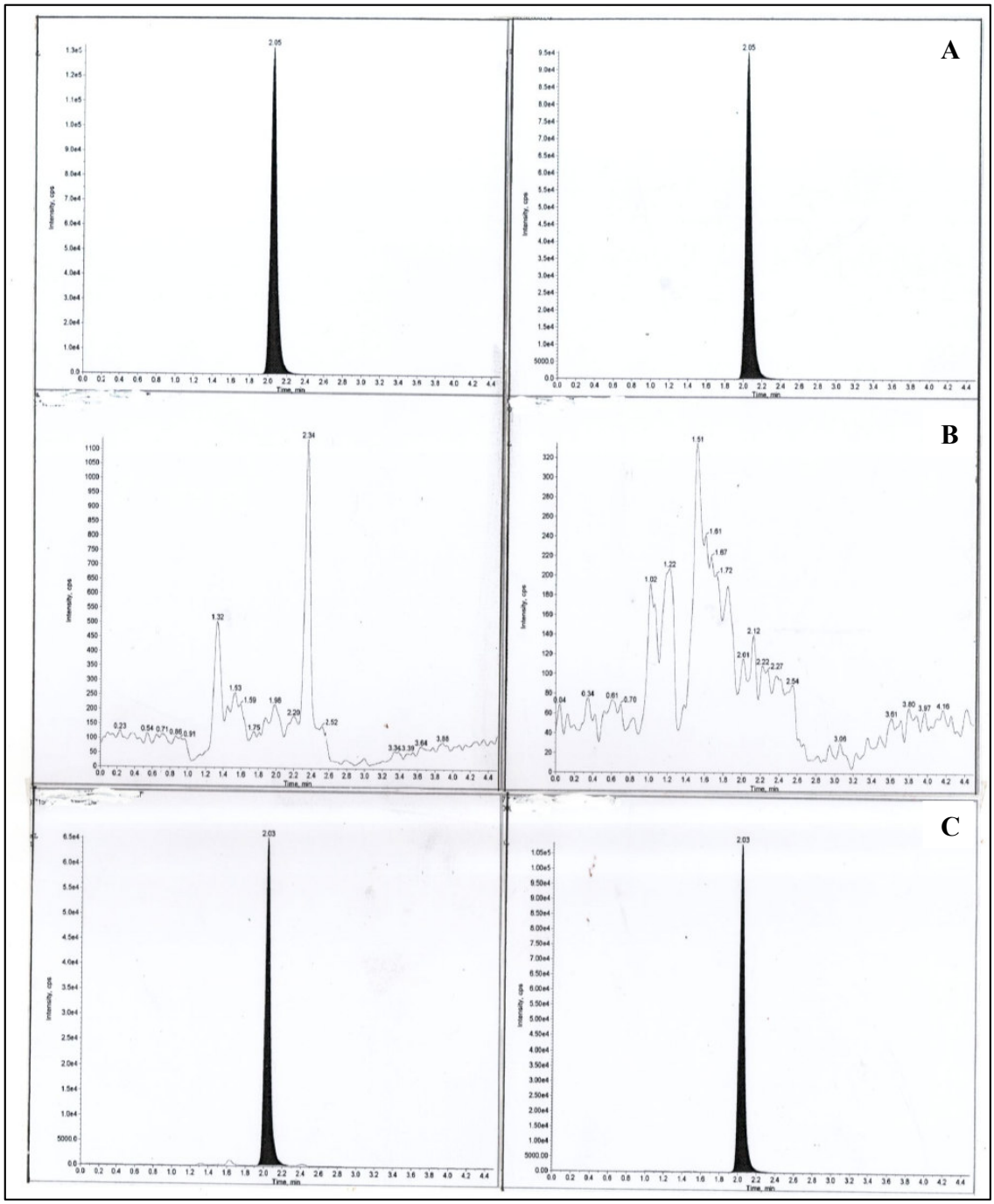

Fig.3.Representative chromatograms of D-Penicillamine and IS in (A) a blank plasma sample spiked with 1375 ng/mL D-Penicillamine and IS blank plasma samples, (B) a blank plasma samples and (C) a plasma sample at 0.5 h after an oral administration of 25 mg/kg D-Penicillamine. The retention time of D-Penicillamine and IS was 2.03 and 2.03 min, respectively.

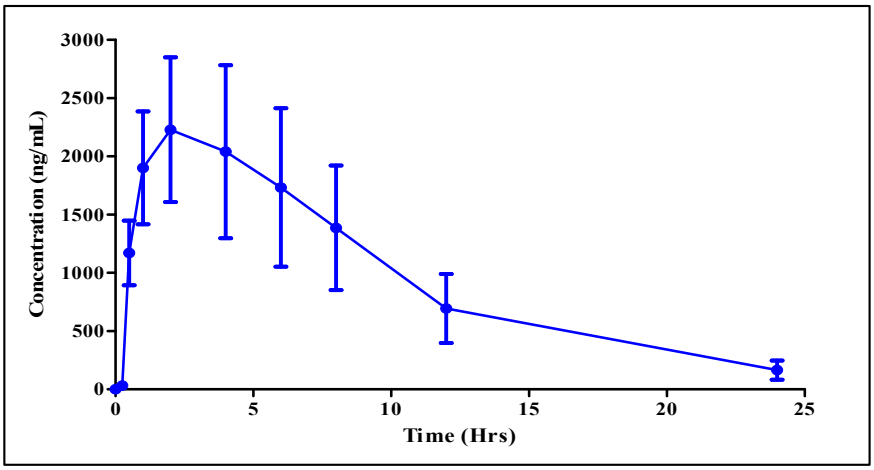

Fig.4.Mean plasma concentration–time profiles of D-Penicillamine in rats after a oral administration of 25 mg/kg. All data are expressed as the mean ± SD (n = 6).

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RESEARCH ARTICLE

Isorhamnetin Interacts with the SARS-CoV-2 Main Protease

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ABSTRACT

2019 Novel corona-virus (2019-nCoV) also referred to as severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2) emerged as a global risk and put the entire globe into unrest. Unavailability of specific drug against the virus is more imperative. This challenging situation requires development of biomolecules for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) has been released, thus can be used for fast *in silico* docking. This may result into identification of active biomolecules primarily phytochemical. *In silico* Molecular Docking revealed that the phytochemical, isorhamnetin effectively binds at the active pocket of the SARS-CoV-2 main protease.

Key words: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, isorhamnetin, phytochemicals.

INTRODUCTION

The pandemic situation caused due to the 2019-nCoV represents a severe public health calamity across the globe. The city of Wuhan was the epicentre where the outbreak of this human pathogen emerged, and resulted to human ailment, termed as COVID-19 [1, 2]. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The

effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that isorhamnetin, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of isorhamnetin to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:6052 corresponding to the isorhamnetin (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

It was found that isorhamnetin binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like isorhamnetin effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of isorhamnetin and eventually can be used in the pharmaceutical sector. Chemical synthesis of isorhamnetin can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current *in silico* molecular docking based study reveals that isorhamnetin can target the reported SARS-CoV-2 M^{pro}. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like isorhamnetin is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like isorhamnetin which can be employed for designing novel therapeutics.

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Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

GKP conceived the idea. GKP, RN, SKS, PKP, CR performed the experiments. GKP analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

The present study was financially supported by Centurion University of Technology and Management, Odisha, India.

Conflict of interest

The authors declare that they have no conflict of interest.

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12. Panigrahi Gagan Kumar, Sahoo Shraban Kumar and Satapathy Kunja Bihari. 2020. In silico Molecular Docking-Based Screening of Phytochemicals Targeted against Glypican-1. IJONS. 59(10):18708-18712.

Table 1.CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Isorhamnetin with the active site of SARS-CoV-2 main protease (M^{pro})

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:6052	Isorhamnetin	COVID-19 Main Protease	6M03	POSITIVE	14.23	16.37

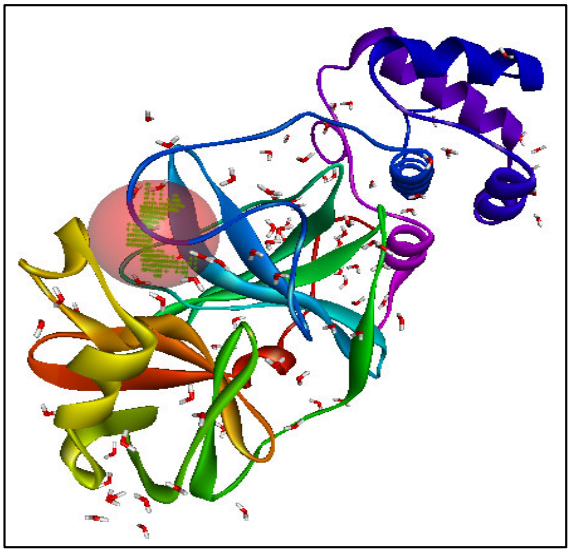

Fig. 1: 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

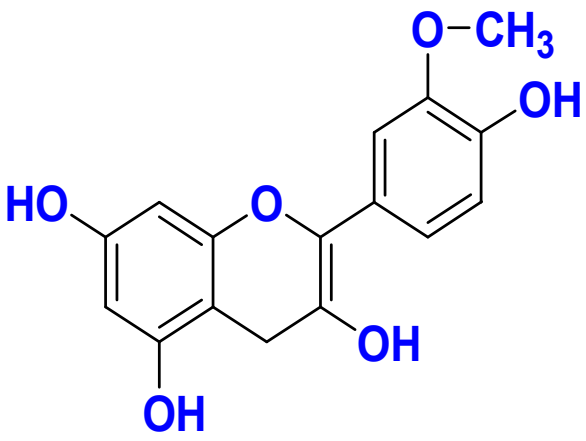

Fig. 2: Chemical structure of Isorhamnetin

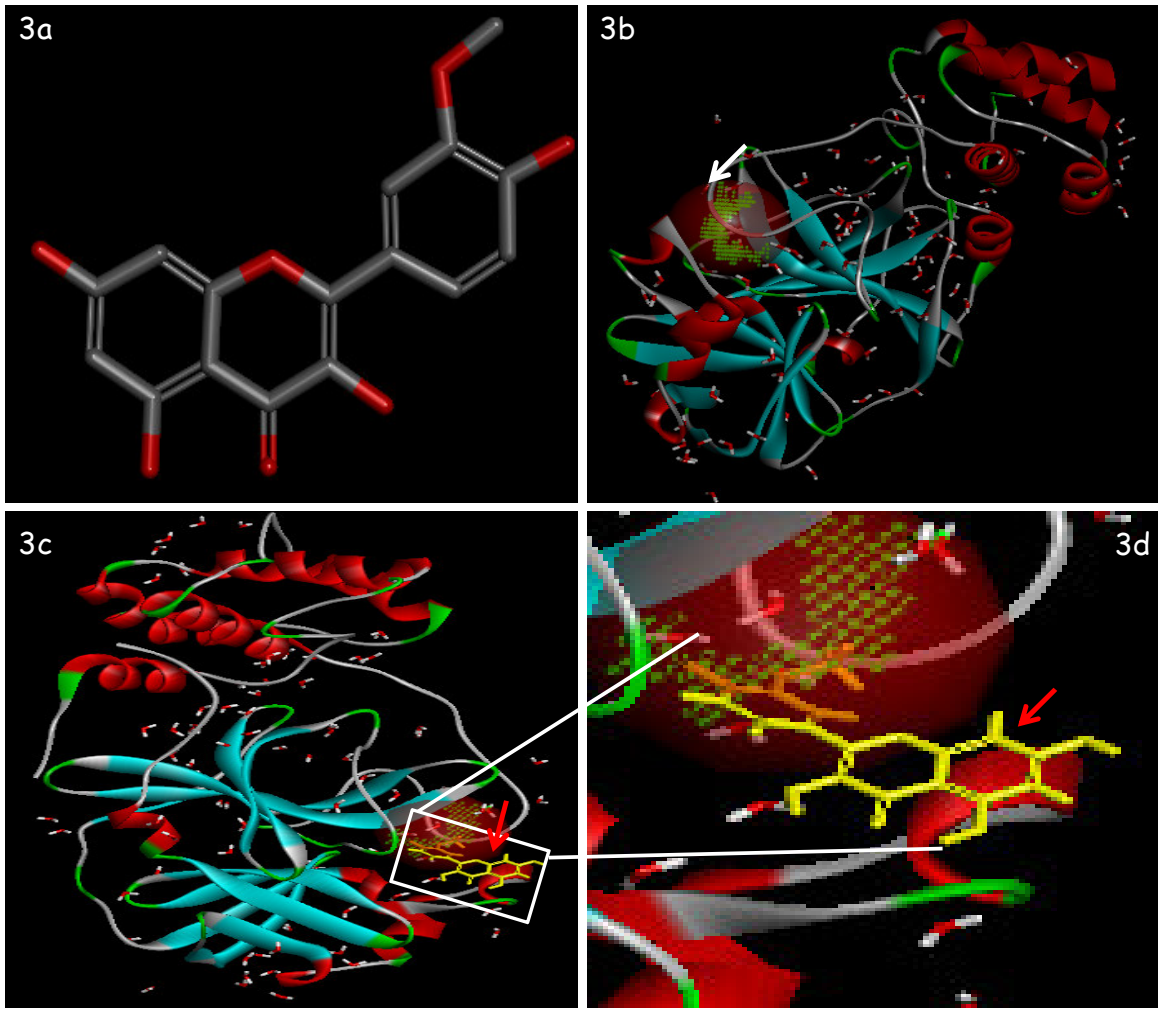

Fig. 3. The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Isorhamnetin. 3a: Phytochemical, Isorhamnetin. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Isorhamnetin. 3d: Magnified image showing the association of the Isorhamnetin with the M^{pro}. (The white colored arrow and the red colored arrow indicate the active site of the M^{pro} and binding of Isorhamnetin respectively).

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RESEARCH ARTICLE

In silico Molecular Docking Reveals the Interaction of Myricetin with the SARS-CoV-2 Main Protease

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ABSTRACT

Severe Acute Respiratory Syndrome Corona-virus 2 (SARS-CoV-2) also referred to as 2019 novel corona-virus (2019-nCoV) emerged as a global risk. Unavailability of specific drug against the virus is more imperative. This situation requires development of pharmacophores for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) can be used for fast *in silico* molecular docking. This may result into identification of active bio-molecules primarily phytochemicals. *In silico* Molecular Docking revealed that the phytochemical, myricetin effectively binds at the active pocket of the SARS-CoV-2 main protease.

Key words: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, molecular docking, myricetin.

INTRODUCTION

In the last weeks of December 2019, many hospitals of Wuhan, China reported unusual cases of severe pneumonia without a clear cause and they were not responding to any form of vaccines or medicines. The initial cases mostly had links to the seafood wholesale market of Wuhan region) [1, 2, 3, 4, 5]. It was called SARS-CoV-2 (causing the coronavirus disease 2019, COVID-19) and rapidly spread from animals (pangolins or bats as possible sources) to humans. The diffusion in humans was very rapid. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [6, 7]. An initial hypothesis was formulated that it was a new type of Corona Virus of zoonotic type. It infected hundreds of others locally which escalated to thousands and quickly stated spreading to the other Chinese provinces (which had international tourist hotspots) within few weeks (with the Chinese New Year further worsening the situation). The

situation became more critical when other cases started cropping up in other countries when after they had returned from China. By January 2020, it emerged as a global risk and was declared as a pandemic as the death toll started crossing the danger level. The word "Corona Virus" has been derived from the latin word "Corona" which means crown because of the characteristic appearance of the virus. The virus consists of core genetic material as RNA and surrounded by protein spikes. The latest corona virus is the 2019 Novel Corona Virus (Formally referred to as Severe Acute Respiratory Syndrome Corona Virus 2- SARS-COV-2) or informally known as Wuhan Corona Virus. It spreads through droplet infections like cough, sneeze or used towels, clothes etc. Its incubation period is 1-14 days. Some mild to serious symptoms are fever, cough, shortness of breath, pneumonia, kidney failure and death. There is currently no vaccine or antiviral treatment, though the research is still going on. Efforts are aimed at managing symptoms and supportive therapy. Some recommended preventive measures include Social Distancing, Monitoring self isolation and sanitizing hands. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [4, 8, 9]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [10]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [11, 12, 13]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Myricetin, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of myricetin to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:18152 corresponding to the Myricetin (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [14] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [15].

RESULTS AND DISCUSSION

It was found that myricetin binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like myricetin effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of myricetin and eventually can be used in the pharmaceutical sector. Chemical synthesis of myricetin can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current *in silico* molecular docking based study reveals that myricetin can target the reported SARS-CoV-2 M^{pro}. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like myricetin is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like myricetin which can be employed for designing novel therapeutics.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

GKP conceived the idea. GKP, PP, MD, SKS, CR, PKP performed the experiments. GKP and SKS analyzed the data. All authors have significant contribution in drafting the manuscript.

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Conflict of interest

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Table 1: CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Myricetin with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:18152	Myricetin	COVID-19 Main Protease	6M03	POSITIVE	20.39	22.01

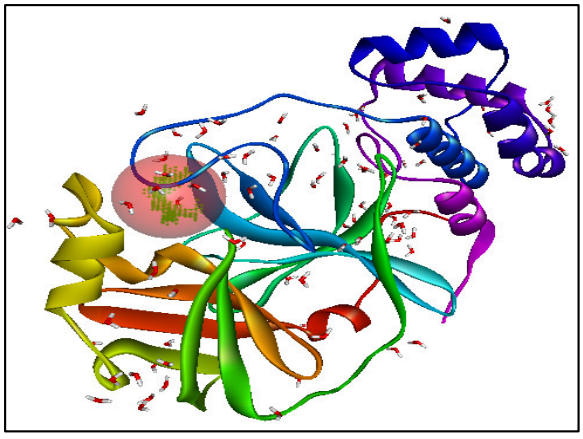

Fig. 1. 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

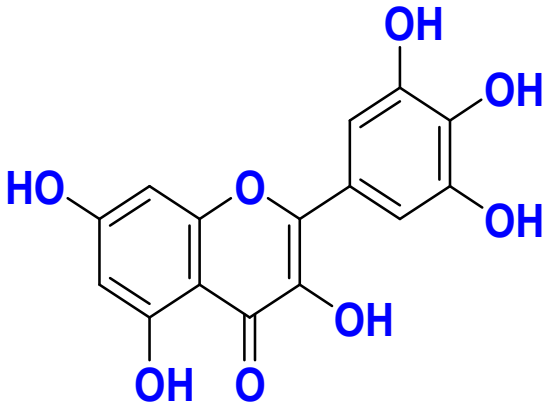

Fig. 2.Chemical structure of Myricetin

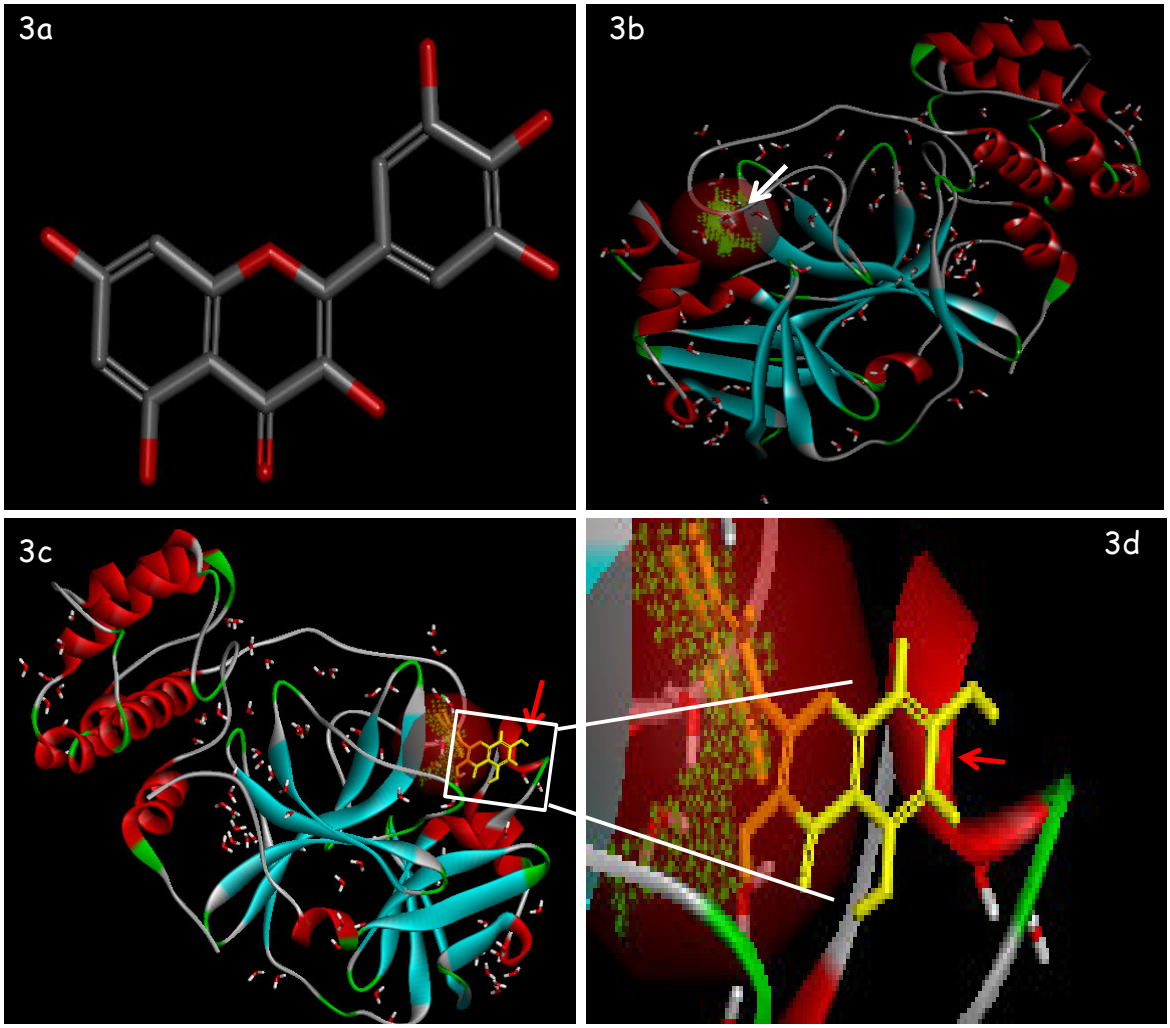

Fig. 3.The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Myricetin. 3a: Phytochemical, Myricetin. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Myricetin. 3d: Magnified image showing the association of the Myricetin with the M^{pro}. (The white colored arrow and the red colored arrow indicate the active site of the M^{pro} and binding of Myricetin respectively).

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RESEARCH ARTICLE

In silico Molecular Docking Reveals the Interaction of Caffeine with the SARS-CoV-2 Main Protease

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ABSTRACT

2019 Novel corona-virus (2019-nCoV) also referred to as severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2) emerged as a global risk and put the entire globe into unrest. Unavailability of specific drug against the virus is more imperative. This challenging situation requires development of biomolecules for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) has been released, thus can be used for fast *in silico* docking. This may result into identification of active biomolecules primarily phytochemical. *In silico* Molecular Docking revealed that the phytochemical, Caffeine effectively binds at the active pocket of the SARS-CoV-2 main protease.

Key words: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, phytochemicals.

INTRODUCTION

Corona Virus is a large family of virus whose causes vary from illness, common cold to severe other diseases such as MERS (Middle East Respiratory Syndrome) or SARS (Severe Acute Respiratory Syndrome). The latest addition to the Corona Virus is termed as Novel Corona Virus and also termed as "SARS-Covid-2" severe acute respiratory system. It is zoonotic disease meaning "transmitted between animals such as bats, chickens, rats etc. and humans" and spread through droplets. The pandemic situation caused due to the 2019-nCoV represents a severe public health calamity across the globe. The city of Wuhan was the epicentre where the outbreak of this human pathogen emerged, and resulted to human ailment, termed as COVID-19 [1, 2]. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing

to its fast rate of transmission within the humans [1, 5, 6]. Some symptoms of these diseases are fever, continuous sneezing whereas in some cases, severe pneumonia can be a symptom and in mild cases, shortness of breath and many more. Recently, there has been no vaccine for this disease though the research is still in progress. Some preventive measures to stop the widespread are recommended as follows: wearing masks, sanitizing hands, social distancing g and self quarantine for travelers.Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear.

The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Caffeine, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of Caffeine to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:27732 corresponding to the Caffeine (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

It was found that Caffeine, a common phytochemical specifically binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like Caffeine effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of Caffeine and eventually can be used in the pharmaceutical sector. Chemical synthesis of Caffeine can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current *in silico* molecular docking based study reveals that Caffeine can target the reported SARS-CoV-2 M^{pro}. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like Caffeine is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like Caffeine which can be employed for designing novel therapeutics.

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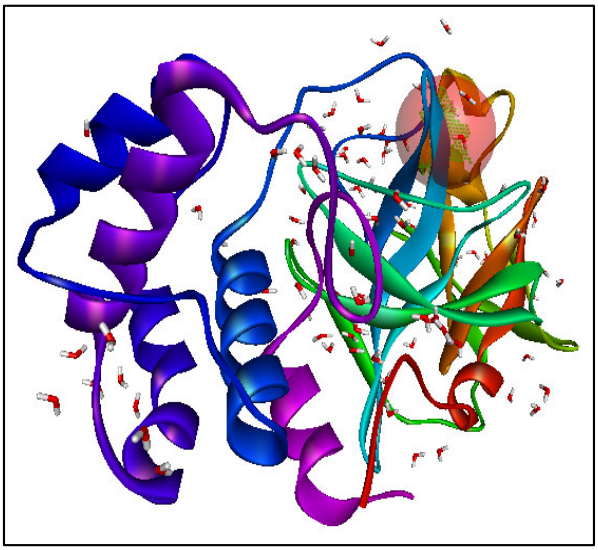
CHEBI:27732	Caffeine	COVID-19 Main Protease	6M03	POSITIVE	9.68	12.37



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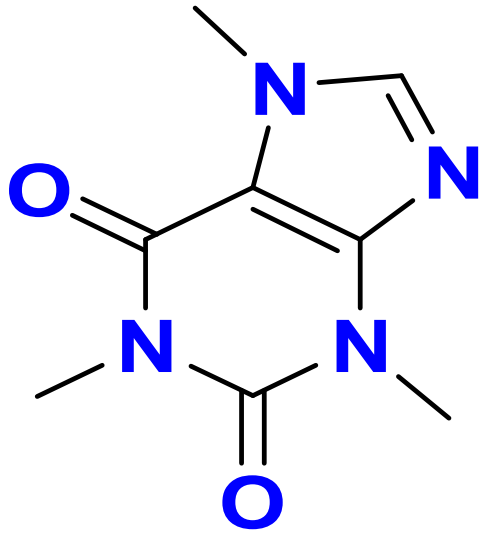

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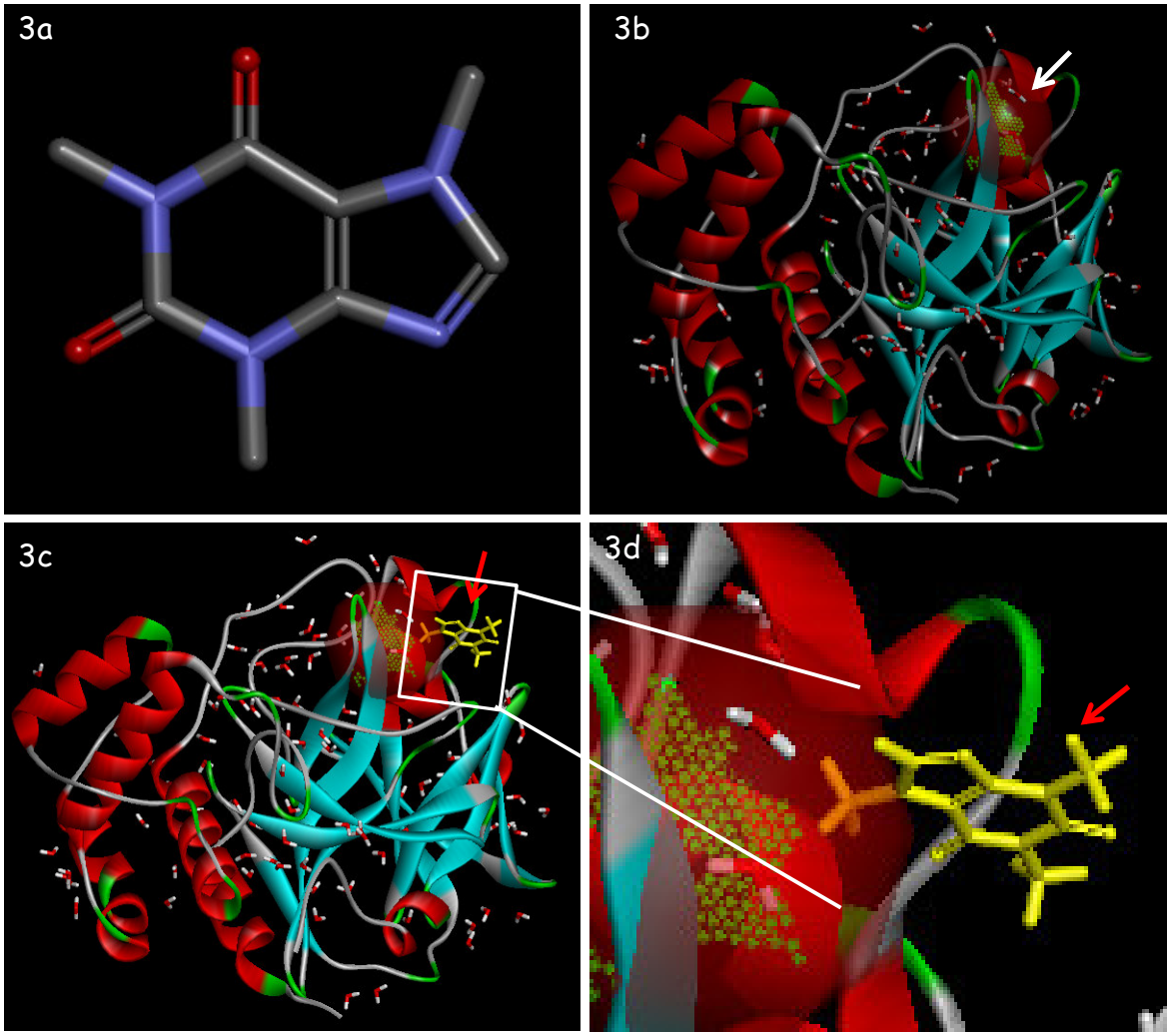

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RESEARCH ARTICLE

Salicylic Acid against the SARS-CoV-2 Main Protease

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ABSTRACT

2019 Novel corona-virus (2019-nCoV) also referred to as severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2) emerged as a global risk and put the entire globe into unrest. Unavailability of specific drug against the virus is more imperative. This challenging situation requires development of biomolecules for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) has been released, thus can be used for fast *in silico* docking. This may result into identification of active biomolecules primarily phytochemical. *In silico* Molecular Docking revealed that the phytochemical, salicylic acid effectively binds at the active pocket of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, phytochemicals, salicylic acid.

INTRODUCTION

The pandemic situation caused due to the 2019-nCoV represents a severe public health calamity across the globe. The city of Wuhan was the epicentre where the outbreak of this human pathogen emerged, and resulted to human ailment, termed as COVID-19 [1, 2]. The 2019 Novel coronavirus (2019-nCoV) which first originated from Wuhan, Hubei province, China has been declared pandemic for its significant threats to international health and the economy. 2019-nCoV is also referred to as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and is the seventh coronavirus that has been confirmed to infect humans. It has 50% genomic similarity to the Middle East respiratory syndrome coronavirus (MERS-CoV), 75-80% to the severe acute respiratory syndrome coronavirus (SARS-CoV) and 96% to a coronavirus found in bats. Specific drug against the virus is yet to be discovered. Development of bio molecules for proficient treatment against severe acute SARS-CoV-2 is challenging. 2019-nCoV

encodes at least 27 proteins, including 15 non-structural proteins, 4 structural proteins, and 8 auxiliary proteins. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins.

The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that salicylic acid, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of Salicylic acid to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:16914 corresponding to the salicylic acid (Fig.2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

It was found that salicylic acid; a common phytochemical specifically binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like Salicylic acid effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of salicylic acid and eventually can be used in the pharmaceutical sector. Chemical synthesis of salicylic acid can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current *in silico* molecular docking based study reveals that salicylic acid can target the reported SARS-CoV-2 M^{pro}. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like salicylic acid is commercially

available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like salicylic acid which can be employed for designing novel therapeutics.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

GKP conceived the idea. GKP, SJ, TD, SKS, PKP, CR performed the experiments. GKP analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

The present study was financially supported by Centurion University of Technology and Management, Odisha, India.

Conflict of interest

The authors declare that they have no conflict of interest.

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12. Panigrahi Gagan Kumar, Sahoo Shraban Kumar and Satapathy Kunja Bihari. 2020. In silico Molecular Docking-Based Screening of Phytochemicals Targeted against Glypican-1. IJONS. 59(10):18708-18712.

Table 1.CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Salicylic acid with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor			Interaction Status	
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:16914	Salicylic acid	COVID-19 Main Protease	6M03	POSITIVE	12.38	14.82

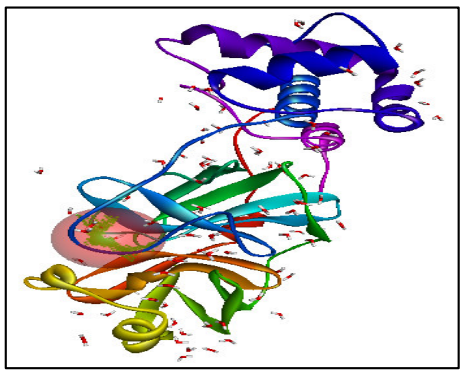

Fig. 1. 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

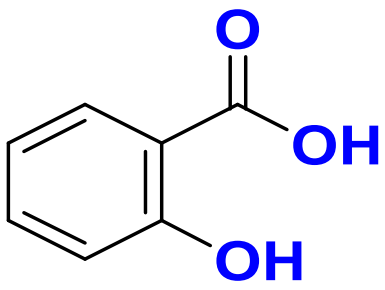

Fig. 2.Chemical structure of Salicylic acid

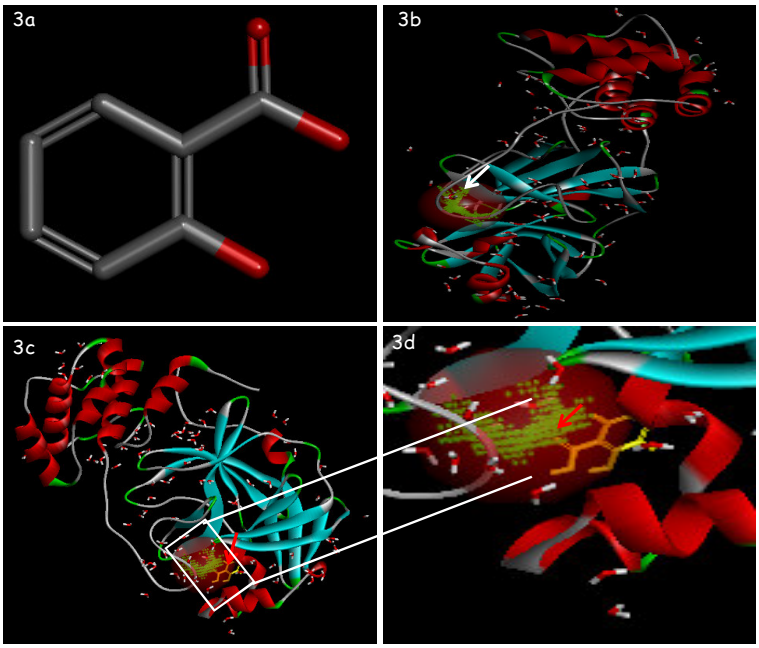

Fig. 3.The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Salicylic acid. 3a: Phytochemical, Salicylic acid. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Salicylic acid. 3d: Magnified image showing the association of the Salicylic acid with the M^{pro}. (The white colored arrow and the red colored arrow indicate the active site of the M^{pro} and binding of Salicylic acid respectively).

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RESEARCH ARTICLE

In silico Molecular Docking Reveals the Interaction of Ellagic acid with the SARS-CoV-2 Main Protease

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ABSTRACT

2019 Novel corona-virus (2019-nCoV) also referred to as severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2) emerged as a global risk and put the entire globe into unrest. Unavailability of specific drug against the virus is more imperative. This challenging situation requires development of biomolecules for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) has been released, thus can be used for fast *in silico* docking. This may result into identification of active bio-molecules primarily phytochemical. *In silico* Molecular Docking revealed that the phytochemical, ellagic acid effectively binds at the active pocket of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, phytochemicals, ellagic acid.

INTRODUCTION

In 2019-20, Corona Virus is an ongoing public health emergency of international health concern. It was caused by (SARS-Covid-2) Severe Acute Respiratory System Corona Virus 2 first identified in Wuhan, China. Within a short span of time, it spread globally and was declared as a pandemic by World Health Organization (WHO). The pandemic situation caused due to the 2019-nCoV represents a severe public health calamity across the globe. The city of Wuhan was the epicentre where the outbreak of this human pathogen emerged, and resulted to human ailment, termed as COVID-19 [1, 2]. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. Till date, more than 2.8 million infections have been confirmed in at least 185 countries and territories including some 2,00,000 deaths worldwide

have been confirmed. The virus primarily spreads between people in a similar way as influenza does via respiratory droplets produced during coughing or sneezing. The time between the exposure and symptoms onset is typically 5 days. But it may also range from 2-14 days. Symptoms may include fever, cough and shortness of breath whereas complications may include pneumonia and Acute Respiratory Distress Syndrome. The word "Corona" has been derived from a Latin word "Corona" meaning crown as the virus consists of RNA as core genetic material surrounded by crown like structures of protein. There is currently no vaccine available at the market whereas efforts on research of vaccine are ongoing. The pandemic outbreak cannot be come to stop but the escalation can be decreased by taking some preventive measures such as wearing of masks, Hand Sanitization, Social Distancing, Self monitoring, Self isolation for 14 days for people who suspect they are infected. Public Health Emergency of International Concern (PHEIC) was declared by the WHO owing to its fast rate of transmission within the humans [1, 5, 6]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins.

The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Ellagic acid, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of ellagic acid to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:4775 corresponding to the ellagic acid (Fig. 2)was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

It was found that ellagic acid binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like ellagic acid effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of ellagic acid and eventually can be used in the pharmaceutical sector. Chemical synthesis of ellagic acid can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current *in silico* molecular docking based study reveals that Ellagic acid can target the reported SARS-CoV-2 M^{pro}. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like ellagic acid is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like ellagic acid which can be employed for designing novel therapeutics.

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Author contribution statement

GKP conceived the idea. GKP, PP, MD, SKS, PKP performed the experiments. GKP and SKS analyzed the data. All authors have significant contribution in drafting the manuscript.

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Conflict of interest

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9. Lung Jrhau, Yu-Shih Lin, Yao-Hsu Yang, et al. 2020. The potential chemical structure of anti-SARS-CoV-2 RNA-dependent RNA polymerase. J Med Virol 0–1.
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Table 1: CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Ellagic acid with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:4775	Ellagic acid	COVID-19 Main Protease	6M03	POSITIVE	10.57	16.37

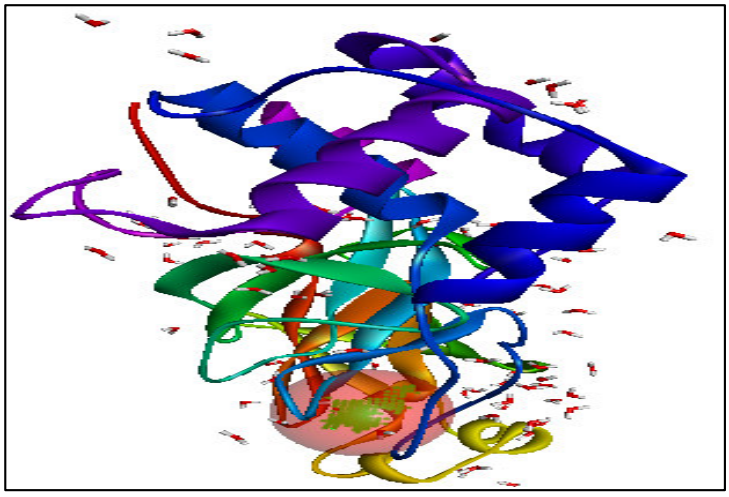

Fig. 1. 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

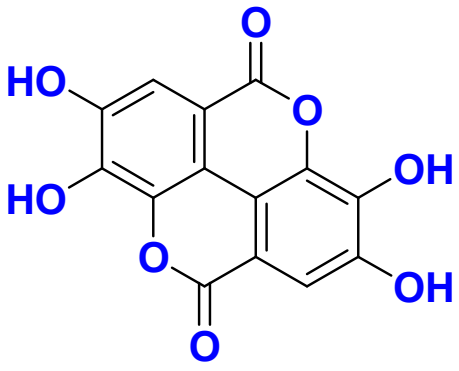

Fig. 2.Chemical structure of Ellagic acid

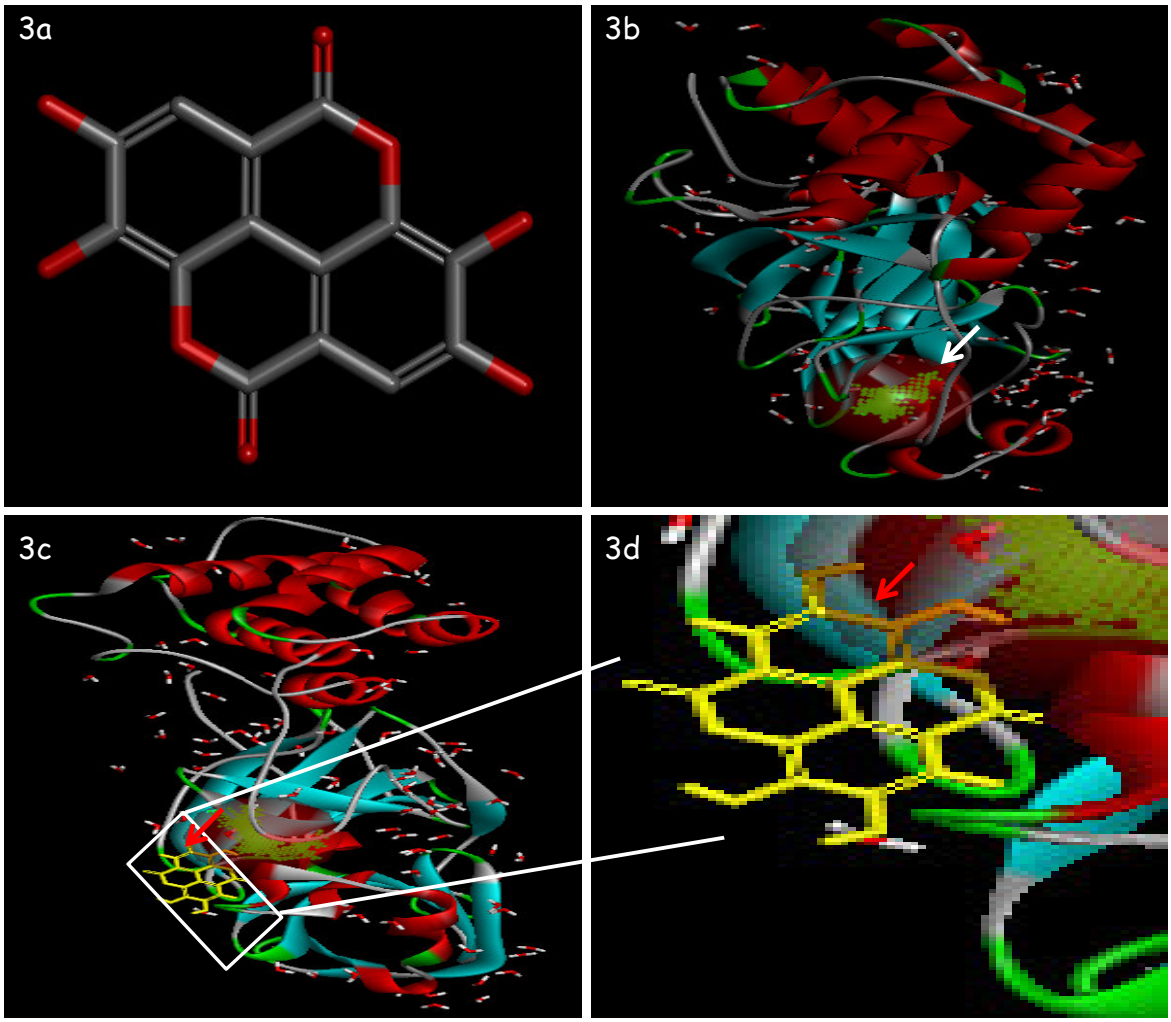

Fig. 3: The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Ellagic acid. 3a: Phytochemical, Ellagic acid. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Ellagic acid. 3d: Magnified image showing the association of the Ellagic acid with the M^{pro}. (The white colored arrow and the red colored arrow indicate the active site of the M^{pro} and binding of Ellagic acid respectively).

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RESEARCH ARTICLE

In silico Molecular Docking Reveals the Interaction of Genistein with the SARS-CoV-2 Main Protease

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ABSTRACT

Developing specific drug against the severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2) also termed as 2019 Novel corona-virus (2019-nCoV) is challenging. This situation requires development of bio-molecules for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) is available, thus can be used for fast *in silico* docking. This may result into identification of active bio-molecules primarily phytochemical. *In silico* Molecular Docking revealed that the phytochemical, genistein which belongs to isoflavone group effectively binds to the active pocket of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, molecular docking, phytochemicals.

INTRODUCTION

A new coronavirus, named SARS-CoV 2 was implicated on 7th January, 2020 in an alarming outbreak of like COVID-19, originated from Wuhan City, Hubei, China. It was first confirmed in Guangdong, China [1, 2]. On 15th February, 2020 more than 65,000 cases are reported. By 1st April, 2020 it became a pandemic with more than 850,000 infected and around 42,000 dead across 180 countries. Coronavirus is evolutionarily related with the Beta- coronavirus, which implicate with the severe acute respiratory syndrome (SARS), which is generally originated from Bats [3, 4]. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. The viral genome encodes for more than 20 proteins out of which SARS-CoV-2 main protease (M^{pro}) is one and the solved crystal structure revealing the three dimensional profile of M^{pro} provides strong ground for screening specific ligands [7]. M^{pro} and other known viral proteins are key features of the SARS-CoV-2 [8, 9, 10]. M^{pro} can be targeted to weaken the viral replications within the host cells. Here,

we report that Genistein, a phytochemical binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking. The phytochemicals are essentially the bioactive compounds. Further studies may reveal the effectiveness of Genistein as one of the COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:28088 corresponding to the Genistein (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [11, 12].

RESULTS AND DISCUSSION

It was found that Genistein, a common phytochemical specifically binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy (Table 1). Since, simple active biomolecule like Genistein effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of Genistein and eventually can be used in the pharmaceutical sector. Chemical synthesis of Genistein can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

Various clinical trials are under progress among which essentially antiviral and immunomodulatory drugs are taken into account. Presently there is no effective drug against SARS-CoV-2. WHO recommends social distancing as one of the preventive measures and also issued several guidelines in accordance with other national and international institutions like European Society of Intensive Care Medicine and Society of Critical Care Medicine. *In silico* molecular docking based study revealed that Genistein can target the reported SARS-CoV-2 M^{pro}. It would be tremendously significant being confirmed *in vivo*. Genistein is commercially available and pharmacophores developed from genistein may act against the M^{pro}.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

KBS and GKP conceived the idea. GKP, AP, PKP, SKS, CR performed the experiments. KBS and GKP analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

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Table 1: CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Genistein with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:28088	Genistein	COVID-19 Main Protease	6M03	POSITIVE	12.46	14.27

Fig. 1. 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

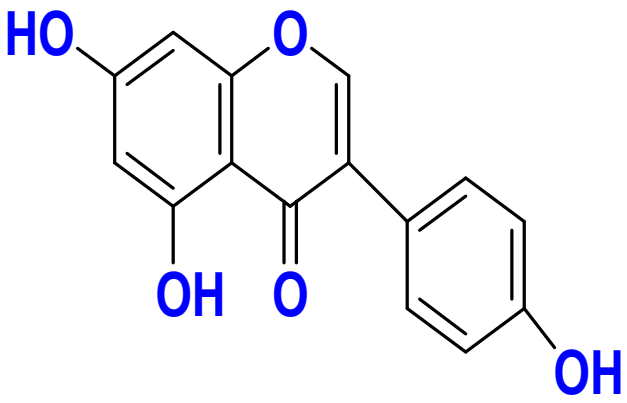

Fig. 2.Chemical structure of Genistein

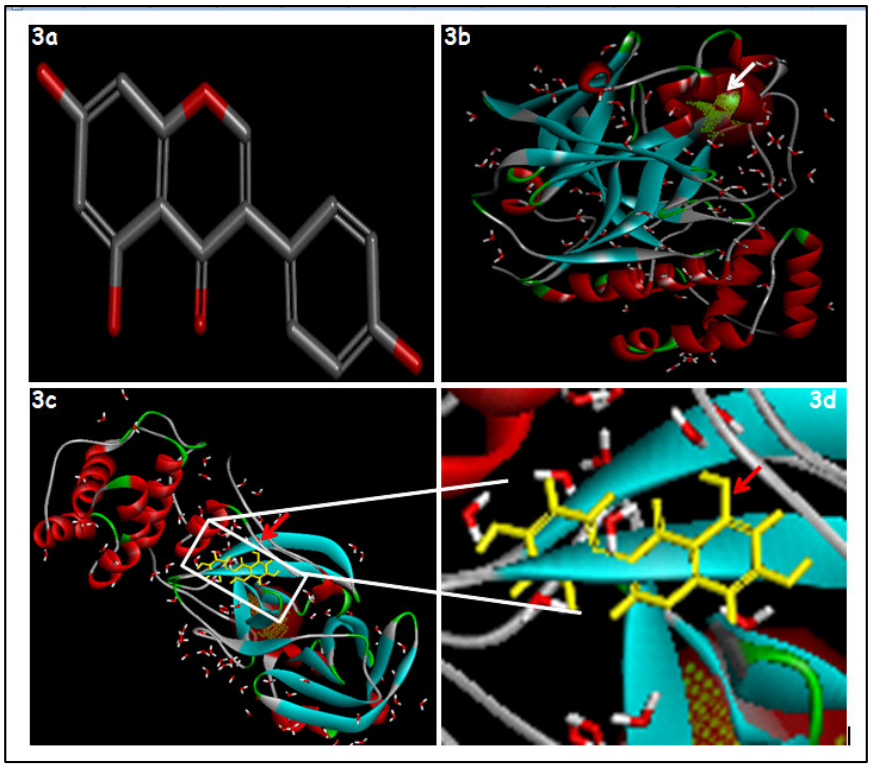

Fig. 3. The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Genistein. 3a: Phytochemical, Genistein. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Genistein. 3d: Magnified image showing the association of the Genistein with the M^{pro}. (The white coloured arrow and the red coloured arrow indicate the active site of the M^{pro} and binding of Genistein respectively).

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RESEARCH ARTICLE

Pelletierine, A Potent Phytochemical Against the SARS-Cov-2 Main Protease

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ABSTRACT

As the 2019 Novel corona-virus (2019-nCoV) also referred to as severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2) has been considered as the global epidemic by World Health Organisation, there is an urgent need to find out the medication against this pandemic. However, by using the available information, *in silico* docking models revealed many effective medications to inhibit the SARS-CoV-2. The three dimensional structure of the SARS-CoV-2 main protease (Mpro) is known, thus can be used for fast *in silico* docking. This may result into identification of phytochemical based pharmacophores. *In silico* Molecular Docking revealed that the phytochemical, Pelletierine effectively binds at the active pocket of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, molecular docking, phytochemicals.

INTRODUCTION

With the starting of 2020, a new virus has been causing the disease called Corona virus disease (COVID-19), which has engulfed the world within a very short period of time. The pandemic situation caused due to the 2019-nCoV represents a severe public health calamity across the globe. The city of Wuhan was the epicentre where the outbreak of this human pathogen emerged, and resulted to human ailment, termed as COVID-19 [1, 2]. It shows the symptoms like fever, cough, pneumonia, nausea and fatigue. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves

to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9,10]. The solved crystal structure of SARS-CoV-2 main protease can be considered as the first step as primary target molecule and possibly inhibitory ligands may be screened using *in silico* docking. Many phytochemicals can be used to detect the potentiality of some bioactive molecules. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Pelletierine, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of Pelletierine to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} was accessed from Protein Data Bank accession 6M03 (Fig. 1). The SDF accession CHEBI:7952 corresponding to the Pelletierine (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

It was found that Pelletierine, a common phytochemical specifically binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active biomolecule like Pelletierine effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of Pelletierine and eventually can be used in the pharmaceutical sector. Chemical synthesis of Pelletierine can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current *in silico* molecular docking based study reveals that Pelletierine can target the reported SARS-CoV-2 M^{pro}. The process of molecular docking has actively been proven to employ for the search of medication that are found in the approved bioactive compound database. The hit compounds reported here have that potential to inhibit the activity of SARS-CoV-2, but these don't hold the guarantee to perform any activity. However, this can build the groundwork for computational drug discovery to reduce transmission of SARS-CoV-2. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like Pelletierine is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemical like Pelletierine which can be employed for designing novel therapeutics. The use of this off-labelled medication might be proved as beneficial.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

KBS and GKP conceived the idea. GKP, SBN, PKP, SKS performed the experiments. KBS and GKP analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

The present study was financially supported by Centurion University of Technology and Management, Odisha, India.

Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1.CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Pelletierine with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:7952	Pelletierine	COVID-19 Main Protease	6M03	POSITIVE	9.37	14.67

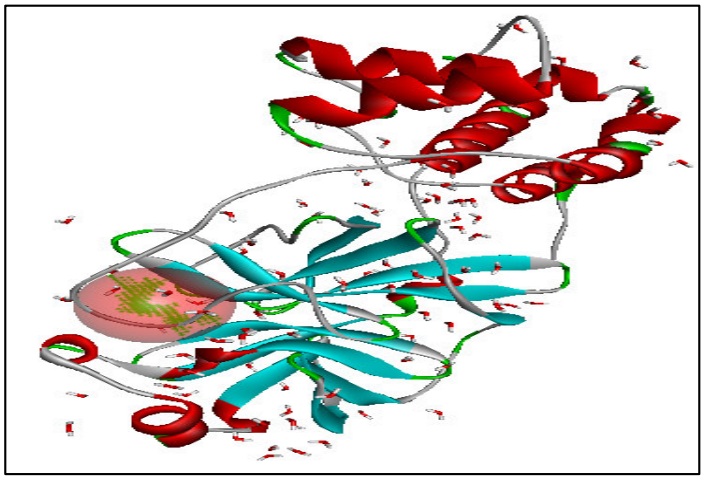

Fig. 1. 3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

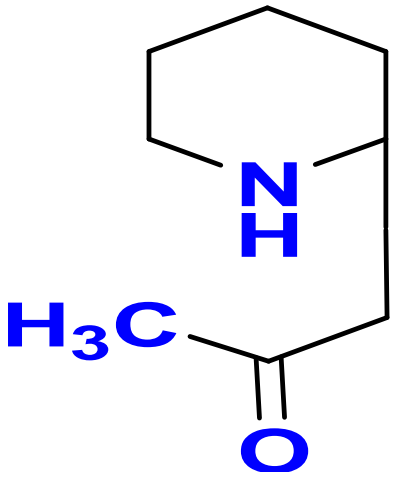

Fig. 2.Chemical structure of Pelletierine

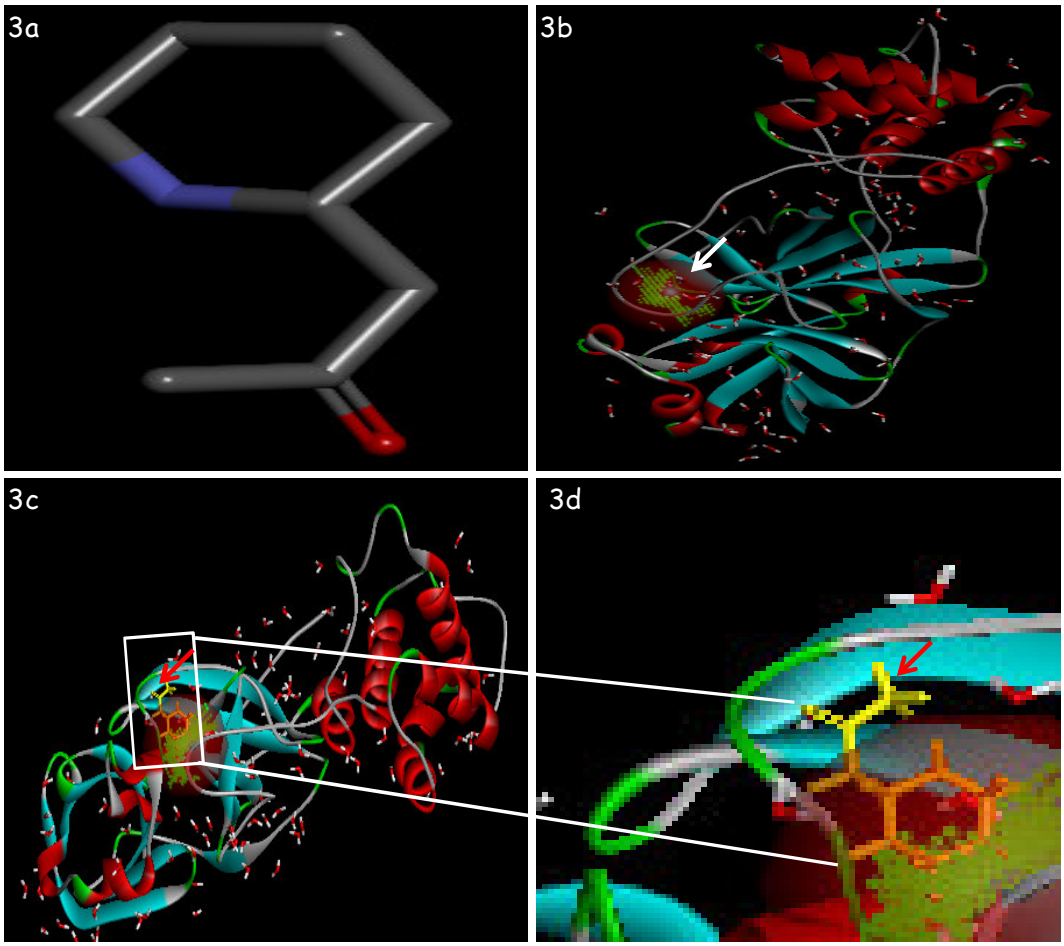

Fig. 3: The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Pelletierine. 3a: Phytochemical, Pelletierine. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Pelletierine. 3d: Magnified image showing the association of the Pelletierine with the M^{pro}. (The white coloured arrow and the red coloured arrow indicate the active site of the M^{pro} and binding of Pelletierine respectively).

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RESEARCH ARTICLE

Quercetin, a Potential Inhibitor of the SARS-CoV-2 Main Protease

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ABSTRACT

2019 Novel corona-virus (2019-nCoV) also referred to as severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2) emerged as a global risk and put the entire globe into unrest. Specific anti-viral drug against the virus is not yet available. This exigent situation requires development of pharmacophores for efficient treatment against severe acute SARS-CoV-2. The crystal structure of SARS-CoV-2 main protease (M^{pro}) can be used for fast *in silico* screening of potential candidate bio-molecules including phytochemicals. *In silico* Molecular Docking revealed that the phytochemical, Quercitin effectively binds to the active pocket of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, molecular docking, phytochemicals.

INTRODUCTION

The coronavirus outbreak came to light on December 31, 2019 when China informed the World Health Organisation of a cluster of cases of pneumonia of an unknown cause in Wuhan City in Hubei Province [1, 2]. The emerging 2019 Novel coronavirus (2019-nCoV) threatens public health. 2019-nCoV is also referred to as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Subsequently the disease spread to more Provinces in China, and to the rest of the world. Within no time it emerged as a global risk and was declared as pandemic. Specific drug against the virus is yet to be discovered. Development of biomolecules for proficient treatment against severe acute SARS-CoV-2 is challenging. The solved crystal structure of SARS-CoV-2 main protease (M^{pro}) can be used as one of the primary target molecule and possible inhibitory ligands may be screened using *in silico* docking. The current *in silico* molecular docking based study reveals that benzyl isothiocyanate and phenyl isothiocyanate can effectively target the SARS-CoV-2 M^{pro}. 2019-nCoV is a positive-single-stranded RNA virus belonging to the subfamily

Orthocoronavirinae of the Coronaviridae family with a crown-like appearance [3, 4]. Members of this large family of viruses can cause respiratory, enteric, hepatic, and neurological diseases in different animal species, including camels, cattle, cats, and bats. The SARS-CoV-2 belongs to the beta coronavirus category of the family Coronaviridae. It has round or elliptic and often pleomorphic form, and a diameter of approximately 60–140 nm. Like other CoVs, it is sensitive to ultraviolet rays and heat. Furthermore, these viruses can be effectively inactivated by lipid solvents including ether (75%), ethanol, chlorine-containing disinfectant, peroxyacetic acid and chloroform except for chlorhexidine.These viruses are responsible for about 5% to 10% of acute respiratory infections. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Among the structural elements of CoVs, there is the spike glycoproteins composed of two subunits (S1 and S2). In SARS-CoV-2, the S2 subunit containing a fusion peptide, a transmembrane domain, and cytoplasmic domain is highly conserved. Thus, it could be a target for antiviral (anti-S2) compounds. On the contrary, the spike receptor-binding domain presents only a 40% amino acid identity with other SARS-CoVs. Typical clinical symptoms of COVID-19 are fever, dry cough, and fatigue within 3-7 days of latency on average after infection.

This is relatively slower than severe acute respiratory syndrome (SARS), which was caused by SARS-CoV. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Quercitin, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of Quercitin to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} (Fig. 1) was accessed from Protein Data Bank accession 6M03. The SDF accession CHEBI:16243 corresponding to the Quercitin (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

It was found that Quercitin, a common phytochemical specifically binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like Quercitin effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite

possible to design pharmacophore molecules based on the structural and functional identity of Quercitin and eventually can be used in the pharmaceutical sector. Chemical synthesis of Quercitin can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

In the worst cases of 2019-nCoV, the virus not only attacks and destroys tissue in the lungs but also triggers an overreaction of the immune system, creating dangerous levels of inflammation. Many of these patients are left unable to breathe on their own, and some die in hospital intensive care units, or at home. Although much intensive effort is being made worldwide to develop drugs or vaccines for SARS-CoV-2, patients currently suffering from 2019-nCoV cannot expect benefits from them due to the slow development process of novel drugs or vaccines. Thus, a rapid drug application strategy that can be immediately applied to the patient is necessary. Currently, the only way to address this matter is to repurpose commercially available drugs for the pathogen in so-called "drug-repurposing". The current *in silico* molecular docking based study reveals that Quercitin can target the reported SARS-CoV-2 M^{pro}. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the 2019-nCoV proteins. Phytochemicals like Quercitin is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like Quercitin which can be employed for designing novel therapeutics.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

KBS and GKP conceived the idea. AS, GKP, PKP, SKS, CR performed the experiments. KBS and GKP analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

The present study was financially supported by Centurion University of Technology and Management, Odisha, India.

Conflict of interest

The authors declare that they have no conflict of interest.

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4. Wu F, Zhao S, Yu B, et al. 2020. A new coronavirus associated with human respiratory disease in China. Nature

579: 265-269.

5. Chan JFW, Yuan S, Kok KH, et al. 2020. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 395: 514-523.
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Table 1. CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Quercitin with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:16243	Quercetin	COVID-19 Main Protease	6M03	POSITIVE	19.35	22.17

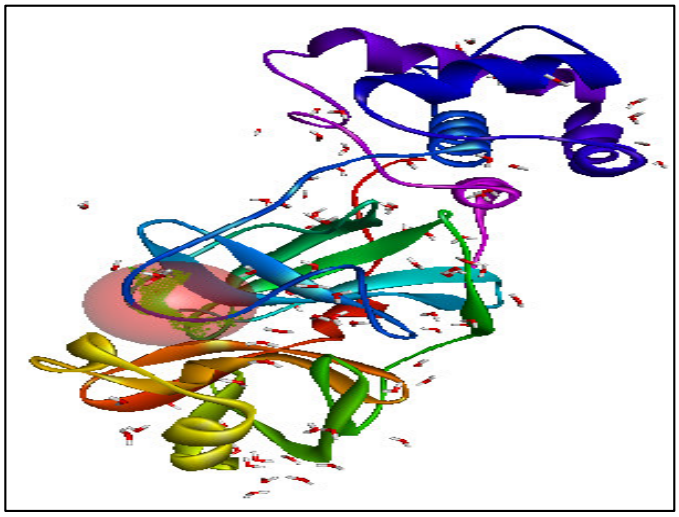

Fig. 1.3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

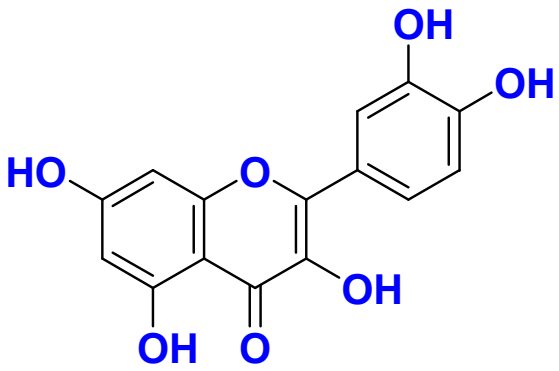

Fig. 2. Chemical structure of Quercitin

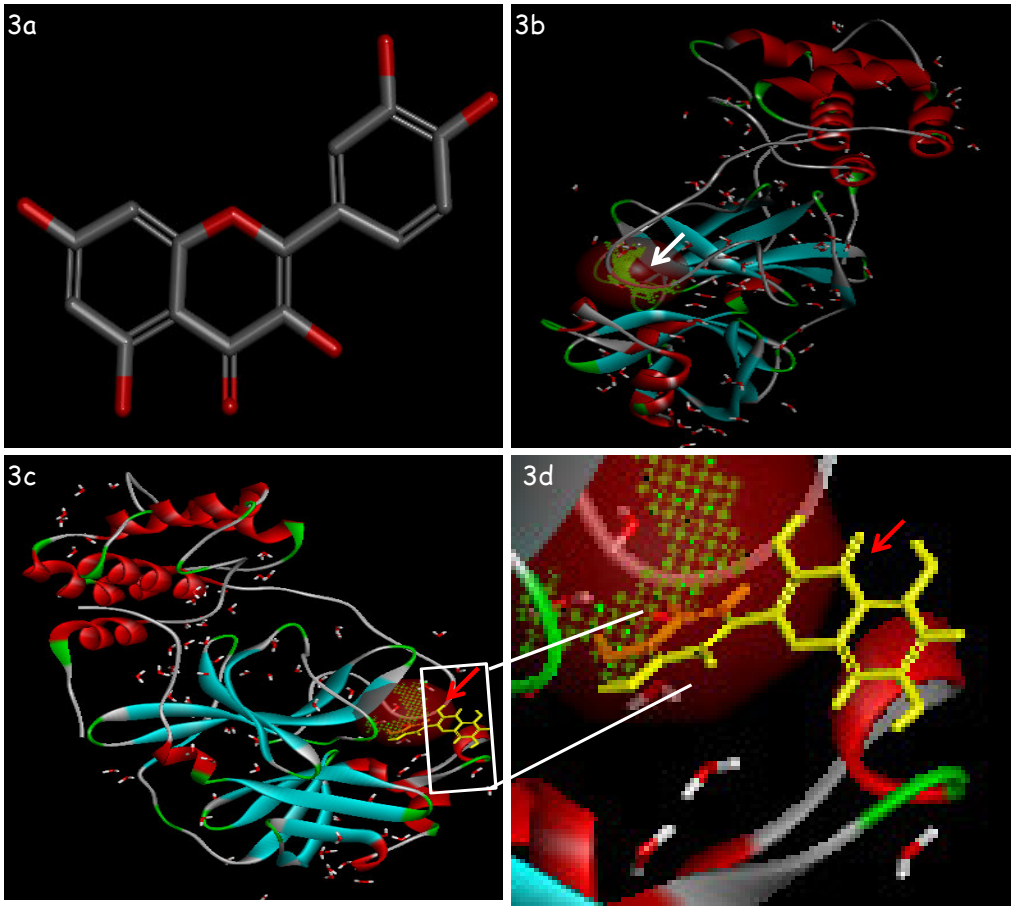

Fig. 3. The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Quercitin. 3a: Phytochemical, Quercitin. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Quercitin. 3d: Magnified image showing the association of the Quercitin with the M^{pro}. (The white coloured arrow and the red coloured arrow indicate the active site of the M^{pro} and binding of Quercitin respectively).

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RESEARCH ARTICLE

Theobromine May Inhibit the Activity of the SARS-CoV-2 Main Protease

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ABSTRACT

2019 Novel corona-virus (2019-nCoV), a large family of single-stranded RNA viruses, is very contagious and has quickly spread globally. It is also referred to as severe acute respiratory syndrome Corona-virus 2 (SARS-CoV-2). The absence of an effective treatment or a vaccine against this deadly virus is challenging. This demanding situation requires development of pharmacophores for treatment against severe acute SARS-CoV-2. The available structure of the SARS-CoV-2 main protease (M^{pro}) can be used for screening phytochemical based pharmacophores. *In silico* molecular docking revealed that the phytochemical, theobromine effectively binds with the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, pharmacophores, phytochemicals.

INTRODUCTION

The emerging 2019 Novel coronavirus (2019-nCoV) threatens public health. 2019-nCoV is also referred as a severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It was first reported on Dec 31, 2019 in Wuhan [1, 2], the largest metropolitan area in China and by Apr 24, 2020, it had spread to 185 countries and territories, with more than 27 lakh confirmed cases and over 1.9 lakh deaths. Within no time it was appeared as one of the global hazards and was declared as pandemic. The death toll from COVID-19 pandemic was highest in USA. In the last twenty years, several viral pandemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 to 2003, and H1N1 influenza in 2009, have been recorded. Most recently, the Middle East respiratory syndrome coronavirus (MERS-CoV) was first identified in Saudi Arabia in 2012. Coronavirus disease 2019 (COVID-19) is an infectious disease caused by SARS-CoV-2, a virus closely related to the SARS virus. For most people, COVID-19 infection will cause mild illness however, it can make some people very ill and, in some people, it can be fatal. Older people and those with pre-existing medical conditions (such as cardiovascular disease, chronic respiratory disease or diabetes)

are at risk for severe disease. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. It has a crown-like appearance due to presence of spike glycoproteins on the envelope. Before the identification of its causative agent, it was named as "pneumonia of unknown etiology". Specific drug against the virus is yet to be discovered. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) [1, 5, 6]. The solved crystal structure of SARS-CoV-2 main protease (M^{pro}) can be used as one of the primary target molecules and possible inhibitory ligands may be screened using *in silico* docking [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10].

Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Theobromine, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 main protease as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of Theobromine to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of M^{pro} (Fig. 1) was accessed from Protein Data Bank accession 6M03. The SDF accession CHEBI:28946 (Fig. 2) corresponding to the Theobromine was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the M^{pro} protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

It was found that Theobromine, a common phytochemical specifically binds to the active pocket of the SARS-CoV-2 M^{pro} (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like Theobromine effectively binds into the active pocket of the M^{pro} under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of Theobromine and eventually can be used in the pharmaceutical sector. Chemical synthesis of Theobromine can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The absence of an effective treatment or a vaccine combined with an exponential growth in infections from late February 2020, led many countries to implement non-pharmaceutical interventions such as 'stay-at-home' policies

(recommended or enforced) alongside other community and physical distancing measures such as the cancellation of mass gatherings, closure of educational institutions and public spaces. In order to find out any potential anti viral pharmacophores, fast *in silco* tools may be used to for the process of screening. The current *in silico* molecular docking based study reveals that Theobromine can target the reported SARS-CoV-2 M^{pro}. Essentially, this study makes an attempt to reveal simple phytochemicals like Theobromine which can be employed for designing novel therapeutics.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

KBS and GKP conceived the idea. GKP, MMA, PKP, SKS performed the experiments. KBS and GKP analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

The present study was financially supported by Centurion University of Technology and Management, Odisha, India.

Conflict of interest

The authors declare that they have no conflict of interest.

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12. Panigrahi Gagan Kumar, Sahoo Shraban Kumar and Satapathy Kunja Bihari. 2020. In silico Molecular Docking-Based Screening of Phytochemicals Targeted against Glypican-1. IJONS. 59(10): 18708-18712.

Table 1.CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Theobromine with the active site of SARS-CoV-2 main protease (M^{pro}).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:28946	Theobromine	COVID-19 Main Protease	6M03	POSITIVE	9.36	12.47

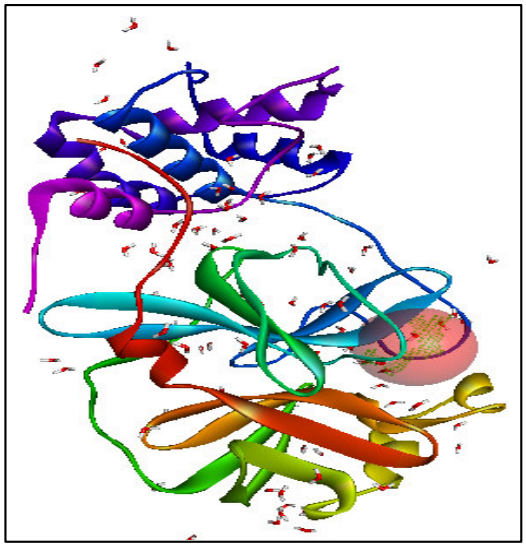

Fig. 1.3-D Structure of the SARS-CoV-2 M^{pro} showing the active site of the protein.

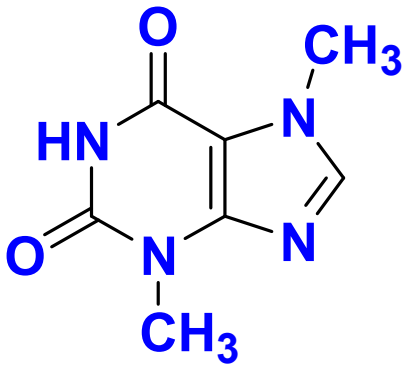

Fig. 2. Chemical structure of Theobromine

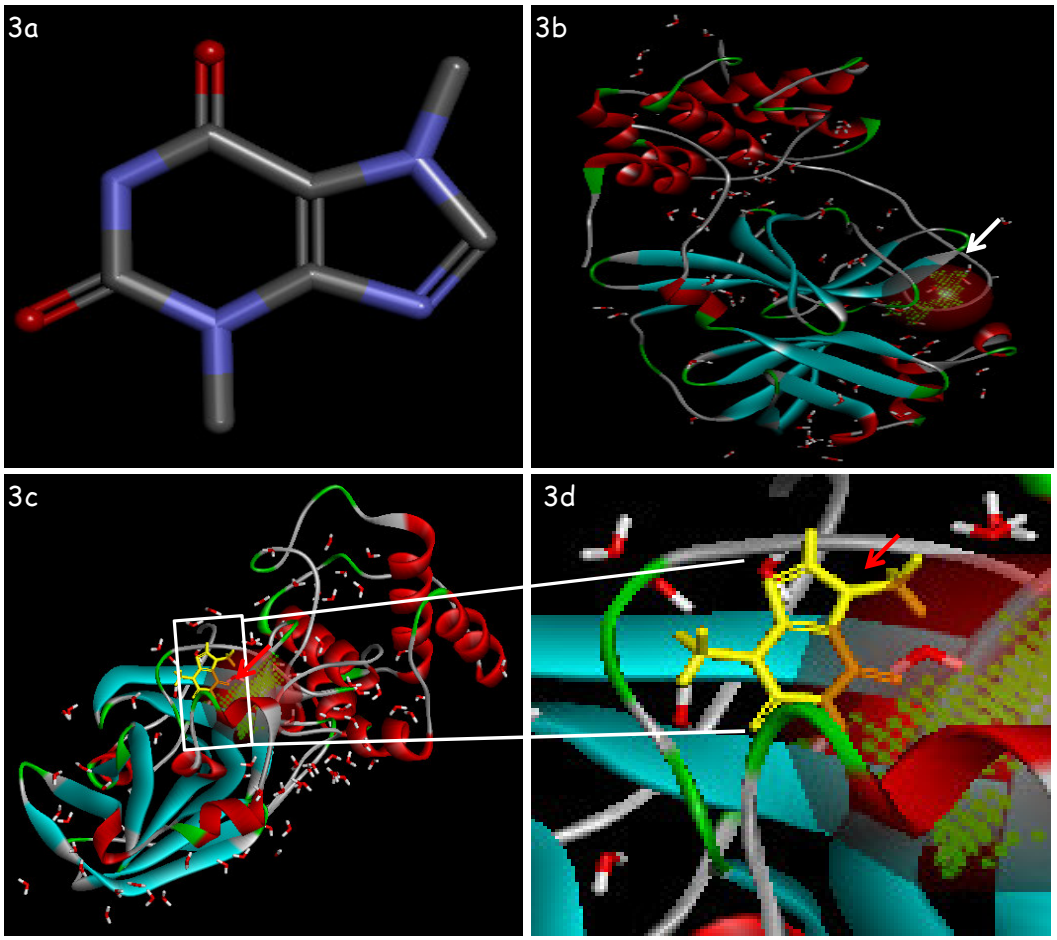

Fig. 3.The active site of the SARS-CoV-2 main protease (M^{pro}) interacts with Theobromine. 3a: Phytochemical, Theobromine. 3b: Free form of M^{pro}. 3c: M^{pro} associated with the ligand, Theobromine. 3d: Magnified image showing the association of the Theobromine with the M^{pro}. (The white colored arrow and the red colored arrow indicate the active site of the M^{pro} and binding of Theobromine respectively).

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RESEARCH ARTICLE

Quercitin against the RNA Dependent RNA polymerase of the SARS-CoV-2

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ABSTRACT

The 2019 Novel coronavirus (2019-nCoV) threatens public health. The 2019-nCoV is also referred to as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Specific drug against the virus is yet to be discovered. Development of pharmacophores for proficient treatment against severe acute SARS-CoV-2 is challenging. The solved cryo-EM structure of SARS-CoV-2 RNA dependent RNA polymerase (RdRp) can be used as one of the primary target molecule and possible inhibitory ligands may be screened using *in silico* molecular docking. Primarily phytochemicals can be screened to detect any potential bio active molecules. *In silico* molecular docking revealed that the phytochemical, Quercitin may effectively bind to the active site of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, phytochemicals, Quercitin.

INTRODUCTION

Coronavirus (COVID19) has become a critical public issue across the global since December 2019 which was suspected to be originated from a wet market in Wuhan, Hubei province, China [1, 2]. As of 24thof April 2020, more than 2.6 million cases have been reported in 213 countries and territories. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. It was named as a coronavirus because corona represents crown-like spikes on the outer surface of the virus. Coronaviruses are minute in size (65-125 nm in diameter), enveloped viruses with a single-standard RNA genome. COVID19 ranges from 26 to 32 kilobases which makes it the largest RNA virus. There are four subgroups of coronaviruses family alpha (α), beta (β), gamma (γ) and delta (δ) coronavirus. Among these types, only alpha and

beta CoV can infect humans. The coronavirus disease 19 (COVID-19) is a highly transmittable and pathogenic viral infection caused by sever acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Genomic analysis revealed that SARS-CoV-2 is phylogenetically related to severe acute respiratory syndrome-like (SARS-like) bate viruses, therefore bats could be the possible primary reservoir. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Spike protein (S) of SARS-CoV-2 interacts with human Angiotensin-converting enzyme 2 (ACE2). All coronaviruses contain specific genes in ORF1 downstream regions that encode proteins for viral replication, nucleocapsids and spikes formation. The glycoprotein spikes on the outer surface of coronaviruses are responsible for the attachment and entry of the virus to host cells. The receptor binding domains (RBD) is loosely attached among virus, therefore, the virus may infect multiple hosts. Other coronaviruses mostly recognize aminopeptidases or carbohydrates as a key receptor for entry to human cells while SARS-CoV and MERS-CoV recognize exopeptidases. The entry mechanism of a coronavirus depends upon cellular proteases which include, human airway trypsin-like protease (HAT), cathepsins and transmembrane proteases serine 2 (TMPRSS2) that split the spike protein and establish further penetration changes. MERS-coronavirus employs dipeptidyl peptidase 4 (DPP4), while HCoV-NL63 and SARS-coronavirus require angiotensin-converting enzyme 2 (ACE2) as a key receptor.

SARS-CoV-2 possesses the typical coronavirus structure with spike protein and also expressed other polyproteins, nucleoproteins, and membrane proteins, such as RNA polymerases, 3-chymotrypsin-like proteases, papain-like protease, helical, glycoproteins, and accessory proteins. The spike protein of SARS-CoV-2 contains a 3-D structure in the RBD region to maintain the van der waals forces. The 394 glutamine residue in the RBD region of SARS-CoV-2 is recognized by the critical lysine 31 residue on the human ACE2 receptor. COVID19 causes respiratory diseases in human, from the common cold to more rare and serious diseases such as the severe Acute Respiratory Syndrome (SARS) and the Middle East respiratory Syndrome (MERS), both of which have high mortality rates and were detected for the first time in 2003 and 2012, respectively. According to the WHO, this contamination is spreading with human to human contact, droplets, and fomites. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7].

SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins including RNA dependent RNA Polymerase (RdRp) are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Quercitin, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 RdRp as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of quercitin to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of RdRp was accessed from Protein Data Bank accession 6VYO (Fig. 1). The SDF accession CHEBI:16243 corresponding to the Quercitin (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the RdRp protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

Structure-based virtual screening refers to in silico identification of potential chemical molecules out of large number of compound libraries, which have high affinity to proteins of known structure, based on the binding of the small molecule with the protein binding pocket. It was found that quercitin binds to the active pocket of the SARS-CoV-2 RdRp (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like quercitin effectively binds into the active pocket of the RdRp under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of quercitin and eventually can be used in the pharmaceutical sector. Chemical synthesis of quercitin can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

Phytochemicals are produced by plants as secondary metabolites to protect them from predators. Some phytochemicals have been used as poisons and other as traditional medicine. This work is mainly focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-19. The current *in silico* molecular docking based study reveals that quercitin can target the reported SARS-CoV-2 RdRp. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like quercitin is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like quercitin which can be employed for designing novel therapeutics.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

GKP conceived the idea. GKP, SP, PKP, SKS, CR performed the experiments. GKP and CR analyzed the data. All authors have significant contribution in drafting the manuscript.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1: CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Quercitin with the active site of SARS-CoV-2 RNA dependent RNA polymerase (RdRp).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:16243	Quercetin	RNA-dependent RNA polymerase	6VYO	POSITIVE	10.57	14.6

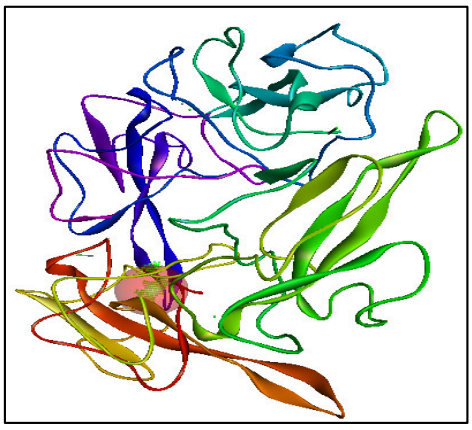

Fig. 1. 3-D Structure of the SARS-CoV-2 RdRp showing the active site of the protein.

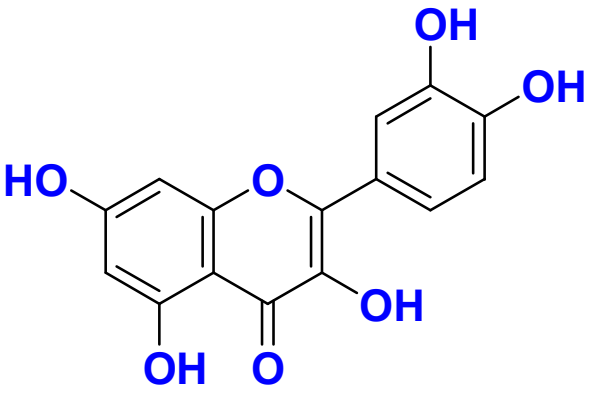

Fig. 2.Chemical structure of Quercitin

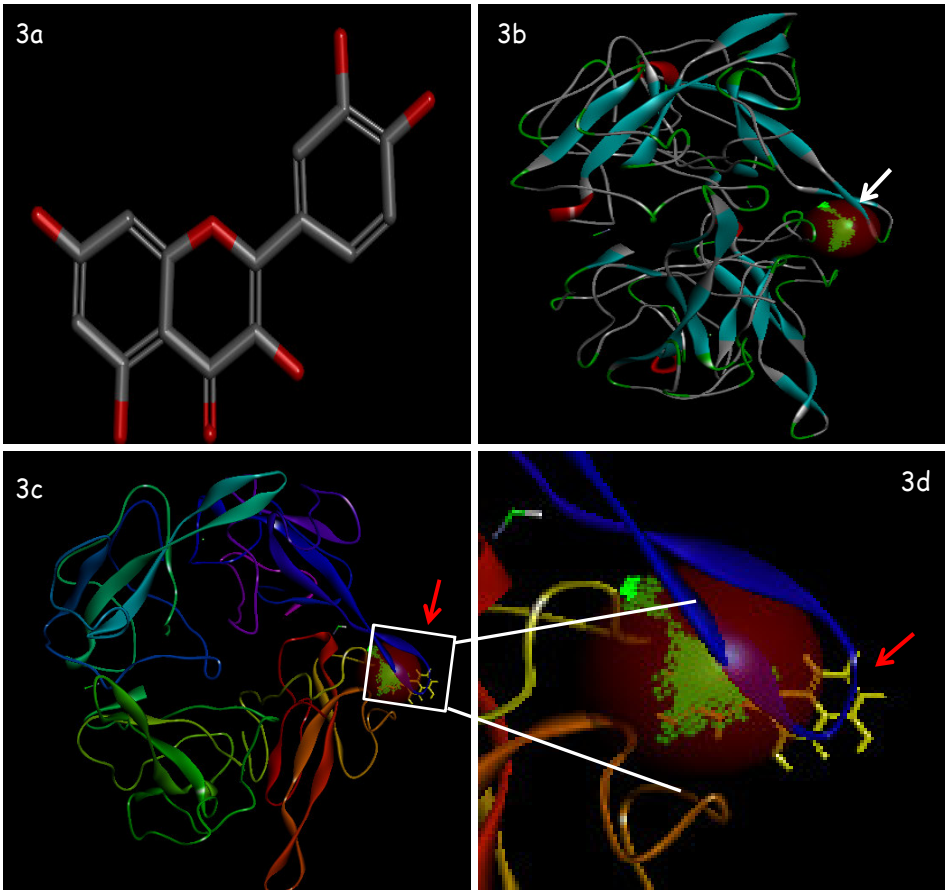

Fig. 3.The active site of the SARS-CoV-2 RdRp with Quercitin. 3a: Phytochemical, Quercitin. 3b: Free form of RdRp. 3c: RdRp associated with the ligand, Quercitin. 3d: Magnified image showing the association of the Quercitin with the RdRp. (The white colored arrow and the red colored arrow indicate the active site of the RdRp and binding of Quercitin respectively).

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RESEARCH ARTICLE

Glutathione may Inhibit the Activity of the RNA Dependent RNA polymerase of the SARS-CoV-2

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ABSTRACT

Specific drug against the emerging 2019 Novel coronavirus (2019-nCoV) also referred to as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is not yet revealed. Development of specific bio-molecules for proficient treatment against severe acute SARS-CoV-2 is demanding. The solved cryo-EM structure of SARS-CoV-2 RNA dependent RNA polymerase (RdRp) may be used as one of the primary target molecule and screening for specific ligands may be done using *in silico* molecular docking. Primarily phytochemical-based pharmacophores can be screened to detect any potential bio active molecules. *In silico* molecular docking revealed that the phytochemical, Glutathione may effectively bind to the active site of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, phytochemicals, Glutathione.

INTRODUCTION

Coronavirus has become a critical public issue across the global since December 2019 which was suspected to be originated from a wet market in Wuhan, Hubei province, China [1, 2]. As of 24thof April 2020, more than 2.6 million cases have been reported in 213 countries and territories. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. CoV ranges from 26 to 32 kilo-bases which make it the largest RNA virus. CoVs are of four kinds which are alpha, beta, delta, and gamma. Among these types, only alpha and beta CoV can infect humans. In 2003 Severe Acute respiratory syndrome CoV (SARS-CoV) and 2012 Middle East respiratory syndrome CoV (MERS-CoV) caused the global epidemic. From 2003 to 2004 SARS-CoV infected 8096 people in 29 countries where 774 people died. MERS-CoV was

even deadly and took 858 lives out of 2494 people since 2012. SARS-CoV-2 belongs to the Beta coronavirus group which is enveloped single-stranded positive sense RNA genome. Coronavirus has able to infect herbs, animals and humans. Bats are being suspected for the SARS-CoV-2 host but there were likely to be involvement of some intermediate host in bat-human transmission because SARS-CoV and MERS-CoV were transmitted from bats to palm civets or dromedary camels, and finally to humans, there should be another animal representing an intermediate host between bat and human. Based on genome sequencing, 2019-nCoV is about89% identical to bat SARS-like-CoVXC21, 82% identical to human SARS-CoV and about 50% to MERS-CoV. Genomic analysis revealed that SARS-CoV-2 is phylogenetically related to severe acute respiratory syndrome-like (SARS-like) bate viruses; therefore bats could be the possible primary reservoir. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins including RNA dependent RNA Polymerase (RdRp) are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10].

Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Glutathione, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 RdRp as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of glutathione to be used as COVID-19 therapeutics.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of RdRp was accessed from Protein Data Bank accession 6VYO (Fig. 1). The SDF accession CHEBI:16856 corresponding to the Glutathione (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the RdRp protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

Structure-based virtual screening refers to in silico identification of potential chemical molecules out of large number of compound libraries, which have high affinity to proteins of known structure, based on the binding of the small molecule with the protein binding pocket. It was found that glutathione binds to the active pocket of the SARS-CoV-2 RdRp (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like glutathione effectively binds into the active pocket of the RdRp under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of glutathione and

eventually can be used in the pharmaceutical sector. Chemical synthesis of glutathione can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

Phytochemicals are produced by plants as secondary metabolites to protect them from predators. Some phytochemicals have been used as poisons and other as traditional medicine. This work is mainly focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-19. The current *in silico* molecular docking based study reveals that glutathione can target the reported SARS-CoV-2 RdRp. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like glutathione is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like glutathione which can be employed for designing novel therapeutics.

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Author contribution statement

GKP conceived the idea. GKP, PKP, SP, SKS, CR performed the experiments. GKP and SKS analyzed the data. All authors have significant contribution in drafting the manuscript.

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SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:16856	Glutathione	RNA-dependent RNA polymerase	6VYO	POSITIVE	16.4	7.76

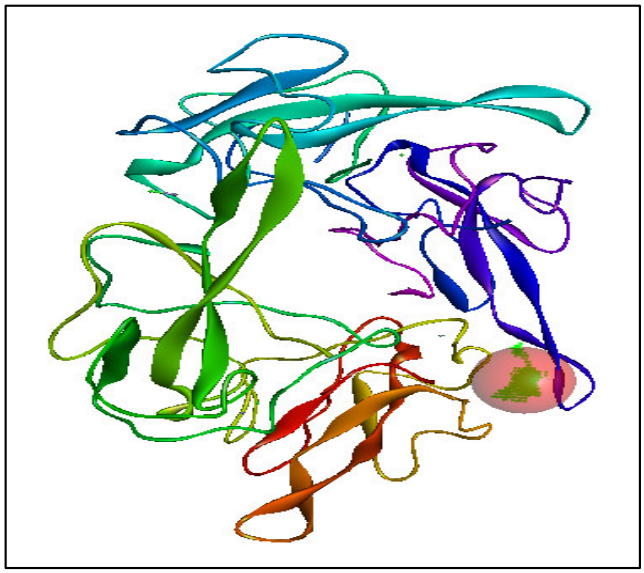

Fig. 1. 3-D Structure of the SARS-CoV-2 RdRp showing the active site of the protein.

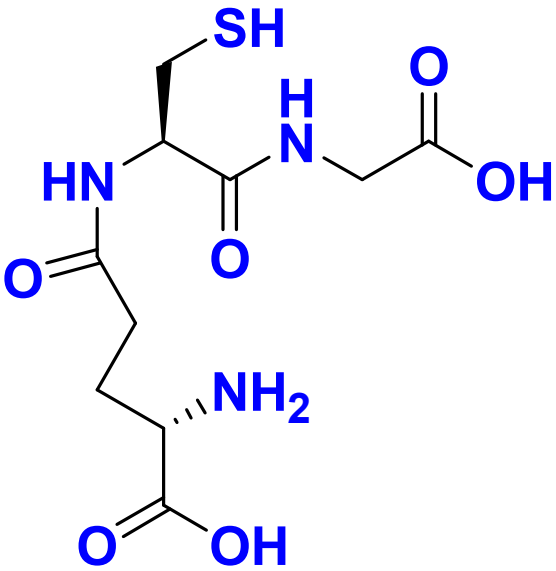

Fig.2.Chemical structure of Glutathione.

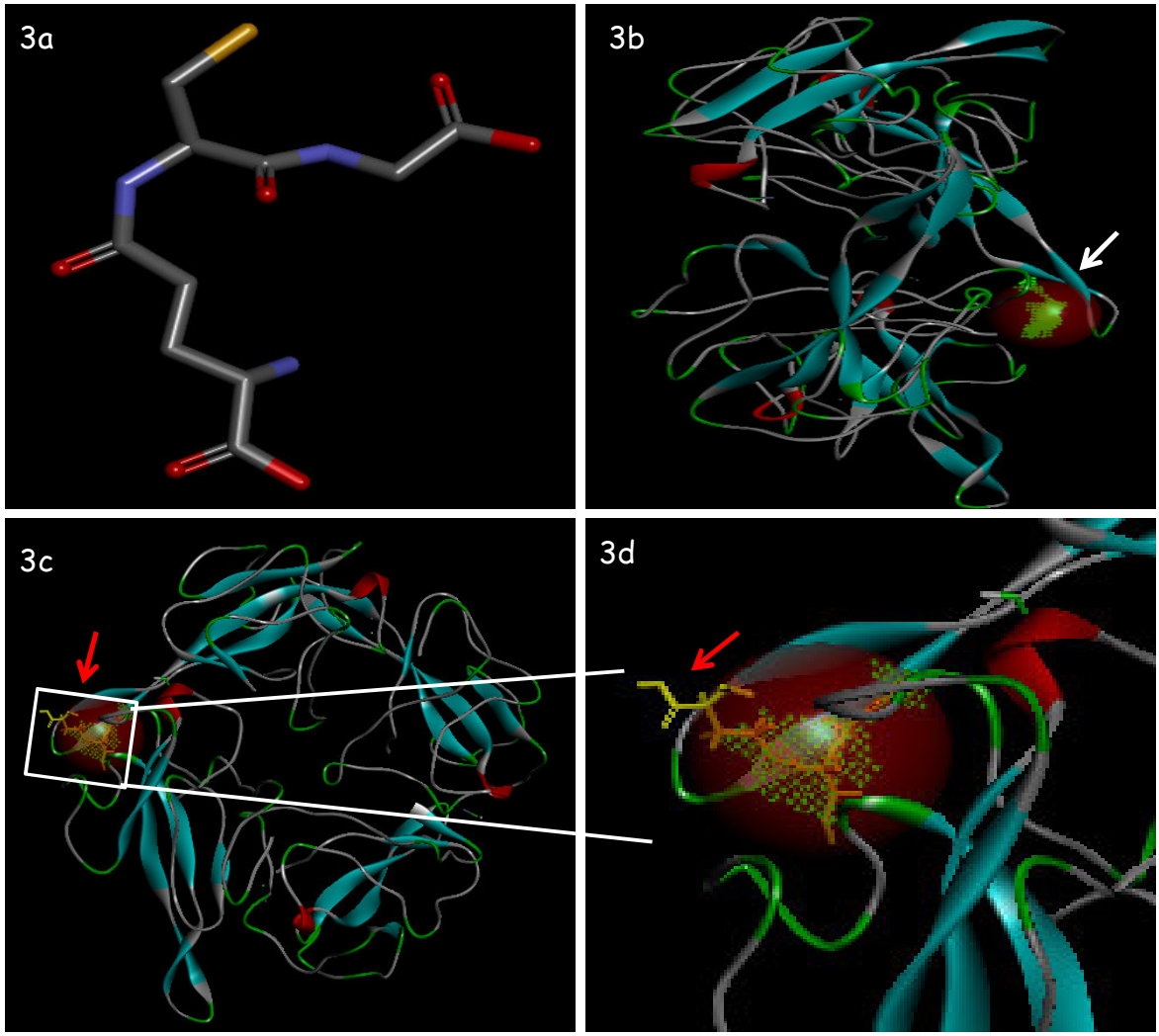

Fig. 3. The active site of the SARS-CoV-2 RdRp with Glutathione. 3a: Phytochemical, Glutathione. 3b: Free form of RdRp. 3c: RdRp associated with the ligand, Glutathione. 3d: Magnified image showing the association of the Glutathione with the RdRp. (The white colored arrow and the red colored arrow indicate the active site of the RdRp and binding of Glutathione respectively).

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RESEARCH ARTICLE

Luteolin, a Phytochemical Interacts with the Activity of the RNA Dependent RNA polymerase of the SARS-CoV-2

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ABSTRACT

The emerging 2019 Novel coronavirus (2019-nCoV) is considered to be an alarming situation. Specific drug against the virus is not yet exposed. Development of pharmacophores for proficient treatment against severe acute SARS-CoV-2 is challenging. The solved cryo-EM structure of SARS-CoV-2 RNA dependent RNA polymerase (RdRp) can be used as one of the primary target molecule and possible inhibitory ligands may be screened using *in silico* docking. Primarily phytochemicals can be screened to detect any potential bio active molecules. *In silico* molecular docking revealed that the phytochemical, Luteolin may effectively bind to the active site of the SARS-CoV-2 main protease.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, phytochemicals, Luteolin.

INTRODUCTION

The rapid spread of coronavirus disease 2019 (COVID-19), caused by zoonotic beta-coronavirus entitled 2019 novel coronavirus (2019-nCoV0, has become a global threat. The genome of 2019-nCoV partially resembled SARS-CoV and MERS-CoV, and indicated a bat origin. The COVID-19 generally had a high reproductive number, a long incubation period, a short serial interval and a low case fatality rate than SARS and MERS. Clinical presentation and pathology of COVID-19 greatly resembled SARS and MARS, with less upper respiratory and gastrointestinal symptoms, and more exudative lesions in post-mortems. Coronavirus has become a critical public issue across the global since December 2019 which was suspected to be originated from a wet market in Wuhan, Hubei province, China [1, 2]. Both SARS-CoV and MERS-CoV were transmitted from bats to palm civets or dromedary camels, and finally to humans, there should be another animal representing an intermediate host between bat and human. Pangolins were suggested as the possible intermediate hosts, because their genome had approximately 85.5%-92.4% similarity to

2019-nCoV, representing two sub-lineages of 2019-nCoV in the phylogenetic tress, one of which (GD/P1L and GDP2S) was extremely closely related to 2019-nCoV. As of 24thof April 2020, more than 2.6 million cases have been reported in 213 countries and territories. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [3, 4]. CoV ranges from 26 to 32 kilo-bases which make it the largest RNA virus. CoVs are of four kinds which are alpha, beta, delta, and gamma. Among these types, only alpha and beta CoV can infect humans. In 2003 Severe Acute respiratory syndrome CoV (SARS-CoV) and 2012 Middle East respiratory syndrome CoV (MERS-CoV) caused the global epidemic. From 2003 to 2004 SARS-CoV infected 8096 people in 29 countries where 774 people died. MERS-CoV was even deadly and took 858 lives out of 2494 people since 2012. SARS-CoV-2 belongs to the Beta coronavirus group which is enveloped single-stranded positive sense RNA genome. Coronavirus has able to infect herbs, animals and humans. Bats are being suspected for the SARS-CoV-2 host but there were likely to be involvement of some intermediate host in bat-human transmission because SARS-CoV and MERS-CoV were transmitted from bats to palm civets or dromedary camels, and finally to humans, there should be another animal representing an intermediate host between bat and human. Based on genome sequencing, 2019-nCoV is about89% identical to bat SARS-like-CoVXC21, 82% identical to human SARS-CoV and about 50% to MERS-CoV. Genomic analysis revealed that SARS-CoV-2 is phylogenetically related to severe acute respiratory syndrome-like (SARS-like) bate viruses; therefore bats could be the possible primary reservoir. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6].

Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins including RNA dependent RNA Polymerase (RdRp) are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear.The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Luteolin, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 RdRp as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of luteolin to be used as COVID-19 therapeutics. Recognizing the need for robust randomized controls trials, the World Health Organization (WHO) recently organized a multinational randomized trial the solidarity trial to study the effect of drugs that have been identified as promising based on in-vitro data and the early clinical experience with COVID-19.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of RdRp was accessed from Protein Data Bank accession 6VYO (Fig. 1). The SDF accession CHEBI:15864 corresponding to the Luteolin (Fig. 2) was obtained and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the RdRp protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

Structure-based virtual screening refers to in silico identification of potential chemical molecules out of large number of compound libraries, which have high affinity to proteins of known structure, based on the binding of the small molecule with the protein binding pocket. It was found that luteolin binds to the active pocket of the SARS-CoV-2 RdRp (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like luteolin effectively binds into the active pocket of the RdRp under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of luteolin and eventually can be used in the pharmaceutical sector. Chemical synthesis of luteolin can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current *in silico* molecular docking based study reveals that luteolin can target the reported SARS-CoV-2 RdRp. It would be extremely noteworthy being confirmed *in vivo*. It is crucial to develop diagnostic tools, potential therapeutics and antibodies selectively for the COVID-19 proteins. Phytochemicals like luteolin is commercially available and thus may be effectively prescribed to circumvent the current global scenario. Essentially, this study makes an attempt to reveal simple phytochemicals like luteolin which can be employed for designing novel therapeutics.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

GKP conceived the idea. GKP, SRK, PKP, SKS, CR performed the experiments. GKP and CR analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

The present study was financially supported by Centurion University of Technology and Management, Odisha, India.

Conflict of interest

The authors declare that they have no conflict of interest.

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1. Chen N, Zhou M, Dong X, et al. 2020. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395:507–513.
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4. Wu F, Zhao S, Yu B, et al. 2020. A new coronavirus associated with human respiratory disease in China. Nature 579:265-269.
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6. Li Q, Guan X, Wu P, et al. 2020. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med 1–9.
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9. Lung Jrhau, Yu-Shih Lin, Yao-Hsu Yang, et al. 2020. The potential chemical structure of anti-SARS-CoV-2 RNA-dependent RNA polymerase. J Med Virol 0–1.
10. Ton A-T, Gentile F, Hsing M, et al. 2020. Rapid Identification of Potential Inhibitors of SARS- CoV-2 Main Protease by Deep Docking of 1.3 Billion Compounds. Mol Inform 1–18.
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12. Panigrahi Gagan Kumar, Sahoo Shraban Kumar and Satapathy Kunja Bihari. 2020. In silico Molecular Docking-Based Screening of Phytochemicals Targeted against Glypican-1. IJONS. 59(10):18708-18712.

Table 1: CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Luteolin with the active site of SARS-CoV-2 RNA dependent RNA polymerase (RdRp).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:15864	Luteolin	RNA-dependent RNA polymerase	6VYO	POSITIVE	7.23	10.5

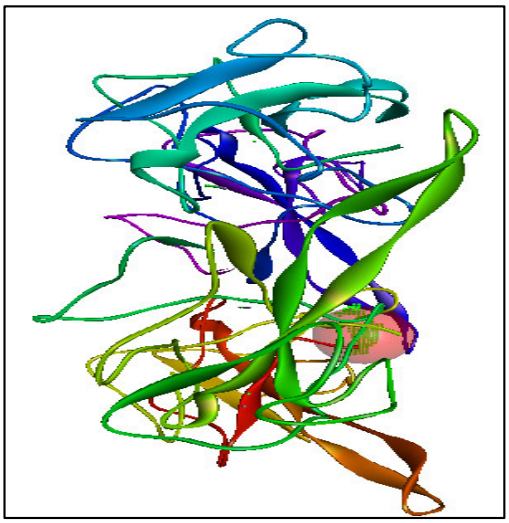

Fig. 1.3-D Structure of the SARS-CoV-2 RdRp showing the active site of the protein.

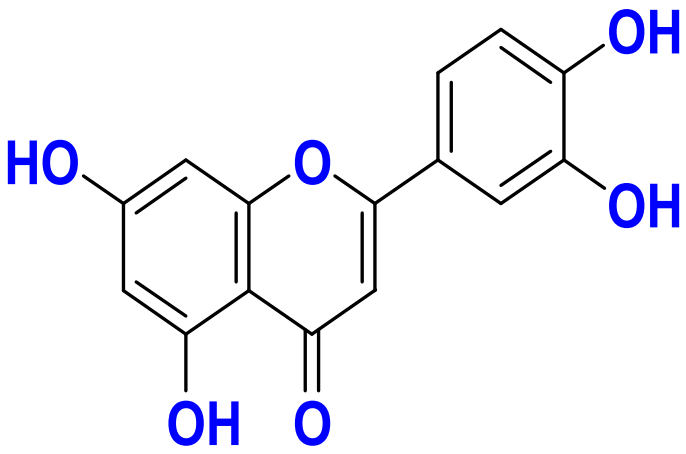

Fig. 2.Chemical structure of Luteolin.

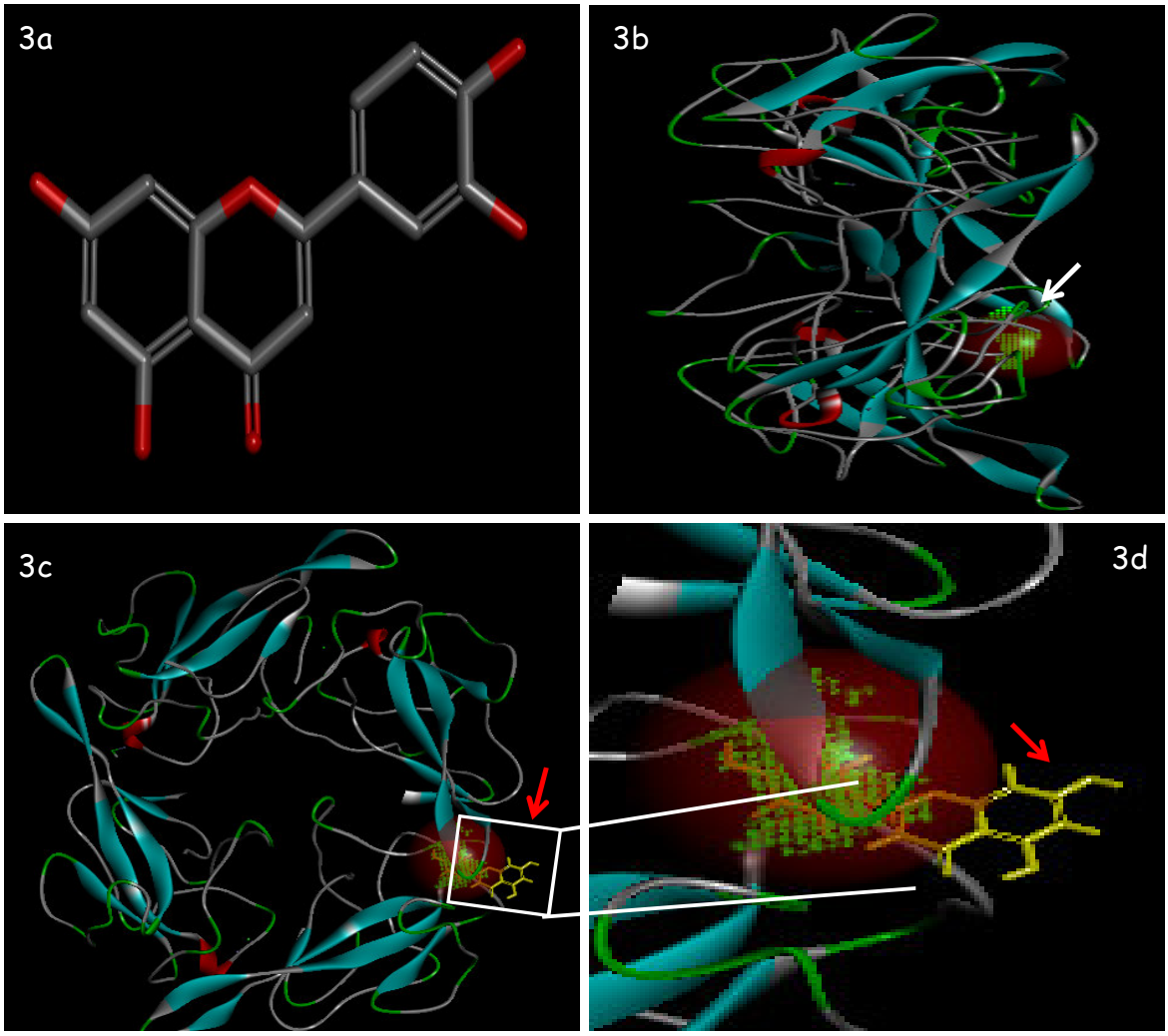

Fig. 3.The active site of the SARS-CoV-2 RdRp with Luteolin. 3a: Phytochemical, Luteolin. 3b: Free form of RdRp. 3c: RdRp associated with the ligand, Luteolin. 3d: Magnified image showing the association of the Luteolin with the RdRp. (The white colored arrow and the red colored arrow indicate the active site of the RdRp and binding of Luteolin respectively).

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RESEARCH ARTICLE

Caffeine against the Activity of the RNA Dependent RNA polymerase of the 2019-nCoV

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ABSTRACT

Public health is threatened by the emerging 2019 Novel coronavirus (2019-nCoV). 2019-nCoV is also referred to as Coronavirus-2 (SARS-CoV-2), a severe acute respiratory syndrome. It emerged as a global risk within no time and was announced a pandemic. A specific anti-viral drug has not yet been discovered. It is challenging to develop bio-molecules for competent treatment against severe acute SARS-CoV-2. RNA dependent RNA polymerase (RdRp) solved Cryo-EM structure can be used as one of the primary target molecules and possible inhibitory ligands can be monitored using in silico docking. Any potential bioactive molecules can be screened primarily with phytochemicals. *In silico* molecular docking revealed that the phytochemical, Caffeine effectively binds to the active site of the SARS-CoV-2 RdRp.

Keywords: 2019-nCoV, SARS-CoV-2, SARS-CoV-2 main protease, docking, phytochemicals, Caffeine.

INTRODUCTION

In the Chinese province of Wuhan, the novel coronavirus 2019 (COVID-19) caused extreme involvement of the lower respiratory tract that led to an acute respiratory syndrome in December 2019 [1, 2]. Coronavirus 2 (SARS-CoV-2) subsequently caused a pandemic that is considered a life-threatening illness. SARS-CoV-2, a family member of beta coronaviruses, has single-stranded positive-sense RNA [3, 4] with standard structural proteins, including the shell, membrane, nucleocapsid, and spike proteins responsible for viral infection, and non-structural proteins. Effective host immune response, including intrinsic and evolutionary immunity against SARS-Cov-2, appears to be crucial to the control and resolution of viral infection. However, the exact nature of COVID-19 may be correlated with the excessive production of pro-inflammatory cytokines "cytokine storm" leading to acute respiratory distress syndrome.

Needless to say, the exact pathophysiology and treatment, especially for severe COVID-19, is still unclear. Early studies have shown that immune-modulatory or immunosuppressive treatments such as hydroxychloroquine, interleukin (IL)-6 and IL-1 antagonists, frequently used in rheumatology, may be considered as possible treatments for COVID-19, particularly in severe diseases. In this review, we concentrated on the structural elements of SARS-CoV-2, the host immune response against SARS-CoV-2, and its association with the cytokine storm to acquire better information on adequate anti-inflammatory treatments, mostly used in COVID-19 rheumatology. Public Health Emergency of International Concern (PHEIC) was declared by the World Health Organization (WHO) owing to its fast rate of transmission within the humans [1, 5, 6]. Crystal structure of the SARS-CoV-2 main protease (M^{pro}) proves to be an exceptional ground for screening specific ligands [7]. SARS-CoV-2 main protease can be beleaguered for developing antibodies, diagnostics and vaccines. Reportedly, M^{pro} and other known viral proteins including RNA dependent RNA Polymerase (RdRp) are defining features paving the path of virus from entry to infection in the host cell [8, 9, 10]. Moreover, M^{pro} can also be an effectual target to diminish the viral replications within the host cells since it facilitates the synthesis of functional viral proteins. The effectiveness of traditional medications on the restriction of COVID-19 growth does not have any scientific back up as of now, since the underlying molecular mechanisms are unclear. The phytochemicals are fundamentally bioactive compounds and has the potential to amend cellular physiology. Here, we report that Caffeine, a phytochemical mostly enriched in some selected plants binds into the active site of the SARS-CoV-2 RdRp as revealed by the *in silico* molecular docking and thus further studies may reveal the effectiveness of caffeine to be used as COVID-19 therapeutics. Recognizing the need for robust randomized controls trials, the World Health Organization (WHO) recently organized a multinational randomized trial the solidarity trial to study the effect of drugs that have been identified as promising based on in-vitro data and the early clinical experience with COVID-19.

MATERIALS AND METHODS

Viral Protein Structure and Phytochemical dataset collection

The 3D structure of RdRp was accessed from Protein Data Bank accession 6VYO (Fig. 1). The SDF accession CHEBI:27732 (Fig. 2) corresponding to the Caffeine was retieved and consequently both the protein and the ligands were used for *in silico* analysis.

Molecular docking

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the RdRp protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [12].

RESULTS AND DISCUSSION

Structure-based virtual screening refers to in silico identification of potential chemical molecules out of large number of compound libraries, which have high affinity to proteins of known structure, based on the binding of the small molecule with the protein binding pocket. It was found that caffeine binds to the active pocket of the SARS-CoV-2 RdRp (Fig. 3), as apparent from higher CDOCKER energy and CDOCKER interaction energy. Since, simple active bio molecule like caffeine effectively binds into the active pocket of the RdRp under *in silico* conditions it is quite possible to design pharmacophore molecules based on the structural and functional identity of caffeine and eventually can be used in the pharmaceutical sector. Chemical synthesis of caffeine can be cost effective as compared to the isolation process from specific plants.

CONCLUSION AND FUTURE PERSPECTIVES

The current study based on silico molecular docking reveals that caffeine can effectively target SARS-CoV-2 RdRp. It would be extremely remarkable to have been confirmed in vivo. Diagnostic tools, prospective therapeutics, and antibodies for COVID-19 proteins must be developed arbitrarily. Phytochemicals such as caffeine may be essentially prescribed to evade the current international situation. Effectively, this study seeks to uncover simple phytochemicals such as caffeine that can be used in the design of novel therapeutics.

ACKNOWLEDGEMENTS

Authors are thankful to the administration and management of Centurion University of Technology and Management, Odisha, India for providing necessary facilities to conduct the experiment.

Author contribution statement

GKP conceived the idea. GKP, SS, PKP, SKS, CR performed the experiments. GKP and CR analyzed the data. All authors have significant contribution in drafting the manuscript.

Funding

The present study was financially supported by Centurion University of Technology and Management, Odisha, India.

Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1: CDOCKER ENERGY and CDOCKER INTERACTION ENERGY values generated for the interaction of Caffeine with the active site of SARS-CoV-2 RNA dependent RNA polymerase (RdRp).

Ligand		Receptor		Interaction Status		
SDF accession	Phytochemical	Protein	PDB accession	Docking Result	CDOCKER ENERGY	CDOCKER INTERACTION ENERGY
CHEBI:27732	Caffeine	RNA-dependent RNA polymerase	6VYO	POSITIVE	5.45	14.1

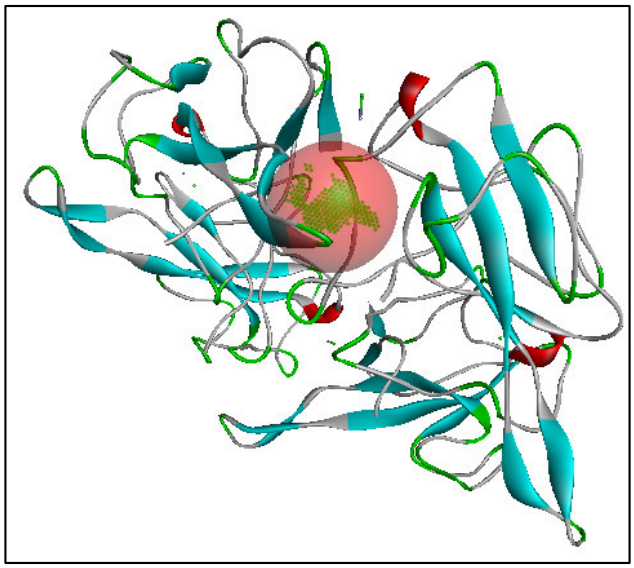

Fig. 1. 3-D Structure of the SARS-CoV-2 RdRp showing the active site of the protein.

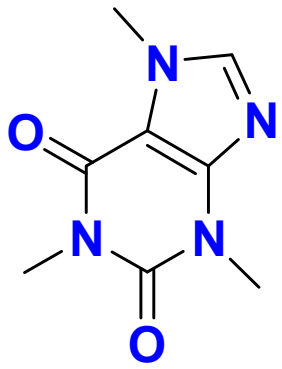

Fig. 2. Chemical structure of Caffeine.

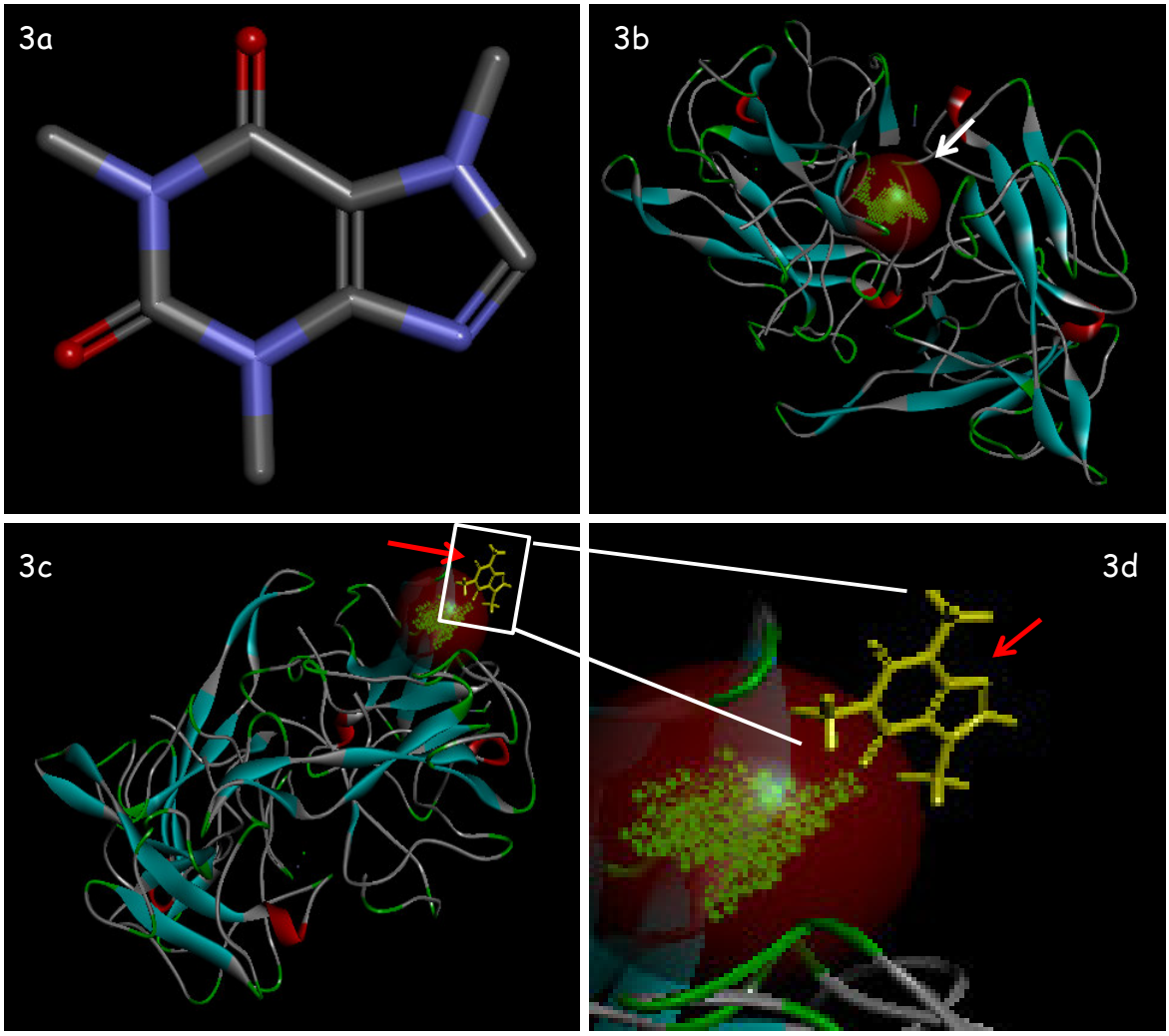

Fig. 3. The active site of the SARS-CoV-2 RdRp with Caffeine. 3a: Phytochemical, Caffeine. 3b: Free form of RdRp. 3c: RdRp associated with the ligand, Caffeine. 3d: Magnified image showing the association of the Caffeine with the RdRp. (The white colored arrow and the red colored arrow indicate the active site of the RdRp and binding of Caffeine respectively).

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RESEARCH ARTICLE

Efficient Method of Mining Frequent Itemset from Large Data Set using Hadoop Technique

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ABSTRACT

Mining Large Data has become an essential aspect in the field of Computer Science. The huge amount of data available need to be turned into useful information. This information can be used for various applications like market analysis, customer retention, production control, analysis, etc.In such scenarios, the huge data need to be processed by using various frameworks. This is beneficial in many application areas, like analysis of the frequently used items by a consumer.The Proposed system is for generating frequent itemsets for large datasets. The method can be efficiently handled by using Hadoop MapReduce framework. Hadoop is a software framework for handling huge data. We implement the MapReduce where the data are divided into various parts and each part is processed individually. This enhances parallel computations and makes the job faster.We have implemented the Distributed and Parallel Frequent Mining Algorithm(DPFPM) for a large dataset.The processing is done by the MapReduce job as specified.This Project uses Hadoop MapReduce, Eclipse, Ubuntu platform, Eclipse. This Approach has an advantage of being fast as compared to previous approaches.

Keywords: Big Data Infrastructure (BDI), Big Data Architecture Framework (BDAF), Big Data Lifecycle Management (BDLM).

INTRODUCTION

To generate frequent itemsets for large datasets using Hadoop MapReduce framework. This project includes working with a large dataset and processing it. When data is taken into consideration, it has been since years that the storage of the data and its processing is confined to databases. These databases handle the data of that particular organization. But, in the recent world, with the rapid growth of increasing applications and the use of Internet, the data has increased .Also, the increase in the computational power has led to a large flow of data. With this, the size

of datasets created by organizations due to availability of low-cost storage and evolution in the data capturing technology is also increasing. Such data is usually referred to as Big Data[6]. For the analysis to be done on the data, it needs to be processed. The manipulation of data to process useful information is referred to be data processing. This data processing includes various aspects like Generation of useful information, Validation, Analysis, Summarization, sorting, aggregation, Reporting and classification. Our project focuses on analysis and generation of useful information. The evolution of data processing is through the manual to electronic procedures.

Manual Data Processing

Data processing functions have been performed manually for millennia. For example, Book-keeping involves functions such as posting transactions and producing reports like the balance sheet and cash flow statement. Completely manual methods were augmented by the application of mechanical or electronic calculators[8]. It used to take years to process this datawithout any mining techniques.

Electronic Data Processing

With the evolution of computers, tapes etc. the data processing has been done with the electronic techniques. Small data can be handled by these devices [9].

Commercial Data Processing

It involves large volume of input data, relatively few computational operations, and a large volume of output. For example, a company needs to keep track of various records on tens or hundreds or thousands of policies, print and mail bills, and receive and post payments [7]. All the above techniques are mostly implied for data that is small. But as referred above, day by day the data is emerging at a pace. For example, the famous social site Facebook serves 570 billion page views per month, stores 3 billion new photos per month, manages 25 pieces of content every month. Business applications include lots of artificial intelligence tricks, requiring parsing of large quantities of data and making decisions [7]. The organisation sectors usually include Retail, Telecommunications, Utilities, Manufacturing, transport, credit cards, Insurance, Banking and many others. Extracting the valuable data is necessary to explore the data efficiently. This valuable information can help the dealer to make more analysis.

Knowledge discovery in databases is very essential for identifying precious information from a large database. This helps in decision making, analysis, measurable benefits, reduced cost of doing business, enhanced profitability, and improved quality of service. If a business organization want to check how frequently a good is being sold so that this analysis can improve the profit on that particular item, this analysis is very helpful. Hence generation of the frequent itemsets is a part of business analysis. In order to handle such huge data, Hadoop is the tool. It is a software framework for working with large amounts of data.

DESCRIPTION

This project deals with large data and to process it using Hadoop Map Reduce framework. The data can be handled easily by the Hadoop Distributed File System (HDFS). The frequent itemsets of a transactional dataset are used by a MapReduce program [5].

PURPOSE

Mining frequent itemsets from large-scale databases has emerged as an important problem in the data mining and knowledge discovery research community. The need for frequent itemsets is to analyse business logic. By finding

frequent itemsets, for example, a retailer can learn what is commonly bought together. Especially important are pairs or larger sets of items that occur much more frequently than would be expected were the items bought independently. This helps in more analysis of his business and further measures can be taken based on these results for more profits. Similarly, web log analysis also follows the same strategy [3].

APPLICATIONS

Frequent patterns and itemsets, reflecting strong associations among multiple items or objects, capture the underlying semantics in data. They were successfully applied to inter-disciplinary domains beyond data mining [7].

Some of the successful applications are:
(1) Indexing and similarity search of complex structured data
(2) Spatiotemporal and multimedia data mining
(3) Stream data mining
(4) Web mining and
(5) Software bug mining and page-fetch prediction

SCOPE

As the project is concerned with mining of frequent patterns of big data, it is well equipped with the latest implementation which has an ease in every aspect like resource sharing, computation latency, etc... This implementation is very much helpful for the Big data where the data analysis is becoming difficult. The MapReduce programming of Hadoop simplifies the task of data processing. Hadoop has no clear boundaries. As the data increases extensively, the scope for mining and use of Hadoop increases. As well, Data mining technologies economic value has been recognized from its birth to now, and many companies have started to use the data mining technology to create economic value. The frequent pattern mining research has substantially broadened the scope of data analysis and will have deep impact on data mining methodologies and applications in the long run [3]. We can Extract, Transform and Load Big Data using Hadoop. Further scope of the project can also include distributed node processing.

For example, if a shopping mall has 30 branches over the world, all the data need to be processed and find what items are being sold most frequently. For this, we can use Hadoop that happens to be the best platform for processing of distributed data. Frequent pattern mining has been a focused theme in data mining research for over a decade. Abundant literature has been dedicated to this research and tremendous progress has been made, ranging from efficient and scalable algorithms for frequent itemset mining in transaction databases to numerous research frontiers, such as sequential pattern mining, structured pattern mining, correlation mining, associative classification, and frequent pattern based clustering, as well as their broad applications[1]. In this article, we provide a brief overview of the current status of frequent pattern mining and discuss a few promising research directions. Already, companies such as Wibidata and Continuity are trying to make it easier for companies to build Hadoop applications specific to their own needs. Frequent pattern mining has been a focused theme in data mining research for over a decade. Abundant literature has been dedicated to this research and tremendous progress has been made, ranging from efficient and scalable algorithms for frequent itemset mining in transaction databases to numerous research frontiers, such as sequential pattern mining, structured pattern mining, correlation mining, associative classification, and frequent pattern-based clustering, as well as their broad applications. It is believed that frequent pattern mining research has substantially broadened the scope of data analysis and will have deep impact on data mining methodologies and applications in the long run.

LITERATURE SURVEY

There has been a growing interest in the development of methods for generation of frequent itemsets. Here we present the literature on the mining, processing of data along with generation of itemsets.

BACKGROUND

It should be noted that there is a significant body of work on generation of frequent itemsets for a normal transaction. First of all, the project takes its initiation from the discipline of data mining. When we ponder the concepts of datamining, processing huge data comes under the scenario. Mining and Processing of large data has been a part of datamining. Many approaches are being done for frequent pattern mining.

Data Mining

Data Mining is an analytical process designed to explore data usually large amounts of data typically business or market related in search of consistent patterns and/or systematic relationships between fields, and to validate the findings by applying the detected patterns to new subsets of data[2].
The process of mining consists of three stages:

Stage 1: Exploration

As the project is concerned with large data, we consider a large dataset consisting of around 1000 transactions. This stage usually starts with data preparation which may involve selecting records data sets with large numbers of fields - performing some preliminary feature selection operations to bring the number of fields to a manageable range (depending on the statistical methods which are being considered). Then, depending on the nature of the analytic problem, this first stage of the process of data mining may involve anywhere between a simple choice of identifying the most relevant variables and determine the complexity and/or the general nature of models that can be taken into account in the next stage.

Stage 2: Model building and validation

This stage involves considering various models and choosing the best one based on their predictive performance . This is a very elaborate process. There are a variety of techniques developed to achieve that goal. The project is designed to work with Hadoop and for the MapReduce programming, we used Eclipse as our programming environment Out of all those we have chosen the DPFPM algorithm.

Stage 3: Deployment

That final stage involves using the model selected as best in the previous stage and applying it to new data in order to generate predictions or estimates of the expected outcome. The concept of datamining is becoming increasingly popular as a business information management tool where it is expected to reveal knowledge structures that can guide decisions in conditions of limited certainty.

Big Data

In the aspect of DataMining, the data is never confined to a particular volume. As mentioned above, the data is growing higher day by day. Big data is a popular term used to describe the exponential growth and availability of data, both structured and unstructured. And big data may be as important to business – and society – as the Internet has become. This data is difficult to be processed using regular transaction data processing techniques [6]. The main issue why the Bigdata really matters is: The real issue is not about acquiring large amounts of data. It's what to be done with the data counts. The hopeful vision is that organizations will be able to take data from any source, harness relevant data and analyse it to find answers that enable cost reductions, time reductions, new product development and optimized offerings, and smarter business decision making.

Data Analysis

When Bigdata comes into scenario, the issue of how to mine such large data is the major concern. This data needs to be mined for data analysis and getting the desired knowledge. If the traditional data mining functions are used, it takes months and years to mine and output the desired result. Hence we need a tool that processes the data with faster computations [7]. The huge data can be processed by a tool named "Hadoop". Hadoop has a programming framework that is designed in such a way that it does parallel computations.

For the transaction dataset that we are considering, it is related to business transactions. Using this, we need to analyse the data and generate the frequently occurring items. This helps in acquiring decision making procedures to profit.

Frequent Itemsets

Frequent sets play an essential role in many Data Mining tasks that try to find interesting patterns from databases, such as association rules, correlations, sequences, episodes, classifiers and clusters. The original motivation for searching frequent sets came from the need to analyse so called supermarket transaction data here, that is, to examine customer behaviour in terms of the purchased products. Frequent sets of products describe how often items are purchased together [5]. Formally let I be the set of items.

A transaction over I is a couple T = (tid, I) where tid is the transaction identifier and I is the set of items from I. A database D over I is a set of transactions over I such that each transaction has a unique identifier. We omit I whenever it is clear from the context A transaction T = (tid, I) is said to support a set X, if X C I. The cover of a set X in D consists of the set of transaction identifiers of transactions in D that support X. The support of a set X in D is the number of transactions in the cover of X in D. The frequency of a set X in D is the probability that X occurs in a transaction, or in other words, the support of X divided by the total number of transactions in the database. We omit D whenever it is clear from the context. A set is called frequent if its support is no less than a given absolute minimal support threshold

min_sup with 0≤min_supabs≤|D|. When working with frequencies of sets instead of their support,

we use the relative minimal frequency threshold min_suprel, w**ith 0≤min_suprel≤1. Obviously**min_supabs = [min_suprel * |D|]. In this paper we will mostly use the absolute minimal support threshold and omit the infrequent itemsets.

The task of discovering all frequent sets is quite challenging. The search space is exponential in the number of items occurring in the database and the targeted databases tend to be massive, containing millions of transactions. Both these characteristics make it a worthwhile effort to seek the most efficient techniques to solve this task.

VARIOUS APPROACHES FOR FREQUENT ITEMSET GENERATION

There are various approaches for the generation of frequent itemsets. Some of them are as follows. For smaller datasets, it is very easy task to find the frequent itemsets. But for large datasets, it is a typical task[1].

Some of the approaches for smaller datasets are:

- Apriori algorithm
- PP tree based parallel and Distributed algorithm
- TPFP tree and BTP tree based parallel and distributed algorithm For the larger datasets, the following are the approaches:

Apriori algorithm using MapReduce

The Apriori algorithm is improved using MapReduce model to handle huge datasets on Hadoop distributed computing environment. It first finds frequent 1-itemsets in first database scan. Then it uses MapReduce model where each mapper generate subset of candidate itemsets. These candidate itemsets are given to reducer to prune candidates based onminimum support threshold and to generate subset of frequent itemsets. At final stage output of all reducers is combined to generate final frequent itemsets.

Disadvantage of Apriori

Multiple iterations to MapReduce are necessary to produce frequent itemsets.
It also suffers from drawback of multiple database scans and huge candidate set generation. It faces the bottleneck problem [2].

DH-Tire algorithm using Map Reduce

The Distributed DH-TRIE frequent pattern mining algorithm is proposed using Hadoop MapReduce programming model. It is based on Dynamic Hash (DH) Trie algorithm. In first phase, first two database scans are assigned to map tasks which results into building of DH-TRIE. In second phase mining is carried out using breadth-first search model by using queue instead of recursive processing for mining. This is carried out by multiple mapper tasks where number of mappers is equal to number of elements in thequeue[5].

Disadvantages of DH-Trie algorithm

Three problems are focused in this approach. They are globalization, random-write and duration which are tried to solve using Java Persistent. It still faces some drawbacks like in first phase two database scans are handled by only map tasks, no reducer is used to construct FP-tree. In second phase mining is also carried out by map tasks to handle sub FP-tree, slowdowns mining process [4]. As all these algorithms have few disadvantages, we are implementing DPFPM algorithm that deals with all the disadvantages of the above approaches.

Related Work

Frequent pattern mining problem is to find all frequent k-itemsets where all itemset support should be more than minimum support threshold.

Support (**k) >= min_sup_threshold**ξ**for given threshold (1 ≤** ξ **≤ |DB|).**

- Apriori based algorithms tried to solve the FPM problem but faced a performance bottleneck of either multiple database scan or huge search space or both. Prefix tree based algorithms like FP-growth tried to optimize performance but suffer performance issues with huge database and small support values where it takes more time for mining or it fails to execute. In this section previous work in the field of distributed and parallel frequent pattern mining is covered. Distributed algorithms based on prefix tree structure and MapReduce framework is discussed [3].
- In PP tree based parallel and distributed algorithm, it proposes parallel and distributed algorithm using PP tree (parallel pattern tree) where it requires only one database scan to construct PP tree and in a way reduces I/O cost. It considers a distributed memory architecture where each node contains all resources locally [4]. Algorithm is divided in three phases –

- Phase I: It first accept database contents in horizontal partitions in any canonical order, construct tree in one scan and then restructure it in global frequency descending sequence of items.
- Phase II: Local Mining – Individually mine local PP tree in parallel for discovering global frequent patterns (FPpg).
- Phase III: Final sequential step which collects frequent patterns from all local PP trees and generate global frequent patterns.
- Phase I: PP tree construction phase – This phase first partitions original database and distribute it to all nodes. It then performs three steps at each local node.
- Step I: It construct local PP tree with insertion stage by generating local header table at each node.
- Step II: All local header tables are collected in global header table array (HTA).This global HTA is reorganized in frequency descending order.
- Step III: At each node restructuring phase is carried out with the help of global HTA and finally local PP tree is created.

- Phase II: Mining of local PP tree – PP tree generate the set of potential frequent patterns (FPpg) by using FP Growth mining algorithm. For this first local PP trees construct itemset based prefix pattern trees PT(x) for each frequent pattern x. It is constructed by collecting all prefix sub paths/patterns from original local PP tree. From this individual tree for each frequent pattern x it generates new conditional tree CT(x), which contains only potential global items, it prunes all infrequent items. Then it generates the set of frequent patterns (FPpg) at each local node in parallel without any IPC cost [7].
- Phase III: Generating global frequent patterns – In this master node takes local frequent patterns (FPpg) and sequential step of accumulating supports of all local (FPpg) is carried out at master node. The final (FPpg) list may lead to false positive patterns but not false negatives. Master node then removes all infrequent patterns from (FPpg) list and generates final global frequent patterns. For removing infrequent patterns from (FPpg) list algorithm uses hash based technique to speed up the search in (FPpg) list. Although this algorithm tries to reduce Inter Process Communication cost with efficient mining algorithm and also reduces I/O cost by performing single database scan still it requires more time for insertion and restructuring phase while constructing local PP trees. Original database is partitioned but not pruned with infrequent 1-itemsets and original database is only used throughout the algorithm so this may utilizes more memory for huge databases.

- In TPFP tree and BTP tree based parallel and distributed algorithm, two parallel and distributed mining algorithms are proposed based on Tidset concept. Tidset based parallel FP tree (TPFP tree) algorithm is proposed for cluster environment and balanced Tidset based parallel FP tree (BTP tree) algorithm is proposed for grid environment. In both the algorithms Tidset (Transaction identifier set) is used to directly select transactions instead of scanning whole database. Its goal is to reduce IPC cost and tree insertion cost, thus decreasing execution time. TPFP tree based algorithm is proposed for homogeneous cluster environment. In this algorithm load is distributed to all nodes evenly without viewing processor capacity. Its objective is to reduce the execution time of mining information exchange and to shorten the index cost of transaction extraction [5]. BTP tree algorithm is proposed for heterogeneous grid environment where it tries to balance the load. In BTP algorithm all the steps are same as TPFP algorithm only one more step is added to it, where it evaluates the performance index of computing nodes. Depending upon performance index it distributes mining sets. This algorithm performs better than PFP tree and TPFP tree in grid environment.

DISTRIBUTED PARALLEL FREQUENT PATTERN MININGALGORITHM

ACTIVITY DIAGRAM

An activity diagram shows the flow from activity to activity. An activity is an on-going non-atomic execution with a state machine. Activities ultimately result in some action, which is made up of executable atomic computations that result in a change of return of value.

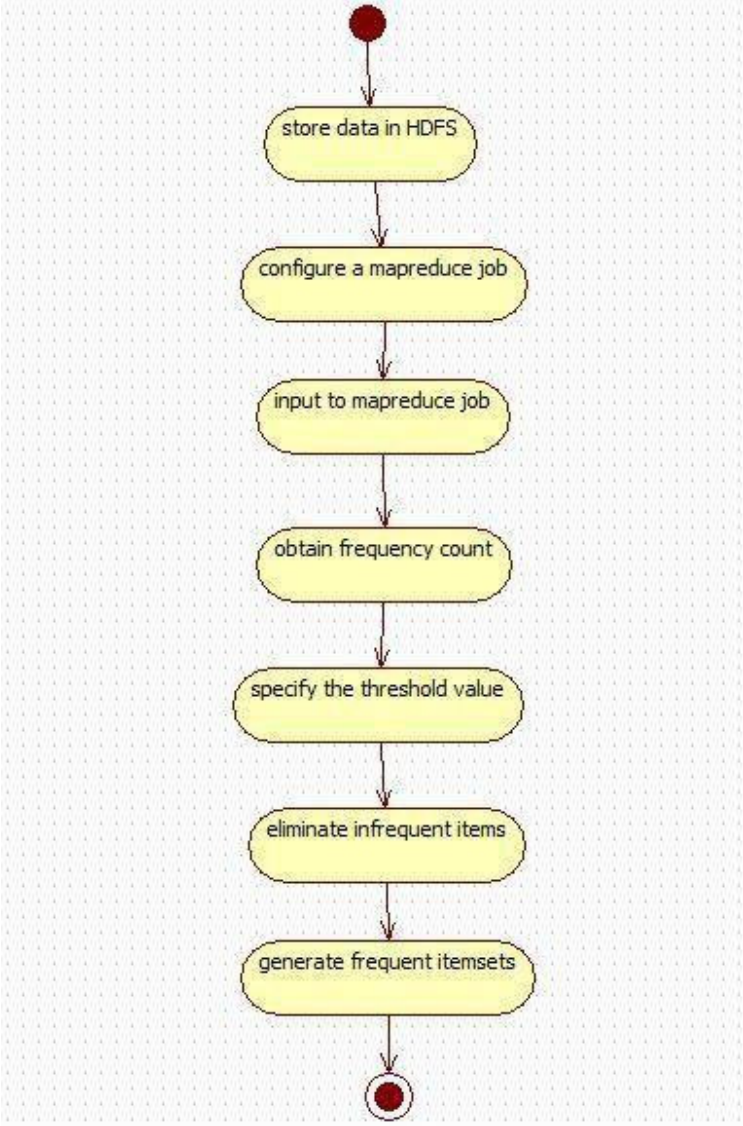

Figure 1. Activity Diagram

The flow of activities which are performed one after the other by the Hadoop job are represented in the activity diagram.

TECHNOLOGY DESCRIPTION

This section explains the various technologies and tools used for development and deployment of the system.

Overview of Hadoop

Hadoop is an open-source software framework for distributed or large storage and distributed processing of very large data sets (Big Data) on computer clusters built from commodity hardware. All the modules in Hadoop are designed with a fundamental assumption that hardware failures (of individual machines or racks of machines) are commonplace and thus should be automatically handled in software by the framework. The core of Hadoop consists of a storage part (Hadoop Distributed File System (HDFS)) and a processing part (MapReduce). Hadoop splits files into large blocks (default 64MB or 128MB) [5] and distributes the blocks amongst the nodes in the cluster. To process the data, Hadoop Map/Reduce transfers code (specifically Jar files) to nodes that have the required data, which the nodes then process in parallel. This approach takes advantage of data locality to allow the data to be processed faster and more efficiently via distributed processing than by using a more conventional supercomputer architecture that relies on a parallel file system where computation and data are connected via high-speed networking.

There are three major components:

Hadoop Distributed File System (HDFS) – a distributed file system that acts as a storage systemfor big data, both structured and unstructured. Users load files to the file system using simple commands and HDFS takes care of making multiple copies of data blocks and distributing those blocks over multiple nodes in the Hadoop system [5].

MapReduce – a parallel programming model for distributed processing of large data sets.The Map phase performs operations such as filtering, transforming and sorting. The Reduce phase takes that output and aggregates it. MapReduce programs are written in Java.

YARN (Yet Another Resource Negotiator) – a general-purpose resource managementframework. It handles and schedules resource requests from distributed applications (MapReduce and others) and supervises their execution.

Installation of Hadoop

This section deals with the installation of Hadoop in the system.
It includes the following phases:
Prerequisites: Ubuntu

1. Installing Java (open JDK):
2. Adding a new group and a new Hadoop user
3. Configuring SSH access
4. Disabling IPv6
5. Downloading and extracting Hadoop .tar file
6. Setting Global Variables
7. Configuring Hadoop Configuration files
8. Formatting namenode
9. Running Hadoop

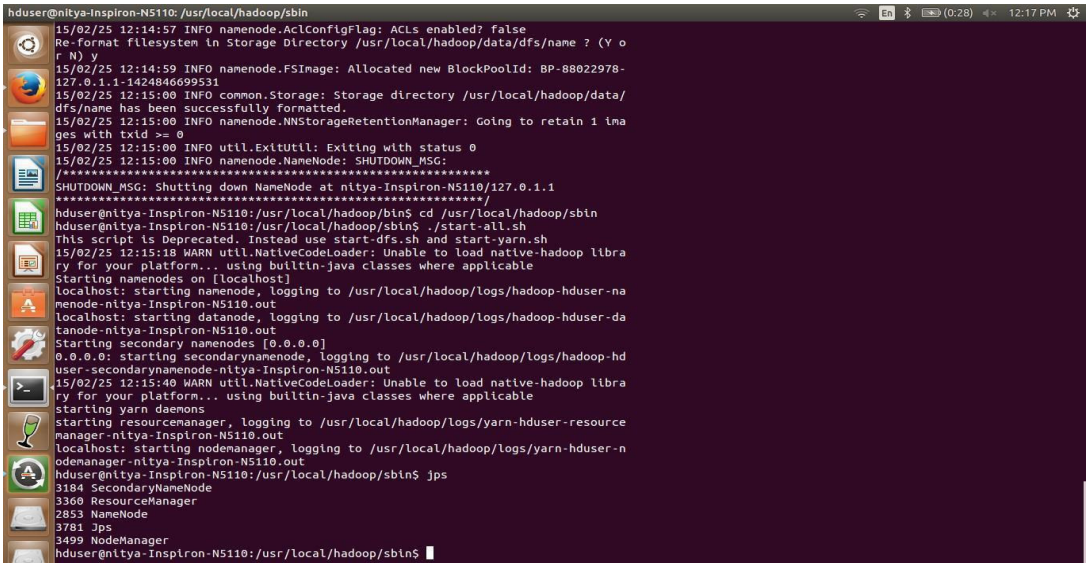

Fig.2. Running of Hadoop

Hadoop LocalHost

We can connect to Hadoop on localhost by configuring SSH. To enable SSH access, we run ssh localhost.

ssh localhost or sshusername@localhost

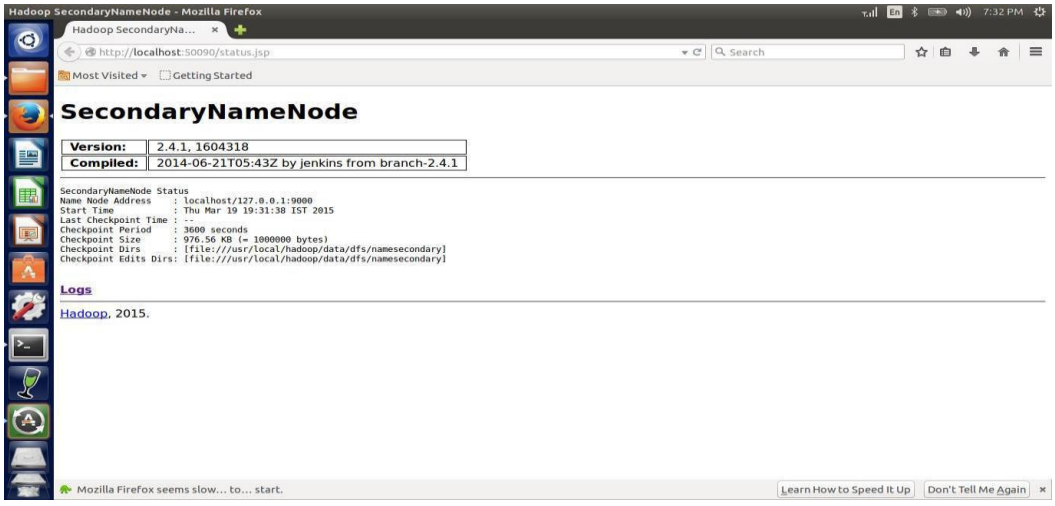

Fig 3. Hadoop on localhost

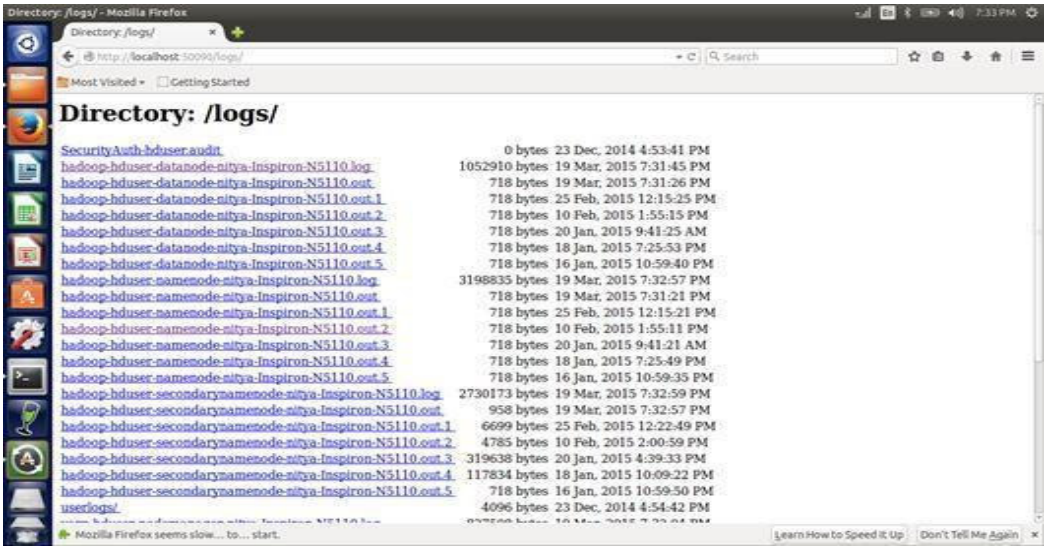

Fig 4. Hadoop-Logs

Overview of Hadoop HDFS

Hadoop Distributed File System (HDFS) is a Java-based file system that provides scalable and reliable data storage that is designed to span large clusters of commodity servers. An HDFS cluster is comprised of a NameNode which manages the cluster metadata and DataNodes that store the data. Files and directories are represented on the NameNode by inodes. Inodes record attributes like permissions, modification and access times, or namespace and disk space quotas [6]. The file content is split into large blocks (typically 128 megabytes), and each block of the file is independently replicated at multiple DataNodes. The blocks are stored on the local file system on the datanodes. The Namenode actively monitors the number of replicas of a block. When a replica of a block is lost due to a DataNode failure or disk failure, the NameNode creates another replica of the block. The NameNode maintains the namespace tree and the mapping of blocks to DataNodes, holding the entire namespace image in RAM. The Name Node does not directly send requests to DataNodes. It sends instructions to the DataNodes by replying to heartbeats sent by those DataNodes. The instructions include commands to: replicate blocks to other nodes, remove local block replicas, re-register and send an immediate block report, or shut down the node.

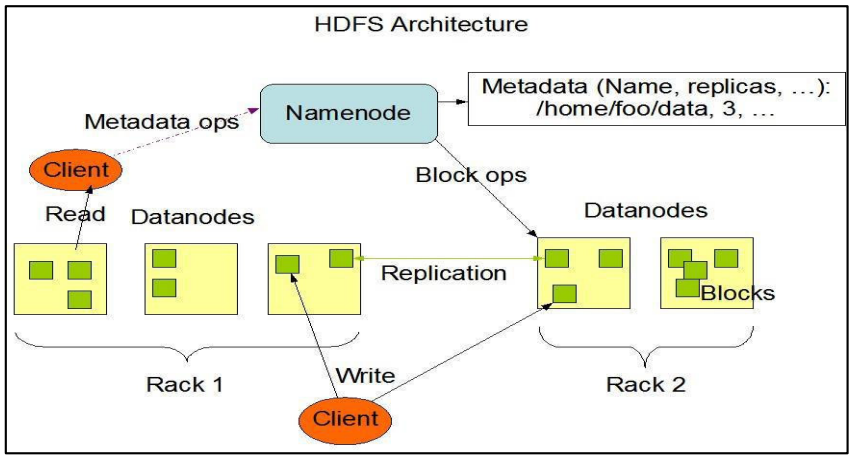

Fig 5. Overview of Hadoop HDFS

Hadoop MapReduce

MapReduce is a programming model for processing and generating large data sets with parallel computations. A MapReduce program is composed of a Map**()** procedure that performs filtering and sorting (such as sorting students by first name into queues, one queue for each name) and a Reduce**()** procedure that performs a summary operation (such as counting the number of students in each queue, yielding name frequencies). The "MapReduce System" (also called "infrastructure" or "framework") orchestrates the processing by marshalling the distributed servers, running the various tasks in parallel, managing all communications and data transfers between the various parts of the system, and providing for redundancy and fault tolerance [6].

Map Reduce is as a 5-step parallel and distributed computation:

Prepare the Map() input – the "MapReduce system" designates Map processors, assignsthe input key value *K1* that each processor would work on, and provides that processor with all the input data associated with that key value.

Run the user-provided Map () code – Map () is run exactly once for each*K1*key value,generating output organized by key values *K2*.

"Shuffle" the Map output to the Reduce processors – the MapReduce system designatesReduce processors, assigns the *K2* key value each processor should work on, and provides that processor with all the Map-generated data associated with that key value.

Run the user-provided Reduce () code – Reduce () is run exactly once for each*K2*keyvalue produced by the Map step.

Produce the final output – the MapReduce system collects all the Reduce output, andsorts it by *K2* to produce the final outcome.

	Input	Output
Map	**<k1,v1>**	**List(<k2,v2>)**
Reduce	**<k2,list(v2)>**	**List(<k3,v3>)**

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Hadoop Daemons

Hadoop Daemon is an interface to help you run a program in Hadoop. List all the daemons required to run the Hadoop cluster:

NameNode– This daemon stores and maintains the metadata for HDFS. Secondary NameNode– Performs housekeeping functions for the NameNode.

JobTracker– Manages MapReduce jobs, distributes individual tasks to machines running the Task Tracker.

DataNode– Stores actual HDFS data blocks.

TaskTracker– Responsible for instantiating and monitoring individual Map and Reduce tasks.

JPS command shows all the daemons of the Hadoop in our system.

Eclipse

Executing a Hadoop job requires a Java programming environment. A powerful development environment for Java-based programming is Eclipse. Eclipse is a free, open-source IDE. It supports multiple languages through a plugin interface, with special attention paid to Java. Tools designed for working with Hadoop can be integrated into Eclipse, making it an attractive platform for Hadoop development. It is also an easier way to manipulate files in HDFS through the Eclipse plugin.

In this project, we have worked on Eclipse Luna by configuring it to work with Hadoop.

Putty

Executing a We have worked on above all mentioned tools but faced problem at reproduction of Frequent Itemsets. So we took the help of IBM Bluemix [11]. We created a Container for Hadoop and dumped in Bluemix and configured that server. Then installed Putty framework on windows and connected to Hadoop configured server. We have dumped our frequent itemset logic code into JAR file and given input into the Bluemix. And followed the below steps.

⚜⚜In putty type root@server address

- hadoop fs -mkdirinput_dir --->if you get this error mkdir: `input_dir': No such file or directory then execute this-->hadoop fs -mkdir -p /user/root

- now execute the below command again

hadoop fs -mkdirinput_dir ---> this time it will be created.

- hadoop fs -put input.txt input_dir --> transfer file to hadoop file system only the sample file java file must not be transferred

- hadoop fs -ls input_dir ---->check if the files exists.

- hadoop jar freq.jar input_diroutput_dir --->run the java file stdcall.jar using hadoop take the input files from input_dir folder and post the output in output_dir (hadoop creates this folder automatically).execution starts and you will recieve

File Output Format Counters

Bytes Written=42

That means job is completed.

- hadoop fs -ls output_dir --->tocheck the output files find the latest file by date and time and copy the name (it will be something like output_dir/part-r-00000).

- then run this --->hadoop fs -cat output_dir/part-r-00000 --->to view the output

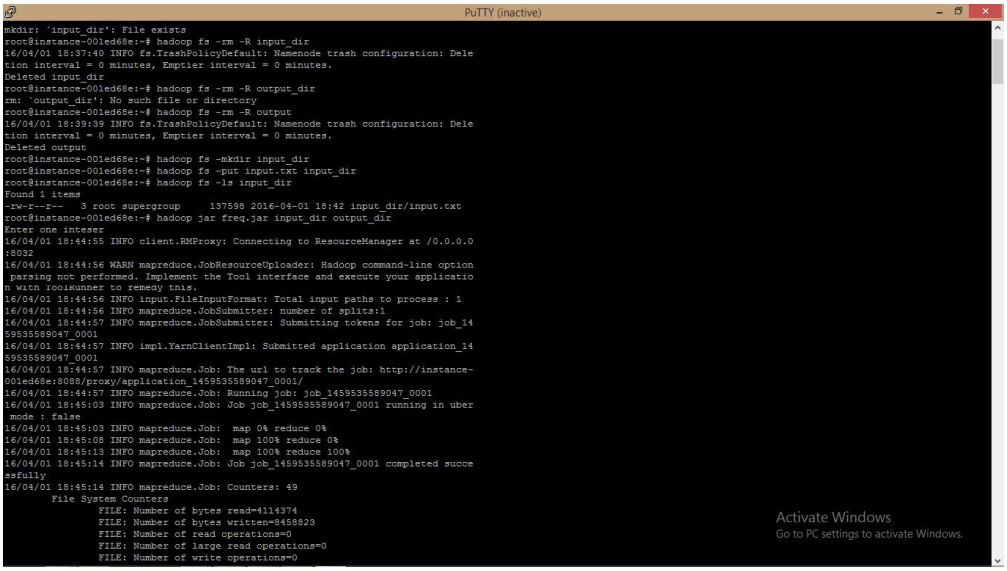


Fig.6. Putty

OUR PROPOSED SYSTEM

Proposed DPFPM algorithm uses Hadoop MapReduce programming framework for frequent pattern mining.

In frequent pattern mining the task of generating conditional frequent patterns and finding global frequent patterns can be done in parallel by distributing the data so MapReduce framework is most suitable for it.

In proposed algorithm MapReduce task is used twice, once for support counting and then for generating frequent patterns, taking more benefits of MapReduce framework. It achieves distributed system goals like high availability, high throughput, load balancing and fault tolerance by using map reduce functionality efficiently and effectively [3].

Advantages of Our System

- It decreases the computational time of the job
- It will be in reach of every organization
- Everything in this project is a open source which makes this app lot cheaper and can be free of cost.
- This can be integrated well with all platforms.
- Gives less computational time when compared with regular java implementation.

DPFPM ALGORITHM

The algorithm specifies a strategy of generating frequent itemsets [1]. It uses the MapReduce programming where the whole dataset is divided into various parts and each one is processed individually. Then the frequency count of every item in all the transactions is being counted and represented as global frequency header table that consists of the items and its frequency count. Based on this count, items are pruned considering some minimal threshold value.

Furthur the conditional patterns are generated as a <key, value> pair. This is done by considering the least count item and mapping the other items to that. At each stage eliminate the successive keys of above pattern. When these conditional patterns are generated, all are combined based on the key value. Then considering the threshold count, pruning of items is done. For the frequent items left out, successive frequent itemsets are generated.

Project has been divided into various modules. They are:

- Divide transaction dataset.
- Construction of Global Frequent Header Table (GFHTable)
- Generating conditional frequent patterns
- Generate frequent item sets.

In first step it divide transaction dataset. In second step it constructs Global Frequent Header Table (GFHTable) using MapReduce tasks for first time. Third step generate conditional frequent patterns using map task second time. In fourth step each reducer combine all conditional frequent patterns of same key to generate frequent sets. In fifth step all reducers output is aggregated to generate final frequent sets [6].

Architecture of Mapreduce task in DPFPM algorithm

It consists of the input data that is splitted into various splits. The data in the splits is sent to the record reader which inputs its data to each Mapper that is generated for each split. The Mapper processes each split individually. Its output is given to every reducer. The reducers then combine the input from all the mappers [2]. They Shuffle and sort. Finally, the output of reducers is combined and the final outcome is generated.

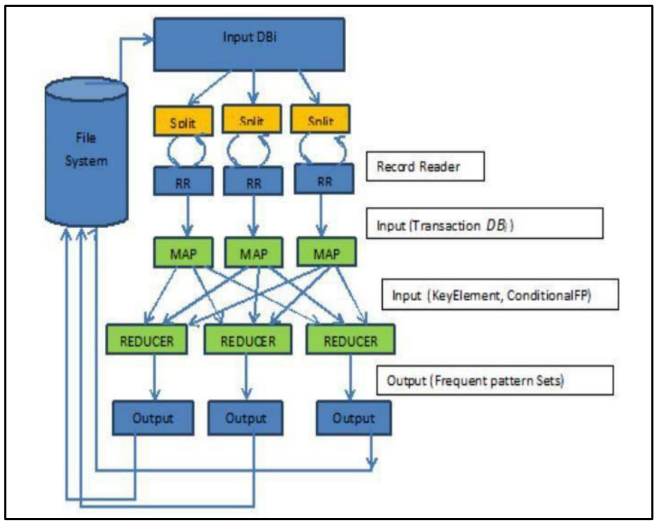


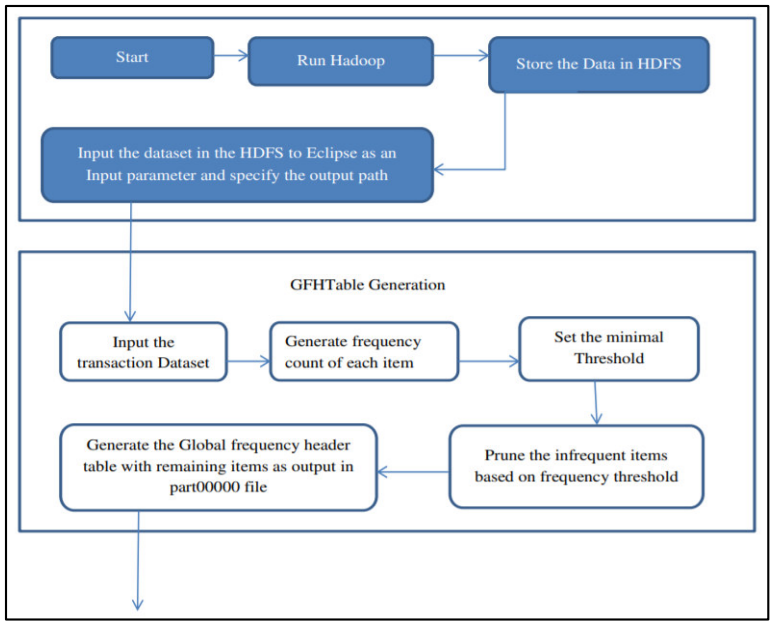
Fig.7. Architecture diagram of DPFPM algorithm using Hadoop MapReduce framework

Architecture diagram of DPFPM algorithm using Hadoop MapReduce framework

The input Data is splitted into several parts based on the size. A split is of 64MB (at most 128MB for very large data).When the size increases more than 64MB, the data goes for the next split. Data from each split is given as an input to the record reader. The record reader inputs to the mapper and the output of mapper is sent to every reducer. The reducer collects, shuffles and sorts the data and generates n outputs for n reducers. All these outputs are combined by Aggregator [2].

Design of the Program Flow

The flow of the program is as follows:



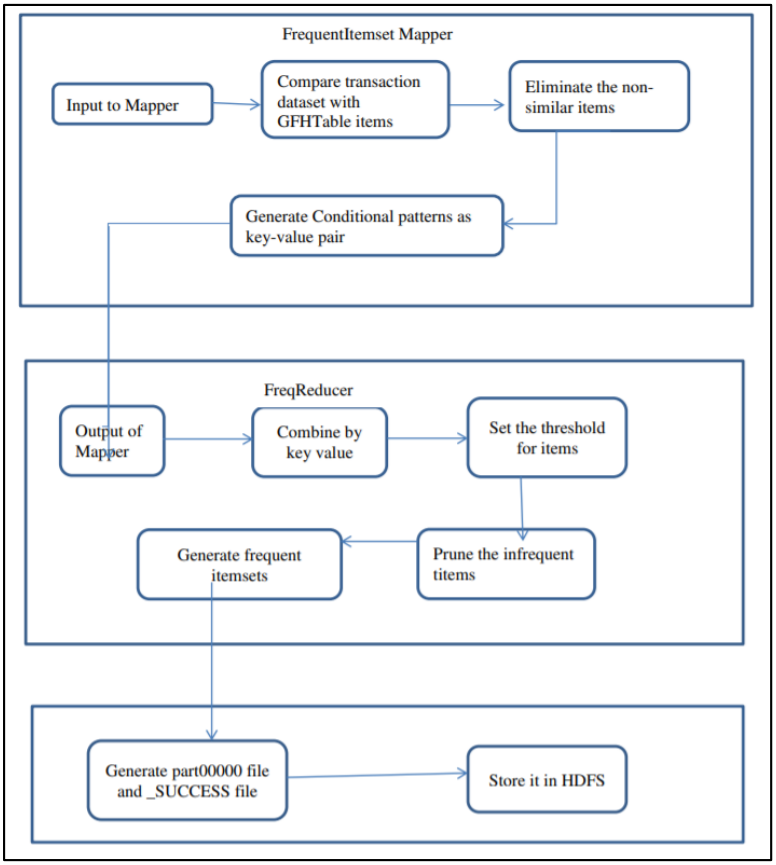


Fig.8. Design of program flow

Input-Output Specifications

Input:	Transactional dataset
Output of GFHT:	Items and their frequency count
Input to Mapper function:	Dataset, GFHTable
Output of Mapper:	Conditional frequent patterns
Input of Reducer:	Conditional frequent patterns, threshold value
Output of Reducer:	Frequent itemsets

IMPLEMENTATION AND RESULTS

As mentioned previously, the whole system is divided into various modules. The output of one module is given as the input for the next module.

This section clearly explains about each module and discusses how the flow of the project goes on along with the results.

MODULE 1: DIVIDING TRANSACTIONAL DATASET

Divide complete transaction dataset into number sub part so that each individual parts. Part is processed individually.
This task is done by the Hadoop Distributed File System.IT allocates 64MBfor each split and the size greater than 64MB goes into the next split.

Ds={D1,D2,D3**…….,D**P}

MODULE 2: CONSTRUCTION OF GFHT

Using MapReduce programming model, the frequent support count of each item is calculated that appeared in the dataset. Then entire locally constructed header tables are merged to generate GFHTable.
It uses two functions: Input-
Transactional dataset Ds
GFHT Mapper- outputs elements and its frequency count 1. GFHT
Reducer-sums up all the counts based on the element
Output- Item of transaction in dataset along with its frequency count.

Pruning of Frequent Itemsets

Once the frequency count of every item is generated, the items that are infrequent are to be eliminated. This is done by considering a minimal threshold frequency.
All the items that have less frequency count than the threshold are eliminated.
Proposed methodology used for constructing GFHTable reduces communication overhead to calculate support of all items. It first calculates frequency count locally of the mapper and then combines.This step effectively uses map and reduce functionality to speed up the operation of mining.

Algorithmic steps for construction of GFHTable

Step 1: Function **GFHTMapper** performs following steps taking transaction ó□ from DS as input.
foreach item from transaction Ti
output write element and its frequency count 1
Hadoop pass the Mapper output to number of reducers it creates.

Step 2: Function **GFHTReducer** performs following steps taking input as elements grouped by element
name
long sum = 0;
foreach element record
  sum = sum + element's frequency count
outputs from each reducer started by Hadoop stack, element name and its global frequency count

Step3: Function aggregator prune infrequent items from GFHTable based on threshold
 foreach element from GHTReducer
     if (element.frequencyCount>= □)
          putInGFHTable(element);

end foreach

Fig.8. Algorithmic steps for GFHT construction

When the program is executed, it generated an output folder which contains 2 files. 1.part00000- holds the output of Hadoop program

2._SUCCESS-specifies that the job is successful.

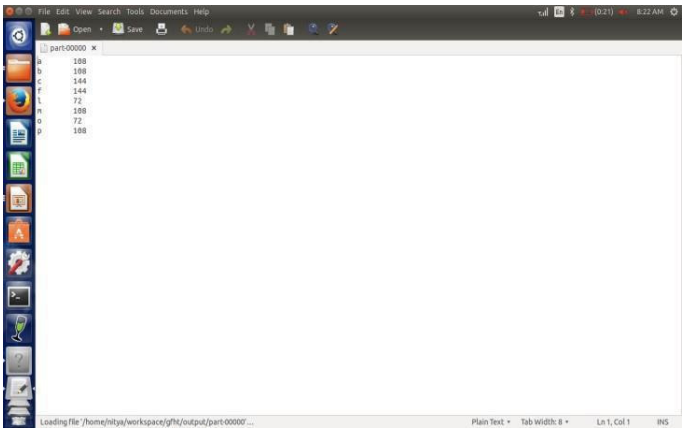


Fig.9. GFHT Output-part00000 file

MODULE 3: GENERATION OF CONDITIONAL PATTERNS

Here Mapper and Reducer per form different tasks than the traditional scatter and gather functionalities.
Here Mapper performs following steps:

i. It prunes the DSi transaction to inline the transaction items as per the available GFHTable.
ii. According to the available GFHTable, it process the transaction and output the key-value pair, where key is conditional element for which conditional frequent pattern set is constructed

Comparision of files

First, the transaction dataset is compared with the items of GFHtable.All the items that are not matching are eliminated. This is done to eliminate the infrequent items.

```
Phase1- Comparision for each
transaction from Ds Collect
pattern elements; for each item
of transaction if

(check If Element exists in GFHTable(element) Then

pattern Eelement.add(element);
}
Endif
```

Fig. 10. Comparision of files

```
Function FreqMapper

Input:GFHTable,Transaction dataset Ds
Output:Conditional Frequent Patterns Steps:
#phase2

#order pattern elements Using
support frequency Prune-
order(pattern elements); #Generate
Conditional patterns

generateConditionalPattern(patternElements); end

#Function-generateconditionalpatternsFor each
elemnt from pattern elements Construct
conditional pattern as key value

HadoopContext.write(element,conditional key-pair) endfor
```

Fig.11 Algorithm for comparison and FPM Mapper

Mapper function

The mapper function takes the least frequent item of a transaction as the first key and maps all the pattern and the loop is followed until the most frequent item is left with no pattern.
This is how the frequent patterns are generated.

Example:
Consider a transaction a,b,c,d,e (e being less frequent and a being more frequent) Conditional patterns for the above transaction are as follows:

e:a,b,c,d

d:a,b
,c
c:a,b
b:a
a:no
ne

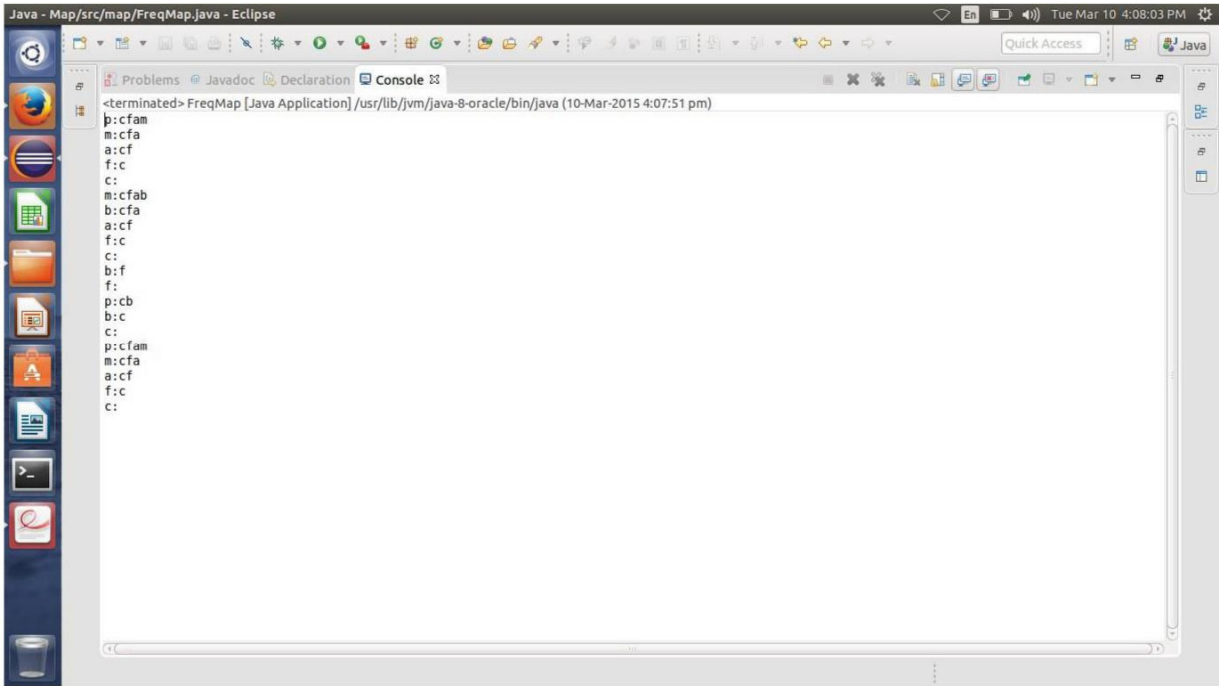


Fig.12. Mapper output-Generation of conditional frequent patterns

MODULE 4: GENERATION OF FREQUENT ITEMSETS

When all mapper instances finished their work of construction of conditional frequent patterns, MapReduce framework helps to group all corresponding conditional frequent patterns transaction over available key element for which conditional frequent patterns are constructed. The Reducer performs following step:

At each reducer instance, it combines the different conditional frequent patterns over the same element key and generates the frequent itemsets as an output.

Pruning

After combining all the patterns for each key, respective reducers do pruning of infrequent itemsets based on Threshold. Each reducer after pruning generates frequent sets for respective keys.

Each reducer after pruning generates frequent sets for respective keys locally at each reducer. This step reduces cost of Inter process communication as for each key frequent set.

For ex**ample first reducer collects all patterns based on element „a□ that is "a: {c, f} | {c, f} |{c, f}". Then it prunes infrequent items from the set**

based on □= 3.For first reducer "a:{c, f}" is frequent so no pruning is done. Finally

conditional patterns of a are generated as {a,ac,af,afc} are created as output .

```
Function FPM-Reducer
Input:Conditional frequent patterns grouped by key
Output:frequentitemsets

Foreach conditional pattern from the mapper output

UpdatcfpHead.intersect(conditionalapattern);
End if;

HadoopContext.write(gfrequentitemset);
endfor

Cfphead=new ConditionalFp(); If(first
conditionalpattern) cfpHead=contains
conditionalPattern; else
merge the already available pattern elements with incoming matched element patterns.

Increment the frequency counts based on the similar elements

HadoopContext.write(freqitemsets);
Endfor;
```

Fig.13 Algorithmic steps for Reducer function

Example:
For a transaction item a.consider the maps as a:c,b|c|b,c| and the threshold is 3.
Then the frequent itemsets are:
After pruning: a:{c}
Eliminating b as it has count=2<threshold(3)
Frequent iemsets: {a},{a,c}

Analysis

With the emergence of large data, Hadoop came into existence. MapReduce programming enables ease in th**e job of data processing. But the question can be arised that Can□t the programming be** done with Java alone? For this question to be answered, we have done analysis of the MapReduce job with the Java Program.

Analysis with respect to time

Initially, a normal word count program has been tested for analysis.
A word count program that counts the occurrences of each word is done using both MapReduce and Java programming.

A data file of 180MB is given to the program and is checked. The data file as input to java took 5min18sec approx. for generating the output. Whereas the same file when is given as input to MapReduce job, it took 1:40minutes.

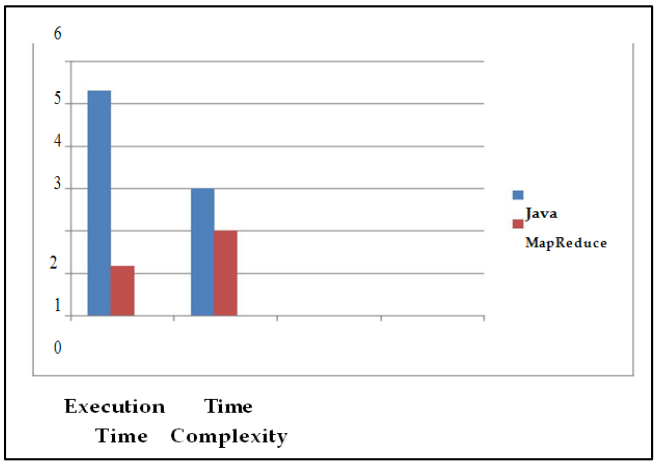


Fig.14 Analysis in terms of Time

Analysis with respect to size of Data-

We can also know from the below analysis that why Hadoop MapReduce programming is feasible for large data. Traditional languages show less performance results when considering the size of data. We have performed analysis by considering various datasets of different sizes, from Kilobytes to Megabytes.

The analysis is done in terms of Execution time, InputSplitBytes, GC time elapsed, Shuffled Maps, Merged MapOutputs.

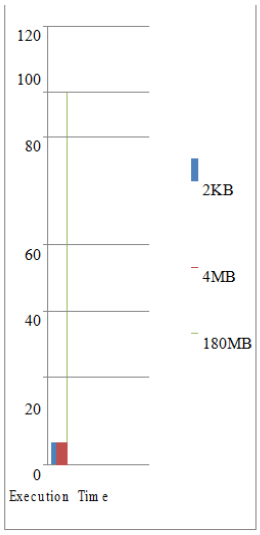


Fig. 15. Execution Time

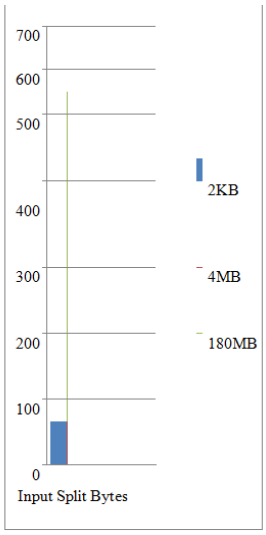


Fig. 16. Input Split Bytes

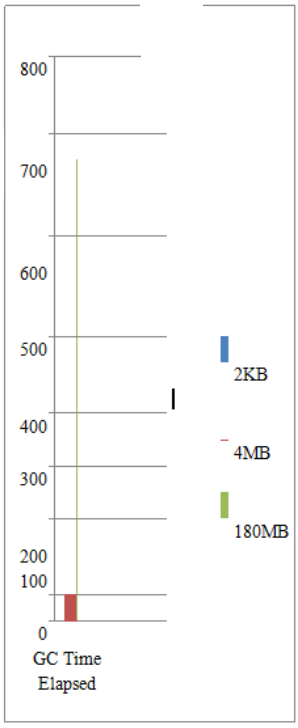


Fig.17 GC Time elapsed

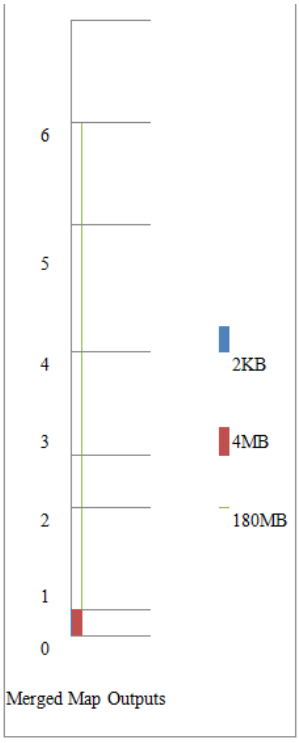


Fig. 18.Merged Map Outputs

Execution Time-

The total time that is taken to run a Hadoop job is referred to as its execution time.The main use of MapReduce programming is that ,when it is compared with other languages,it offers the best results in terms of Execution time. Map Reduce jobs offer comparatively very less execution time while working with large data

GC Time Elapsed-

It referes to the time that is elapsed by the Garbage Collector in Memory Management.This comes with the Mapper.The GC time elapsed will be high as the input data increases and the no of processing modules increase for a job.

Input Split–

It represents the data to be processed by an individual Mapper.

Typically InputSplit presents a byte-oriented view of the input, and it is the responsibility of RecordReader to process and present a record-oriented view.The Input Split Bytes increase with the increase in the size of data so that more the input splits, faster the processing is done.

Merged Map Outputs-

The outputs of the Mapper will be merged by the Reducer.More the splits,then more are the outputs of Mapper to the Reducer.Hence,large data require more mapper outputs.

Sample Input

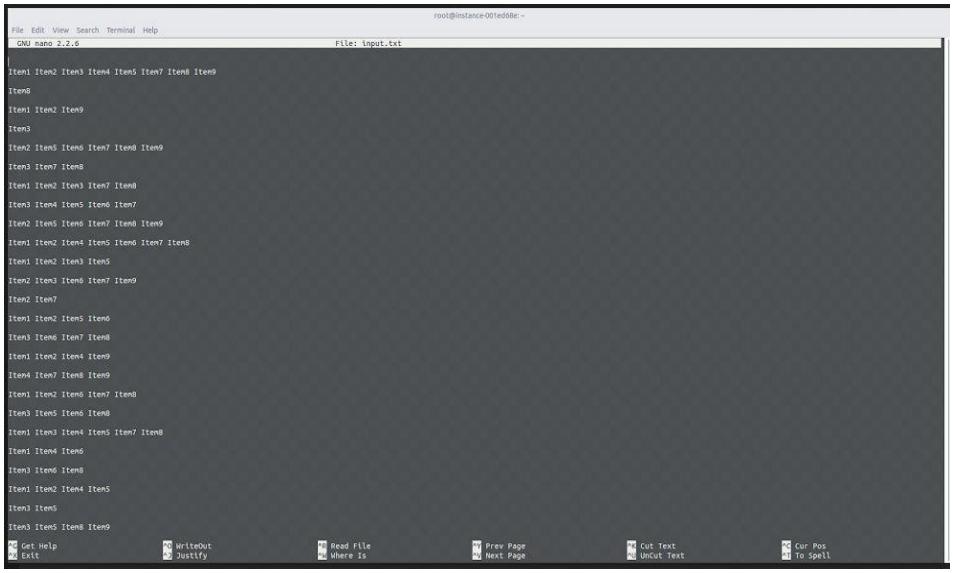


Fig.19. Sample Input

Expected Output

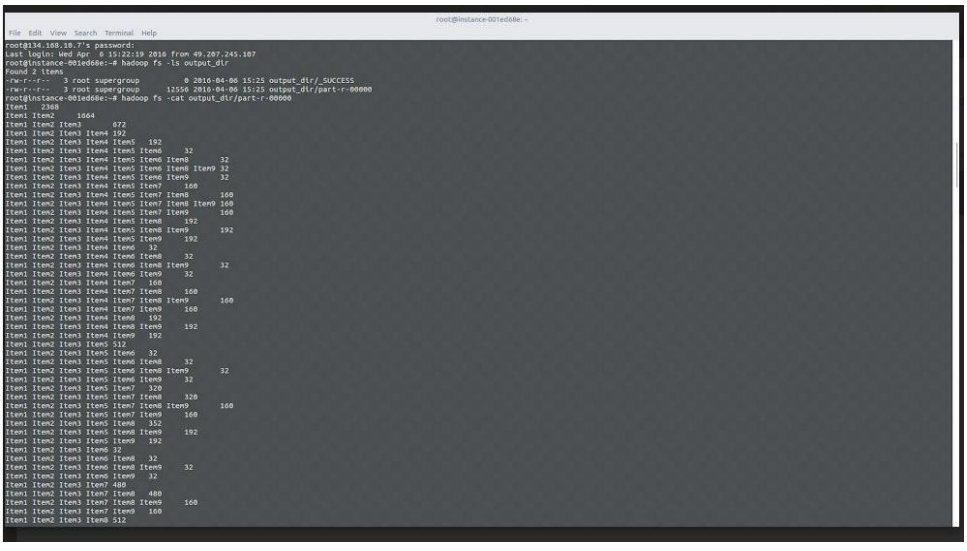


Fig.20 Expected Output

Executed Output

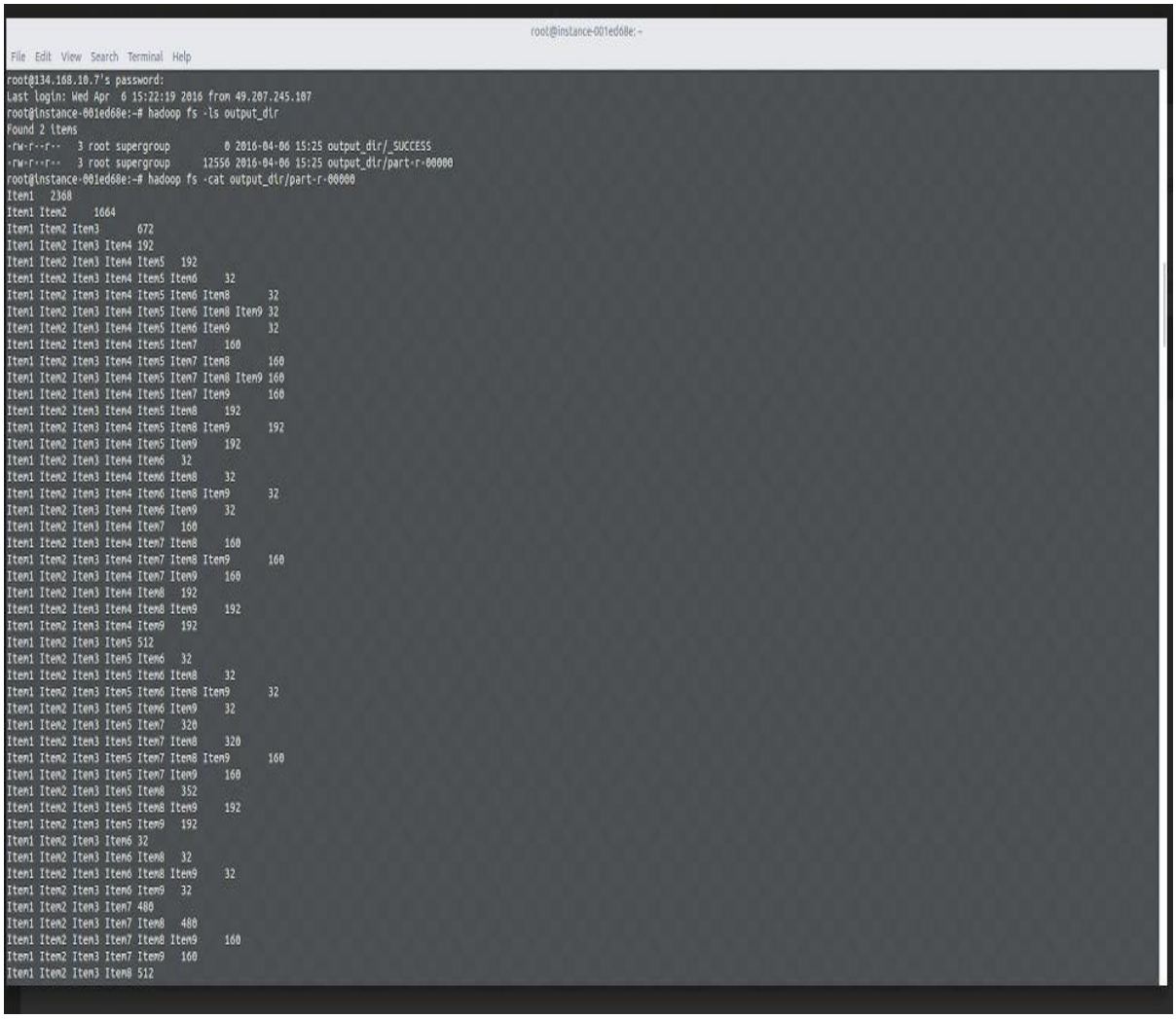


Fig.21.Executed Output

CONCLUSION AND FUTURE SCOPE

CONCLUSION

Proposed DPFPM algorithm shows best performance results for large datasets using Hadoop MapReduce framework. Proposed algorithm implement parallel processing for header table generation and mining frequent pattern both, speeding up the execution. Proposed algorithms partition/distribute the dataset in such a way that, it works independently and parallel. It performs task of frequent itemset generation by speeding up mining process. Experimental result shows that parallel and distributed algorithm efficiently handles the scalability for very large datsets.

FUTURE SCOPE

There are still some challenging research issues that need to be solved before frequent pattern mining can claim a cornerstone approach in data mining applications.Additional steps like pruning in the reducer based on threshold can be done to increase the efficiency and more frequent itemsets are generated.

It is important to go to the core part of pattern mining algorithms, and analyze the theoretical properties of different solutions. Much work is needed to explore new applications of frequent pattern mining. For example, bioinformatics has raised a lot of challenging problems, and we believe frequent pattern mining may contribute a good deal to it with further research efforts.

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RESEARCH ARTICLE

Diffusionof Solar Lights in South Odisha

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ABSTRACT

The objective of this paper is to provide a snapshot on the diffusion of solar lights in the region of South of Odisha. A case study analysis has been adopted to understand the diffusion process of solar lights. The case of decentralized rural electricity through minimum productive energy access is taken into consideration. The case is related to Kundra and Jeypur block of Koraput district of South Odisha. The study was undertaken by a cooperative, Pataneswari Agricultural Cooperative Societyand Centurion University based at the city of Jeypore and Bhubaneswar in the state of Odisha.

Keywords- Diffusion, Solar Light, South Odisha, Decentralized, Rural Electricity.

INTRODUCTION

To end poverty and safeguard sustainability are the important aspects in today's time. Energy is the solution to it. Energy in the form of electricity is an important dimension in country's economic growth. Absence to access to electricity retards the development of the region, state and country. It negatively impacts the economic development and standard of living. In today's era, the demand of electricity has rose drastically. India has become the world's third largest producer and third largest consumer of electricity (BP Report, 2016). With the increase in demand of electricity it has raised the concern of exhausting the reserves of coal, petroleum and other resources. Excavation of these non-conventional resources is causing harmful effect on the health of people and environment as well. According to a report in newspaper, every year 8 billion metric tonnes of carbon goes into our atmosphere, out of which 6.5 billion tonnes comes from fossil fuels and1.5 billion tonnes results from deforestation. These are not

compelling benchmarks in the context of providing quality of electricity to all. India needs to increase its energy base for its people as well as a provision to increase the share of clean energy in the overall energy mix. Clean energy through the use of decentralized products are the solution to it (WWF, 2015).

The objective of this paper is to provide a snapshot on the diffusion of solar lights in the region of South of Odisha. A case study analysis has been adopted to understand the diffusion process of solar lights. The case of decentralized rural electricity through minimum productive energy access is taken into consideration. The case is related to Kundra and Jeypur block of Koraput district of South Odisha. The study was undertaken by a cooperative, Pataneswari Agricultural Cooperative Societyand Centurion University based at the city of Jeypore and Bhubaneswar in the state of Odisha.

Decentralized Rural Electricity through Minimum and Productive Energy Access

About the Study

Koraput district is based at South Odisha with a population of about 14 lakh. About 84 percent of the total population of the district resides in rural areas. This study was undertaken in Jeypur and Kundra blocks of Koraput district which consist of 22 and 12 gram panchayats, with 125 and 85 villages respectively. Whole of the population of two blocks resides in rural areas (Census, 2011).

With 88 percent of the rural households in Kundra block and 67 percent of the rural households in Jeypur block using kerosene light for lighting purpose (Census, 2011), were facing health-related issues, sense of insecurity and danger of fire hazard. As a result, Centurion University and the cooperative, Pataneswari Agricultural Cooperative Society" (PACS) came together to implement the decentralized electricity system for the rural households in the area. "Pataneswari Agricultural Cooperative Society" (PACS) is basically a cooperative working in Jeypur and Kundra blocks of Koraput district dealing with agro forestry products. PACS intention was not to earn profit but rather to promote clean energy usage. The reason for supporting the cooperative was, although the members of the cooperative were getting enough profit from agro-forestry activities, but still they did not have access to modern energy services which was important for improving quality of life. Further the cooperative also decided to open a clean energy vertical through the use clean energy products where it could provide clean energy solutions to its members as well. Kashyap (2012), focused that cooperative can act as new model of distribution for marketing of products into the rural areas. Cooperative management can effectively deliver electricity services to rural areas, achieving greater operational efficiency and improving customer service (ibid). Every product can also be distributed into the rural markets with the help of self help groups (Ramanathan, 1993) as well. The primary objective was to implement a decentralized electricity supply system by the use of solar lights in the rural areas. Decentralized electricity supply system refers to those systems which are not connected to the central electrical grid and are usually underserved by the grid as well. These system ranges from 2 kW to 100 kW. Example of these systems includes solar study lamps, solar lanterns, solar home lighting systems, etc.

A comparison study of different solar lights available in South Odisha was conducted. These included D-Light, Green Light Planet, Bajaj, BPL, RAL, Eureka Forbes, Reliance and FOSERA. Based on the technical features, lumen, storage capacity, operational experience in knowing the services and price it was observed that, FOSERA (PSHS 3200) fitted best for the rural consumers. As a result, FOSERA was introduced to the rural consumers. It was manufactured and supplied by Auroville Energy Products (AEP), Pondicherry, India. FOSERA had two LED lights, one battery and one solar panel. It provided lighting from 6 to 10 hrs in different modes with one-day charging. The product was designed to be affordable for economically sensitive rural consumers and communities. The product introduced was a plug and play type and was virtually unbreakable. It did not require any complicated installation process and can be used without any technical knowledge. This would substantially increase the acceptance rate among the members. In addition, to it the electricity source did not harm the end user. The product also offered the possibility of charging mobile phones. The usage of mobile phones in remote areas was strikingly going high, and

was going beyond the rate of electrification. As a result, the members took enormous efforts to re-charge their mobile phone batteries (often in bulk) and other communication devices to other houses where electricity was available. Sometimes they also go to local shops to recharge their mobile phone batteries and are charged between Rs 5 to 10 per 30 mins charge and some of them even travel miles for charging. With the members facing such problems, it was decided to go for introducing the FOSERA (PSHS 3200) to all the members of the cooperative. With this, the procurement of FOSERA (PSHS 3200) was carried out by PACS from Auroville Energy Products (AEP) based at Pondicherry.

For implementation of the diffusion process, interaction with all the members of the cooperative was conducted. Local youths, key opinion leaders of the area were also involved during the interactions. Interactions through meetings for creating awareness, understanding the benefits of adopting the solar lights and also to develop a sense of consensus for adopting the solar light among all the members was carried out. After discussion, it was observed that apart from the existing activities, there was also potential for the use of solar lights in other activities as well. Activities such as tailoring, bamboo works units, carpentry, dairy farms, pan shop, tiffin stalls, dairy farms, jaggery manufacturing units, roadside eateries, etc. where solar lights could be used. These were in addition to mobile vendors, retail stores, bicycle and auto repair shops, and poultry sheds. It generated the idea that solar lights can address income generation activities.

Workshop and training programs on technical and managerial aspects, financial viability were conducted on the benefits of adopting solar lights. The training programs were provided to all the 21 community service providers (CSP) of PACS. CSPs were earlier working in the community in the field of agro-forestry, agriculture and livestock and were being paid by PACS. For promotion and awareness of solar lights, the products were fixed in the office of the cooperative, where people would come and observe it working. Explaining and demonstrating the use of solar lights to the Self-Help Group (SHG) members at the village level during their weekly meetings, preferably in evenings was also conducted by the CSPs for the diffusion to take place. Door to door demonstration and campaign of the product and comparing it with kerosene lamps and sharing the experiences through photographs was also carried out by the CSPs.

For an easy payment process, the product was bought and given to the members through instalments on a monthly basis. PACS lend the product at the rate of 16 percent per annum to the beneficiary which was effectively recovered by the CSPs within 3 months. The landing cost of solar light at PACS was Rs 2900, out of that down payment of 30 percent of Maximum Retail Price (MRP) was done (30 percent of Rs 3500) Rs 1050 was paid by the beneficiary to PACS and the rest (70 percent of Rs 3500) Rs 2450 was paid in 3 months on installment basis. Out of Rs 2450, the CSPs were paid Rs 500 as incentive towards mobilizing and recovery of the cost from the beneficiary and Rs 100 was kept as interest by PACS. The incentive to the CSPs was only paid when the entire installment was recovered and was paid to PACS. This motivated the CSPs to sensitize people to go for adopting solar lights and close the financial cycle as soon as possible. With the incentive mechanism in place, these 21 CSPs ventured into solar business in addition to their present work and were further called as Clean Energy Entrepreneurs (CEEs).

In addition to this a solar energy pprogramme card was designed for keeping track of payment of the instalments being paid by the members. The card was prepared in two colors, one in green and other in yellow colour. One card was maintained with the CEE and the other card was kept by the member, bearing the same serial number. To keep track of the progress made, it was also decided to conduct a review meeting with the CEEs on a monthly basis for target planned, achievement, query regarding the product if any and repair and maintenance. The meetings were held in the cooperative office. In order to provide after sales-service, the CEEs were also trained on service, repair and maintenance of solar lights. Training materials were provided to the CEEs in the local language, along with the audio-visual tools for easy understanding. Emergence of CEEs helped in establishing an effective supply chain for product and service delivery. Resource person from Centurion University and the researcher were engaged for conducting the technical and managerial workshops and training.

For diffusion of solar lights into the rural areas, a participatory method was adopted involving all the stakeholders. From the diffusion process, all the members of the cooperative started using the solar lights. Four members used the light both in their homes and in poultry-sheds and other two members used it in the grocery shops. Solar lights were also used during the evening time for study purpose by their children and cooking purpose as well. Focused group discussion was carried with the members of the cooperative for understanding the impact of use of solar lights.

In the study, the principle generally involved was sensitizing the local youth to start their own business thus creating a sense of becoming an entrepreneur and the use of solar lights for income generation activity. Solar lights were used in the households, with income generating potential starting from tailoring to roadside eateries. It was also used in poultry sheds, protecting the chicks from snakes and wild animals. Solar lights were also used in tea stalls, vegetable vendors, farmer's fields, variety store, medicine store, cloth store etc. In relation with the application of the framework a process flow diagram has been devised (Fig 1.).

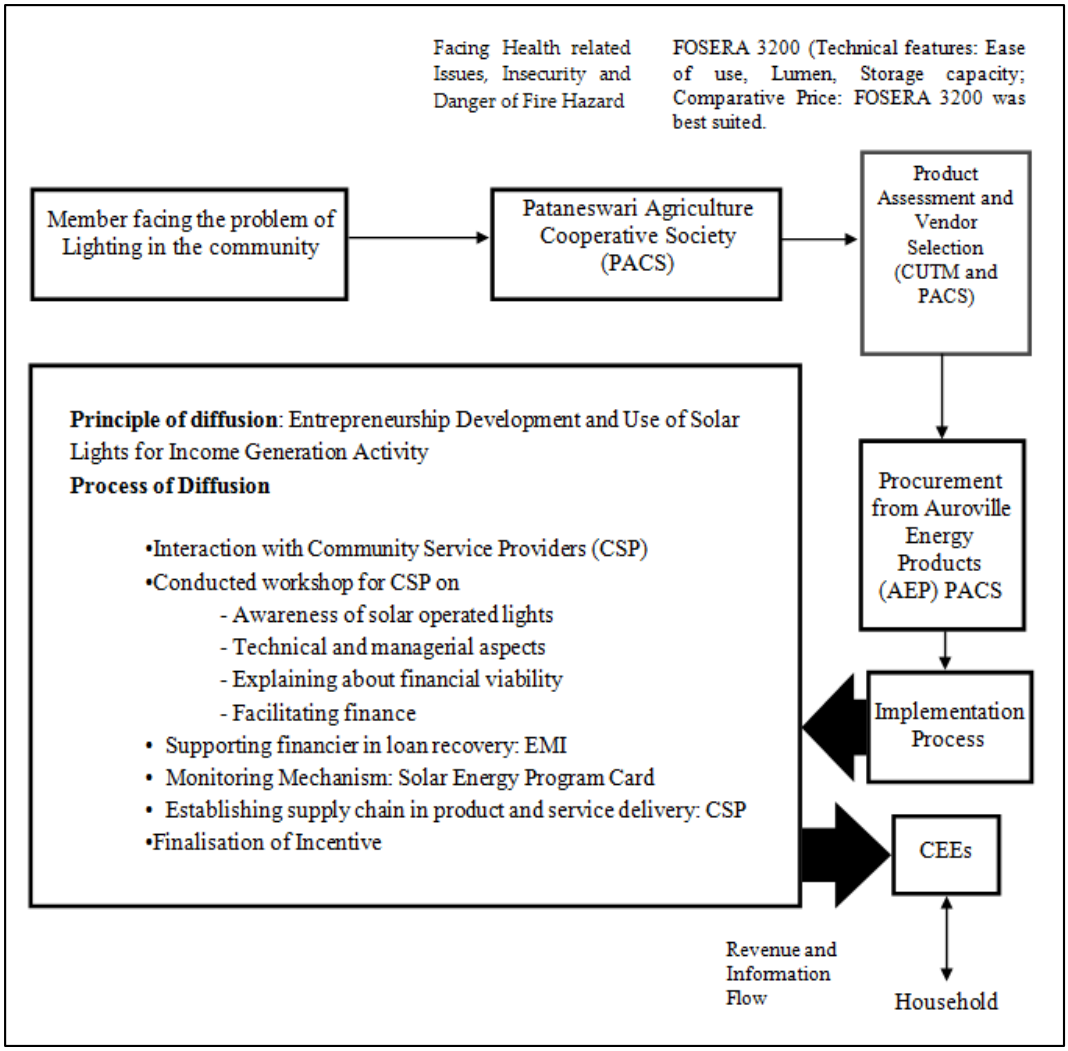

Fig 1. Process Flow for Decentralized Rural Electricity through Minimum and Productive Energy Access

From the above process flow diagram, Pataneswari agriculture cooperative society (PACS) was the implementing agency. PACS with the support from Centurion University conducted the product assessment, selection of vendor and implementation. The major role was played by the implementing agency PACS on implementation aspect. Factors such as technical features of the product, cost of the product, availability of the customized product, ease of use, demonstration of the product, payment through Equated Monthly Installment (EMI), repair and maintenance by CEE, incentive to CEE, were some of the important factors which helped for the diffusion to take place. For successful diffusion of solar lights into the rural areas there was a need for a strong stable supply chain with an innovative financing and recovery mechanism. It was fulfilled by the presence of a go down or a warehouse with availability of spares parts of solar lights.

Provision of training to CEEs on service, repair and maintenance of the product and a designated toll free number was in place for helping the members for quick and service delivery. With the introduction of EMI options and the use solar energy program card, it was easier for the rural consumers to pay for the solar lights and track their payment, which act as an effective monitoring mechanism. Involvement of all these actors and factors helped in the diffusion of to take place.

Impact of Use of Solar Lights

This section of the paper focuses on the impact of use of solar lights by the members of the cooperative. To understand the impact of use of solar lights, Focused Group Discussions (FGD) was held with the members of the cooperative with the involvement of CEEs and officials of PACS. Focused group discussion was held in the PACS office based at Jeypore, a small town based at South Odisha. Focused group discussion was held with the members from Limma village of Kundura tehsil. From the discussion it was found that during the day time they go for daily wage work, and in the evening, after they installed solar lights, they were able to carry out different household chores which were difficult for them to carry out in kerosene lighting. They started making plates out of leaf, making puffed rice, grinding of rice, etc. They sold leaf plates in local haat which helped them in rise of their income. One of the member shared that he carried the solar light in evening to go to toilet, which was earlier difficult with kerosene light. Women of the house were able to cook food comfortably during the evening time as well.

Focused group discussion was held with the members from Dangarpaunsi village of Kundura tehsil. From the discussion it was found that, after they installed solar lights their kerosene consumption had reduced. One of the member said that he was able to save Rs 100 in the earlier month after installing the light. Other members shared that they have totally stopped buying kerosene from market and the money which they were spending in buying kerosene, now they buy other necessary items for their home. Focused group discussion was held with the members from Konga village of Jeypur tehsil. From the discussion it was found that after they installed solar lights they could look after their domestic animals like chickens, goat, sheep, cows, etc. better during evening time due to availability of the light. Member shared that after installation of the lights there was no fear of attack by wild animals. Their kerosene consumption was also reduced and their children also started reading during evening time which was not carried out earlier. One of the member shared that his child had secured 74 percent in the recently concluded examination held in his school.

Focused group discussion was held with the member's fromBagderi village of Kundura tehsil. From the discussion it was found that after they installed the solar operated light, their kerosene consumption has reduced. Earlier they used to buy 6-8 liters of kerosene per month but now they only bring 2-3 liters per month. Due to better lighting condition they were able to spend more time in making bamboo artifacts, carpentry and milking of cows during the evening time. They now sell their bamboo works in local market and also do participate in different events, meals and showcasing their products and selling it. This has helped them in improving their income as well. They now sell milk and other milk products during evening time in the local haat and also deliver it to nearby villages. Earlier they used to earn Rs 500-800 but now with more people coming to buy milk and other products during the evening time

their income has rose to Rs 1000-1400. Focused group discussion was held with the members from Ananta village of Jeypur tehsil. From the discussion it was found that, they have installed solar lights in their homes and poultry. Some of the members were using it in the food stalls. Earlier due to poor lighting in food stalls, it attracted more insects and flies which made the food unhygienic. Now with the installation of solar lights there is a reduction in insects and flies. With better lighting they could able to sell the food items till late evening, which helped them in increasing of their income. Now food is being served in a more hygienic way. During the discussion, it was also found that one of the members from Ananta village, who was differently abled, has opened a small kirana store in his locality and is using solar light for lighting purpose. He is now able to open his store till late evening, selling different items, thus earning his livelihood.

Focused group discussion was held with the members from Badajiuna village of Jeypur tehsil. From the discussion it was found that after using the solar lights their kerosene consumption has reduced. After interacting, it was found that solar lights were also used during marriage ceremony and other social gatherings during evening time. Social gathering like dancing and singing took place during evening time where they used the solar lights. They also used the lights in their fields and in poultry sheds. People were able to move freely during evening time due to better lighting. One member said that, earlier snake and insect bites was common but with the use of solar lights such incidents have reduced. No such incident has happen from last 2 months. This has led to achieve better health condition.

Focused group discussion was held with the other members from Balia village of Jeypur tehsil. They basically earned their living through poultry farming. It was found that they replaced their kerosene lights with solar lights in the poultry sheds. As a result, there was a reductionof mortality of chicks, better feed conversion ratio and the chickens were sold in higher price between Rs 220 to Rs 350 per kg in the village market. Similarly, few other members shared that after they installed solar lights they were able to open their shops till late evening. A member having a cycle repair shop shared the experience that he is now able to open his shop till 8 PM, earlier he used to close during evening hours. He has also employed another person in his shop for helping him in cycle repairing and doing other activity, thus helping in employment generation and earning livelihood.

Similarly, a widow for her living was doing tailoring business in Kerimity village of Kundura tehsil. Unavailability of electricity forced her to depend on the use of kerosene for lighting purpose. She was afraid that the use of kerosene might damage the cloths, result in poor workmanship and there was a danger of fire hazard. But after she started using solar light it resulted in quick delivery of the cloths, having good workmanship and was able to work for longer duration during the evening time. This helped her in increasing of her income. With the installation of solar lights multiple activities were carried out for income generation. Table 1. gives the details of such activity undertaken by the different rural consumers after adoption of solar lights in Kundura and Jeypur block of Koraput District.

Till date more than 1600 number of solar lights are being used by different vendors and 517 number of solar lights are being used in poultry sheds across Kundura and Jeypur block of Koraput district of South Odisha.

Recommendations and Conclusion of the Study

Based on the process of implementation, community interactions carried out with the members of the cooperative and findings from the case study this section of the paper focuses on the recommendation and conclusion for diffusion of solar lights in South Odisha. Use of Local Resource: Although organizations do have access to the rural areas, but they find it difficult to sale their products into the rural areas due to varied reasons, starting from understanding the perception of their consumers whether to buy the product or not, to price of the product, place of its availability and promotion of the product. The possible approach to overcome this problem is to use the local

resources available in the region. Use of local resources basically focuses on involving local opinion leaders, youths of the village, local shop owners, etc. present in the area. It should also focus on the use of solar lights for local value addition.

NGO, Cooperatives and SHG to act distribution channels: Manufacturers, marketers and others find it difficult to access to remote areas to sale their product and services. They become reluctant to build-up a distribution network if they cannot secure a certain amount of sales volume to justify the investment in the first place. For achieving the same they need to diffuse their products, components, services to the rural consumers by involving the members from the cooperative and SHGs present in the local area. Cooperatives and SHG can directly approach the manufacturers, marketers to procure and sell their product to the consumers as well. They need to be made part of their distribution channel so as to achieve a last mile delivery of their product and services to the rural consumers. They should be given incentive or should be made a part of their decision making process pertinent to fixing of margin and pricing of the product. Exposure of the product to women through SHG intervention will affect the purchase decision, thus helping in the diffusion of the product. Here the SHG members can become the selling agent for the rural retailer as well.

Formation of JGLs: The formation of joint liability groups (JLGs) for taking group loans can help in the diffusion process as well where SHG is not feasible. Five to eight members can be mobilized for formation of a joint liability groups (JLGs), who can apply for group loans. There are some reasons for forming JLGs instead of seeking individual loans. Firstly, the branch of the bank will be under pressure for processing individual loans applications and it will be time consuming. Secondly, JLGs automatically could create peer pressure for everyone within the group to pay their share every month. Third, instead of each member going to the bank every month, the members can share that responsibility among each other. Finally, when the members have more income in certain seasons, they can have the option of depositing more money in their JLG accounts, in order to save up for the times when their incomes might be low. Here the branch manager of the bank, needs to be instrumental in facilitating the loans, and should be keen on financing more innovative livelihood initiatives. With getting of loans, the members can buy solar lights, components, systems from the producer directly, which will be sold to end-users to earn revenue. With the cash collected from the end-users, a member can go on buying more solar operated products and getting into a healthy cycle of buying and selling process. Eventually, once the business is well established, the loans have to be paid back with the interest amount.

Product Rent Model: The product rent model needs to be undertaken when the rural consumers when cannot afford high priced solar operated product. They can rent the product to other consumers for specific amount, on hourly basis or on day basis. This model can generate income for the rural consumers and helping in repayment of loans. Demonstration and creating awareness on the benefits of using solar operated products needs to be undertaken among the rural communities for successful diffusion to take place. Raising awareness among the bankers, lenders, donors, MFIs, other private sectors institutions, etc. needs to be undertaken for achieving diffusion. Pursuing international agreement and commitment to achieve the goal of universal access to clean energy needs to be prioritising as well. All the above recommendations will help creating successful diffusion of clean energy products into the rural areas, thus bringing in an inspiring and galvanizing effect in forming a movement for change.

CONCLUSION

From the study some factors were found out which are necessary for diffusion of solar lights in the rural areas. Use of local resource, involvement of cooperative was very much essential for the diffusion to take place. Lastly, all the stakeholders coordinated, cooperate and collaborated with each other so as to achieve diffusion of solar lights in the areas of Kundra and Jeypur tehsil of South Odisha. This not only led to the diffusion of solar lights but also was accompanied with service delivery as well.

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Table 1: Solar lights used for Income Generation Activity

Sl.No	Nature of Income Generation Activity	Number of Users
1	Small shops	716
2	Small eating stalls	577
3	Poultry shed	517
4	Daily market, Pan shop, Chicken shop, Barber shop, Garage etc.	55
5	Medicine store, Variety store, Cloth store	45
6	Farmers Field	64
7	Manufacturing of Agro-Forest Products	31
8	Miscellaneous	33
	Total	**2038**

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RESEARCH ARTICLE

A New Adaptive Filtering Technique to Estimate Common Oscillatory Modes in the Power System Utilizing the Approach of Rotational in-Variance

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ABSTRACT

The dynamic changes in the frequency of power system, needs to be estimated for improving the damping of oscillations. In this paper, we propose a new approach of Least Means Squares Sign Sign Error (LMSSS) with Total Least Square Estimation of Signal Parameters Employing Rotational Invariance Technique (TLS-ESPRIT), in order to reduce the oscillations and estimate the low-frequency oscillatory modes. The proposed estimation scheme LMSSS-TLS-ESPRIT is compared with other schemes such as TLS-ESPRIT, LS-ESPRIT, and ESRIT methods for analyzing the effectiveness of the proposed LMSSS-TLS-ESPRIT method. The robustness of the proposed estimation scheme is checked using Monte-Carlo simulations. The Kundurs two-area system is used to analyze the performance and efficiency of the proposed approach in practical test system .It can be seen from the results that the proposed approach accurately estimates the inter-area modes and reduces its mean and standard deviation(SD) to a minimum value as compared to the aforesaid algorithms.

Key words: Common mode oscillations, ESPRIT, Adaptive LMS filter, Sign-Sign, Noise Cancellation

INTRODUCTION

Aims and difficulties

Nowadays the advancement of power system is considered based on the up gradation of interconnected regional power networks. The distributed power resources of different areas are efficiently utilized by the wide-area interconnected system. The wide area interconnected system is also useful in optimizing the energy resources allocation [1].Low-frequency oscillations (LFOs) or inter-area oscillations (IAOs) ,experienced by the interconnected

systems when subjected to load shedding, line outage, line-to-ground fault, are a matter of concern since these oscillations can cause stability issues on the interconnected lines, and can also inevitably limit the interconnected ability of the power system. Hence it is necessary to record the dynamic behavior of the interconnected power system and stabilize the oscillating modes by using appropriate damping strategy. Using Small Signal Stability Analysis (SSSA) [2], the IAOs modes are obtained by linearizing the entire system to a particular equilibrium point and then representing the system by proper state equations. The limitation to the linear approach is that it fails to linearize the entire system during the occurrence of large disturbance Therefore; it becomes essential that the IAOs modes are identified directly from the measured signal [3].

Literature review

The application of wide area measurement systems (WAMSs) in the power system has increased tremendously in the last couple of years. It gives high accuracy in both the off and ontime estimation of IAOs .The on-line approach for estimation of IAOs is measurement based and is classified as non-parametric and parametric methods. The non-parametric approach normally estimates the parameters of a given signal directly from the measured signal data, whereas in the parametric approach the approximate model of the measured signal is first obtained and then the parameters from the signal data available are estimated.One of the most commonly used non-parametric approach for spectral estimation is the Discrete Fourier Transform (DFT). The performance of DFT is limited to the periodic signals of finite length and stationary behavior. The sliding mode version of DFT, called as Short-Time Fourier Transform (STFT), allows the linear representation of the time-frequency model of the signal. The challenges with STFT is that it suffers from time-frequency resolution problem due to its sliding window operation. Fast Fourier Transform (FFT) is another popular non-parametric approach, which allows fast and easy implementation and is less sensitive to the outliers. Irrespective of this benefits it has limitations due to spectral leakage as well as suffers from frequency resolution problem with short data points. Wavelet Transformation (WT) [4], [5], is another time-frequency estimation approach which has a behavior similar to that of band-pass filter. The variation in window size is one of the benefits of WT which gives the provision of multi-resolution capability for both slow and fast frequency response. But due to its interpretation complexity and high computational burden, the application of WT is limited. Another polynomial approach based parametric method is Prony Analysis(PA), in which the roots of the polynomial are averaged and has low-resolution issue when the noise level is low. Although this method provides poor estimation for changes in data length and placing but with Improved Prony and Modified Prony we can achieve estimation of complete signal parameters from a given sampled sequence i.e frequency,phase, amplitude, damping ratio, and attenuation factor [6], [7]. One of the drawback of all these approaches is that they require substantial computational time and have issues related to signal correlation.

Unlike the above methods there is another parametric approach which is widely used for IAOs modes estimation as it directly estimates the noise and signal subspace from the measured signal and this approach is based on the subspace identification technique(i.e., noise and signal subspace). A recent most powerful subspace approach for estimation of IAOs modes are the variance of Estimation of Signal Parameter using Rotational Invariance Technique (ESPRIT) [8], [9]. The effectiveness of the ESPRIT, Least Square-ESPRIT (LS-ESPRIT), Total least Square-ESPRIT (TLS-ESPRIT), Modified TLS-ESPRIT is in their relation to time-frequency resolution, low sensitivity towards noise and rapid computational time. Apart from all the benefits ESPRIT have its limitations w.r.t. The number of frequency components, variation in SNRs (low SNRs), the presence of outliers and non-linear trends in ambient data. In order to reduce this we propose a new adaptive LMSSS filtering based TLS-ESPRIT approach for estimation of low-frequency modes.

Contributions and novelties

Accurate and effective mode estimation can be done if the measured signal from Phasor Measurement Unit (PMU) is maintained noise free but this is impossible due to presence of sensor network, lightning, hardware fault,

electromagnetic fault and man-made fault. Further due to the presence of outliers higher order harmonics as well as unwanted spikes are formed in the signal. The proposed approach efficiently reduces the effect of coloured noise and compacts the energy contained in the signal to its maximum by breaking the sample into a set of eigenvectors of its correlation matrix. The inter-area modes are calculated by the TLS-ESPRIT approach 1st and 2nd rotational shift in-variance properties to estimate the inter-area modes.

Paper layout

The rest of the paper is arranged as follows. Section II gives a review on the low-frequency oscillation problem occurring in power system with the proper signal model. Section III reviews the configuration of adaptive LMSSS filtering approach. Section IV describes the proposed LMSSS adaptive filtering approach used for modes estimation in power system. Section V gives the TLS-ESPRIT approach for complete error minimization. Section VII gives a conclusion to the paper.

INTER-AREA MODE ESTIMATION PROBLEM IN POWER SYSTEM

The proposed method evaluates the low-frequency mode of power system by using LMSSS adaptive filtering and TLS-ESPRIT. The proposed estimation method uses a signal model which is a linear combination of exponentially damped sinusoidal signals with AWGN.

Signal Model for Power system

The analysis of proposed approach is done with the signal obtained from the real power flowing in the tie-lines of the Kundurs two area test system. let us express this real power in terms exponentially damped sinusoids x(n)

$$x(n) = \sum_{i=1}^{p} \mathrm{a}_i e^{j(2\pi f_i n + \phi_i)} \quad \text{.....(1)}$$

Where *ffig* frequencies and *faig* amplitudes are deterministic values. The *fΦig* phases are uncorrelated random quantities, spaced uniformly over (0; 2π), whereby *fbkn g*is the attenuation parameter and *K* is the total number of sinusoids. Ifthe sinusoids are affected by a zero-mean AWGN *!*(*n*) serieswhere *E*[*j!*(*n*)*j*2] = *σ!*2 . Components consist of signal andnoise can be expressed as:

$$y(n) = x(\mathrm{n}) + \omega(\mathrm{n}) \quad \text{.....(2)}$$

Effect of outliers in power system

The building of automated, interconnected regional electric power networks results generation of diverse and Complex outlier data in the power system. Major causes of outlier are as follows [10].

1) Signal acquisition capability: The limited potentiality of the sensors and WAMSs.
2) Power system Failures: The power system failures such as transmission line outage, faults in the transmission lines.
3) Human influences: The involvement of the human in signal measurement. Nevertheless, for a single out-of-scale measurement, the sample means of the estimation can be affected when the data sequence includes the outliers.

LMSSS ADAPTIVE FILTERING

Adaptive Noise Cancellation Configuration

The key purpose here is the subtraction of the AWGN n_0 from the primary sensor output $s + n_0$. That is achieved by creating an adaptive filter, such that n_0 from n_1 can be estimated. A primary sensor is aligned to capture the s signal, and a secondary reference sensor is configured in such a way to capture the signal n_0 from the same source. Fig.1 presented the noise signal as n_1 [11]. It is assumed that the n_0 and n_1 noise signals are closely associated since this originates from the same sources.

LMS Sign-Sign Algorithm

This is a variation of the LMS sign algorithm, while the LMSSS is the updated version of the regular LMS algorithm. Instance at which its required to implement fast and easier hardware interface, for example digital signal processing devices and other integrated circuits, their preference is given to LMSSS. LMSS implementations need less cycles of computation, compared to the RLS algorithm. The LMS sign function into the standard LMS method, the process are used to develop the LMSSS method. LMSSS error slow or fast reduction depends on the step length. The LMSSS algorithm can be written in v The LMSSS approximation could be provided by the process that uses the standard LMS algorithm with *sign* function. The key approximation of this weight-updating algorithm is given below:

$$sign[x(n)] = \begin{cases} -1, x(n) < 0; \\ 0, x(n) = 0 \\ 1 > x(n) > 0; \end{cases} \quad \text{.....(3)}$$

$$w(n+1) = w(n) + \mu sign[\mathrm{e}(n)]x(n) \text{.....(4)}$$

The $x(n)$ vector includes the data input, the error is $e(n)$the weights added to the filter coefficients are the vector $w(n)$, and is the step length. The LMSSS error may be gradually or rapidly minimized depending on the step size. μ will be inside $0 < \mu < \frac{1}{N\{\text{Inputs Signal Power}\}}$ to maintain strong stability and convergence.

THE POWER SYSTEM MODE ESTIMATION USING LMSSS ADAPTIVE FILTERING

Fig.2 displays the key steps required while estimation of the LFOs using the LMSSS adaptive filtering based on TLSESPRIT. The approach proposed here uses a set of new *N1*samples from the PMU via Phasor Data Concentrator (PDC),which are further passed by a down-sampler via a low-passAdaptive FIR filter. Even though the extracted signal is lessdistorted but it is an ambient signal, the existence of highnoise level causes difficulties in mode extraction. The mode estimated by the adaptive filtering process using LMSSS,and afterwards the SD for estimated modes is minimized by adding the TLS-ESPRIT. To estimate the exact number of the signal parameters, the order of the signal must beproperly approximated. The proposed approach uses SVD toalgorithm must be streamlined on the basis of the above objectives as well as the value to be assigned to using the sign function. Use approximate to a lower-rank of the auto-correlation matrix $\Re$ as in [12] and index is described as:

$$K(\mathrm{i}) = \left[\frac{\sigma_1^2 + \sigma_2^2 +, \ldots, +\sigma_{\mathrm{i}}^2}{\sigma_1^2 + \sigma_2^2 +, \ldots, +\sigma_{\mathrm{i}}^2}\right] \text{.....(5)}$$

where monotonous increase index given by $K(i)$ and σ_i is the singular value of i_{th} As I corresponds to the actual order of signals, as the $K(i)$ reaches unity. This index is used to figure out the sequence of the signals.

TOTAL ERROR REDUCTION BASED ON TLS-ESPRIT APPROACH

Y(*n*) describes the sinusoidal components obtained from the low-pass filter based adaptive filtering of a test signal vector *N*1, is given below:

$$=[\mathrm{y(n)},\mathrm{y(n+1)},...,\mathrm{y(n+M-1)}]^{\mathrm{T}}=\mathbf{x}(\mathrm{n})+\mathbf{w}(\mathrm{n})....(6)$$

Where the signal vector is **x**(*n*), and where the noise vector is **w**(*n*). It is seen that **Y**(*n*) can also be represented in the form of a "v" time frequency window vector.

$$\mathbf{Y}(n)=\sum_{i=1}^{p}\mathrm{a}_i\mathrm{v}(f_i)e^{j(2\pi f_i n+\phi_i)}+\mathbf{w}(n)=\mathbf{V}\Phi^n\mathrm{A}+\mathbf{w}(\mathrm{n})\ldots\ldots(7)$$

where the *p* columns of matrix **V** are length-*M* time-window frequency vectors of the complex exponential.

$$\mathbf{V}\ =\ [v(f_1)\,v(f_2),\ldots,v(f_{\boldsymbol{p}})]\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(8)$$

Amplitudes of the complex exponentials a*i* is present in vector **A**, whereas diagonal Matrix of phase shifts between adjacent time samples of each complex exponential components of **x**(*n*), is the matrix Φ, and is given as:

$$\boldsymbol{\Phi}=\mathrm{diag}[\mathrm{e}^{\mathrm{j}2\pi\mathrm{f}_1},\mathrm{e}^{\mathrm{j}2\pi\mathrm{f}_2},\ldots,\mathrm{e}^{\mathrm{j}2\pi\mathrm{f}_p}]=\mathrm{diag}[\Phi_1,\Phi_2,\ldots,\Phi_p]\ldots\ldots\ldots(9)$$

Where $\Phi_i=e^{j2\pi f_i}$ for $i=1,\ 2,\ldots,\boldsymbol{p}$. Although the frequencies of the $f_{\boldsymbol{p}}$ complex exponentials entirely define this [13] rotating matrix, the estimated frequency can be extracted by identifying **Φ**. Here in order to explore the determinist featuresof the sinusoids we have taken two sub-windows of length (*M-1)*, which are overlapping and are inside the time window matrix *M*. This process under windowing is shown in Fig.3.Find the signal formed by the sum of complex exponentials.We get the signal vector from (6) through the subwindowing process given by

$$\mathbf{x}_{\mathrm{M-1}}(n)\ =\mathbf{V}_{\mathrm{M-1}}\Phi^n\mathbf{A}\ldots\ldots\ldots\ldots\ldots\ldots\ldots(10)$$

Matrix **V***M*-1 although constructed in the same manner as **V**

Yet unlike **V** its time-window frequency vectors have (*M* -1) length, denoted as :

$$\mathbf{V}_{\mathrm{M-1}}=\ [\mathbf{V}_{\mathrm{M-1}}(f_1)\mathbf{V}_{\mathrm{M-2}}(f_1),...,\mathbf{V}_{\mathrm{M-}\boldsymbol{p}}(f_{\boldsymbol{p}})]\ldots\ldots\ldots\ldots\ldots(11)$$

The data should be divided into signal and noise subspaces, i.e the two orthogonal subspaces as recommended by the TLS- ESPRIT algorithm. The classification of subspaces could be achieved through the use of the [14], [15] SVD. Using (8), we describe the matrices using

$$\mathrm{V}_1=\mathrm{V}_{M\text{-}1}\boldsymbol{\Phi}^n\quad\text{and}\ \mathrm{V}_2=\mathrm{V}_{M\text{-}1}\boldsymbol{\Phi}^{n+1}\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(12)$$

where V_1 and V_2 represent the untaggered and staggered windows. TLS-ESPRIT algorithm implementation steps [16] are represented using the following signal flow diagram in Fig.4.

Step 1: Define the dimensional ***N***random vector pertaining to consecutive data samples with frequency vector having length of (M –1)time window and estimate the covariance matrix from the data window.

Step 2: The $\mathbf{Y}(n)$ SVD will give $\mathbf{Y} = \mathrm{L}\Sigma\mathbf{U}^{\mathrm{H}}$, where matrix $\mathbf{L} \in \mathrm{R}^{N\times N}$ gives left singular vectors matrix and $\mathbf{U}\ \mathbf{U} \in \mathrm{R}^{M\times M}$ provides the right singular vectors

Step 3: Ifrequired, estimate the number of signals***p***.

Step 4: For the M-dimensional vector space, U provides an orthonormal basis. The subspace could be separated as followed into subspace for signal and noise.

$$\upsilon = [\upsilon_s \ \ \upsilon_n]$$

Where υ_S fits the subspace belongs to signal, and contains the $v(f)$ time-window frequency vector for all f . $\mathbf{U}_s$ and V mapped onto $V=\mathbf{U}_s T$ because of the same subspace representation.

Step 5: Generate a basis spanning the signal subspace and partition it as two smaller (M-1) dimension subspaces as follows.

$$\upsilon_s = \begin{bmatrix} \upsilon_1 \\ * \ * \ * \ * \end{bmatrix} = \begin{bmatrix} \upsilon_2 \\ * \ * \ * \ * \end{bmatrix} \ldots\ldots\ldots\ldots\ldots\ldots(13)$$

Where $v1$ and $v2$ belong to the same unstaggered and staggered subspace as V1 and V2, such that we can map them as:

$$V_1 = \mathbf{U}_1 T \quad \text{and} \quad V_2 = \mathbf{U}_2 T \ldots\ldots\ldots\ldots\ldots\ldots(14)$$

V_1 and V_2 are related as:

$$V_2 = V_1\Phi \quad \text{and} \quad \mathbf{U}_2 = \mathbf{U}_1\mathbf{\Psi} \ldots\ldots\ldots\ldots\ldots\ldots(15)$$

Where $\mathbf{\Psi}$ is least square approximate rotational operator;

$$\mathbf{\Psi} = (\mathbf{U}_1^{\mathrm{H}}\mathbf{U}_1)^{-1}\mathbf{U}_1^{\mathrm{H}}\mathbf{U}_2 \ldots\ldots\ldots\ldots\ldots\ldots(16)$$

Substituting $\mathbf{U}_2$ and V_1 in V_2 gives:

$$V_2 = \mathbf{U}_2 T = \mathbf{U}_1 \Psi T \text{ or } V_2 = V_1\Phi = \mathbf{U}_1 T\Phi \ldots\ldots\ldots\ldots(17)$$

Step 6: Subsequently, after comparing these two right-sides values of V_2 in (17), the relationship between the two subspace rotations can be described.

$$\Psi T = T\Phi \text{ or } \Psi = T\Phi T^{-1} \ldots\ldots\ldots\ldots\ldots\ldots(18)$$

where Φ_p is the phase of Φ_p

Step 7: The υ_1 and υ_2 subspaces are estimates of the actual subspace that relates to V_1 and V_2 accordingly, computed from the **Y** data matrix.

Step 8: The subspace rotation estimation was extracted by solving $\mathbf{\Upsilon}_2$ through (15) using the [16] LS criterion.

$$\mathbf{\Psi}_{ls} = (\mathbf{\Upsilon}_1^H \mathbf{\Upsilon}_1)^{-1} \mathbf{\Upsilon}_1^H \mathbf{\Upsilon}_2 \quad \ldots\ldots(19)$$

The solution based on LS from (17) is received by reducing the its errors using

$$\mathbf{\Upsilon}_2 + \Delta_2 = \mathbf{\Upsilon}_1 \Psi \quad \ldots\ldots(20)$$

Where Δ_2 is an error vector between $\mathbf{\Upsilon}_2$ and the real subspace V_2.

Step 9: LS approximation predicts an errors only in estimating $\mathbf{\Upsilon}_2$ but no errors within $\mathbf{\Upsilon}_1$ and the V_1 true subspace. So an appropriate formulation is provided by estimating the error against $\mathbf{\Upsilon}_1$ and V_1.

$$\mathbf{\Upsilon}_2 + \Delta_2 = (\mathbf{\Upsilon}_1 + \Delta_1)\Psi \quad \ldots\ldots(21)$$

Where Δ_1 is the vector of the errors between $\mathbf{\Upsilon}_1$ and the true subspace of V_1.

Step 10: Total Least Squares (TLS) is derived by reducing the Frobenius norm of the both [17] error matrices.

$$\|\Delta_1 \quad \Delta_2\| \quad \ldots\ldots(22)$$

Step 11: Compute the matrix $\tilde{\upsilon}$ using SVD of right singular vectors with staggered signal subspace matrices $\mathbf{\Upsilon}_1$ and $\mathbf{\Upsilon}_2$ placed aside.

$$[\mathbf{\Upsilon}_1 \ \mathbf{\Upsilon}_2] = \tilde{L}\tilde{\Sigma}\tilde{\upsilon}^H \quad \ldots\ldots(23)$$

and partition $\tilde{\upsilon} \in \Re^{2p \times 2p}$ into four sub matrices $\tilde{\upsilon} \in \Re^{p \times p}$ quadrants as follows

$$\tilde{\upsilon} = \begin{bmatrix} \tilde{\upsilon}_{11} & \tilde{\upsilon}_{12} \\ \tilde{\upsilon}_{21} & \tilde{\upsilon}_{22} \end{bmatrix} \quad \ldots\ldots(24)$$

Step 12: Compute the singular values $\sigma_1, \sigma_2, \ldots, \sigma_p$ of the matrix Ψ by using subspace rotation

$$\Psi_{\mathbf{tls}} = -\tilde{\upsilon}_{12}\tilde{\upsilon}_{22}^{-1} \quad \ldots\ldots(25)$$

Step 13: The desired frequencies estimates are then obtained from (18) by using $\Psi_{\mathbf{tls}}$ Ψtls from The diagonal element of **Φ**, Φ*p* for *p* = 1; 2; 3 : : : *p* are the singular values of **Ψ**. Thus, the estimated frequency is given by [12]:

$$f_{\boldsymbol{p}} = \frac{\angle \Phi_p}{2\pi} \quad \ldots\ldots(26)$$

where Φ_p is the phase of Φ_p :

RESULTS AND DISCUSSION

For the analysis, a test signal corresponding to the power system mode (i.e. local area and inter-area) is considered. The robustness of the proposed LMSSS adaptive filtering algorithm is also tested at different noise levels, i.e. SNR 10dB and 30dB. The realistic implementation of the proposed method is carried out on the Kundur's test system of two-area, four-machine with simulation of 50,000 Monte Carlo. And in the presence of noise, that is, SNR=30dB, the execution of the proposed approach is completed. The variance of PMU measurements is typically estimated to be 10^{-4}p.u. in the oscillating state at(SNR at 30dB). The North American Synchro Phasor Initiative(NASPI) provides PMU and synchro Phasor with a certain basic guideline under various complex conditions [18], such as energy variability of 0:61 × 10-4p.u.

Test signal Comparing to Inter Area Mode

For the simulation, a test signal with an attenuation factor= -0.07, frequency=0.4Hz, and amplitude=1 is considered.Examination of the proposed solution using SNR=10dB and 30dB for TLS-ESPRIT calculations.

Examination of the proposed approach with TLS-ESPRIT calculations with SNR=10dB and 30dB:

Fig.5 and Fig.6 illustrate how the approximate frequency of the evaluated mode is distributed on a test signal. Table I and Table II provide the SD and mean of the evaluated mode usingthe ESPRIT, LSESPRIT, and TLS-ESPRIT estimation method proposed for SNR 10dB and 30dB. It is observed from thistable that the SD of the approximate mode with the LMSSS is around 29.29 % for 10dB and 31.52 % for 30dB as obtained with the TLS-ESPRIT.

Test signal Comparing to Local Area Mode

For the simulation a test signal with attenuation factor=-0.1, frequency=1Hz and amplitude=1 is considered. Examination of the Proposed approach with TLS-ESPRITcalculations with SNR=10dB and 30dB:

Examination of the proposed method with TLS-ESPRIT measurements using SNR=10dB and 30dB

Fig.7and Fig.8demonstrate the distribution of the approximate mode frequency on a test signal. Table III and Table IV include theSDs and means for SNR 10dB and 30dB in the evaluated mode with LMSSS, ESPRIT, LS-ESPRIT and TLS-ESPRIT.It is found from these tables that the SD of the approximate mode using the LMSSS is around 48.78 % for 10dB and 37.52% for 30dB as obtained with the TLS-ESPRIT.

Practical Application of the Proposed Approach using the Parameters of Two-Area Kundur's Test System

Single Line Schematic of Two-Area Kundur's Power System

The concept of the two-area kundur's test system model takes into consideration from [2]. This network consists of four generators and eleven buses, and is seen in Fig.9. The weak tie-line ties these two zones. Both local and inter-area oscillating modes of the power network was calculated using the SSSA,Table V displays the estimated oscillating modes for the two-area network corresponding to the LFOs of speed in the generator two and four. Such LFOs (corresponding to the ringdown data) are identified, due to the addition to generator 2 ofa disruption of 0.05v for 0.2s at excitation. It is presumed that the measurement is received from a PMU situated at bus 2. Table V displays the average of 50,000 monte-carlo simulated value of the estimated modes. The SD of 2:2787 × 10-5 appeared at the estimated modes through LMSSS adaptive filtering is which occurred in SNR 30dB. The estimated modes are very similar to the meaning derived from SSSA on the basis of eigenvalues of the state matrix.

CONCLUSIONS

LMSSS-TLS-ESPRIT, a new mode estimation method, has been proposed in this paper and it is based on adaptive filtering which gives robust and more precise estimation of modes andis less likely to get affected by the highly correlated colored noise. As compared to the LS-ESPRIT, ESPRIT, TLS-ESPRIT,LMSSS adaptive filtering gives better estimation performance based on the SD, mean of the frequency of the estimated mode. In addition, the two-area test system described by the Kundur's checked the accuracy of the LMSSS-TLS-ESPRIT atSNR 30dB. Results obtained using adaptive filtering from theLMSSS are similar to the estimate obtained with the SSSA

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TABLE I: MEAN AND STANDARD DEVIATION FOR THE ESPRIT, TLS-ESPRIT, AND THE ADAPTIVE LMSSS FILTERING AT SNR=10dB

SNR=10 dB		ESPRIT	LS-ESPRIT	TLS-ESPRIT	Proposed Method
Frequency (Hz)	Standard Deviation	4.5717×10^{-4}	4.5714×10^{-4}	4.5253×10^{-4}	1.3255 × 10−4
	Mean	0.4020	0.4018	0.4018	0.4005

TABLE II: MEAN AND STANDARD DEVIATION FOR THE ESPRIT, TLS-ESPRIT, AND THE ADAPTIVE LMSSS FILTERING AT SNR=30dB

SNR=30 dB		ESPRIT	LS-ESPRIT	TLS-ESPRIT	Proposed Method
Frequency (Hz)	Standard Deviation	4.5337×10^{-5}	4.5335×10^{-5}	4.4682×10^{-5}	1.4335 × 10−5
	Mean	0.4004	0.4003	0.4003	0.4000

TABLE III: MEAN AND STANDARD DEVIATION FOR THE ESPRIT, THE LS-ESPRIT, THE TLS-ESPRIT, AND THE LMSSS ADAPTIVE FILTERING AT SNR=10dB.

SNR=10 dB		ESPRIT	LS-ESPRIT	TLS-ESPRIT	Proposed Method
Frequency (Hz)	Standard Deviation	4.8141×10^{-4}	4.8140×10^{-4}	4.8128×10^{-4}	2.3477 × 10−4
	Mean	1.0019	1.0019	1.0017	1.0009

TABLE IV: MEAN AND STANDARD DEVIATION FOR THE ESPRIT, THE LS-ESPRIT, THE TLS-ESPRIT, AND THE LMSSS ADAPTIVE FILTERING AT SNR=30dB

SNR=30 dB		ESPRIT	LS-ESPRIT	TLS-ESPRIT	Proposed Method
Frequency (Hz)	Standard Deviation	4.7123×10^{-5}	4.7123×10^{-5}	4.7110×10^{-5}	1.7678 × 10−5
	Mean	1.0023	1.0018	1.0018	1.0009

TABLE V: TWO-AREA KUNUR'S POWER SYSTEM AT SNR=30dB TO ESTIMATION OF CRITICAL MODE USING LMSSS ADAPTIVE FILTERING APPROACH

	(Frequency=1.3914 Hz using SSSA)	
Mode-1 Frequency(Hz)	Mean	Standard Deviation
	1.4657	2.8775_10−4
Mode-2 Frequency(Hz)	**Frequency=1.2106 Hz using SSSA**	
	Mean	Standard Deviation
	1.3723	2.5733_10−4
Mode-3 Frequency(Hz)	**Frequency=0.6227 Hz using SSSA**	
	Mean	Standard Deviation
	0.5997	2.2787_10−5

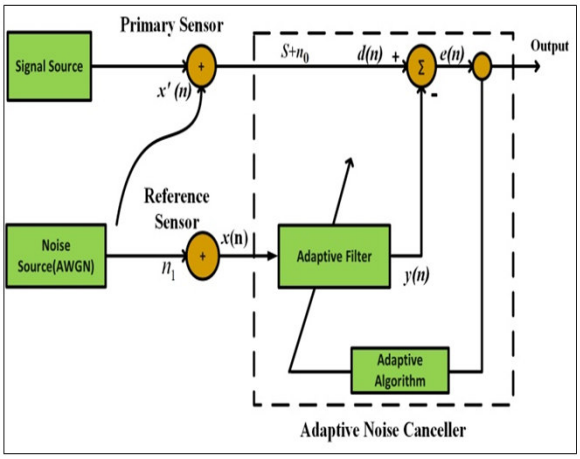

Fig. 1: Adaptive LMSSS filter for noise cancellation

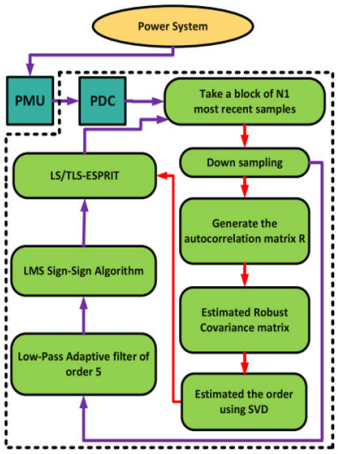

Fig. 2: Block diagram of proposed mode identification method

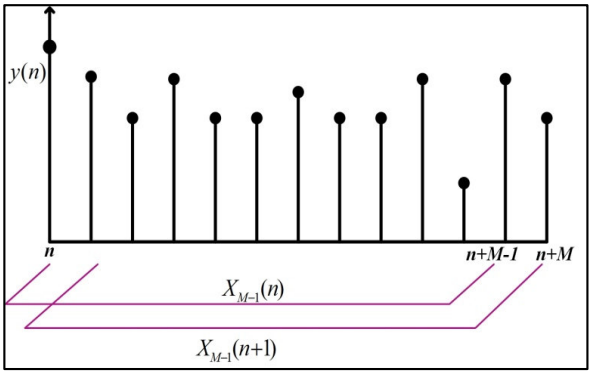

Fig. 3: Time-staggered, overlapping windows used by the LS/TLS ESPRIT algorithm

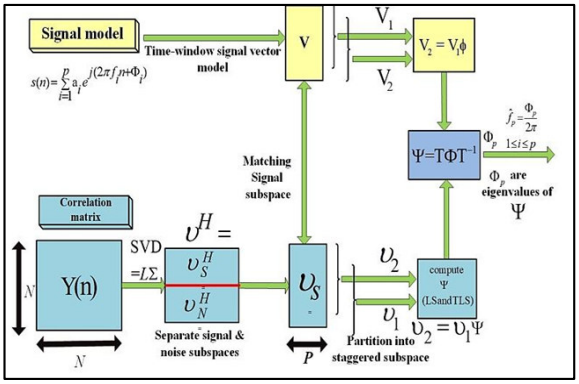

Fig. 4: Steps for application of Adaptive based-TLS-ESPRIT Algorithm for frequency estimation

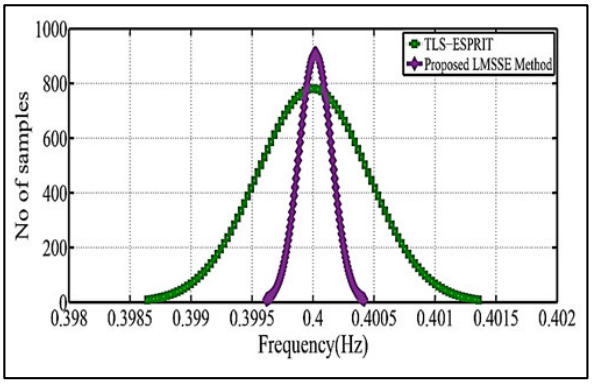

Fig. 5: Distribution of modes using the Monte-Carlo simulation at SNR=10dB

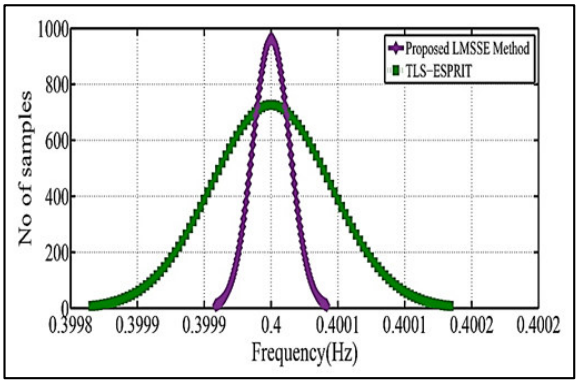

Fig. 6: Distribution of modes using the Monte-Carlo simulation at SNR=30dB

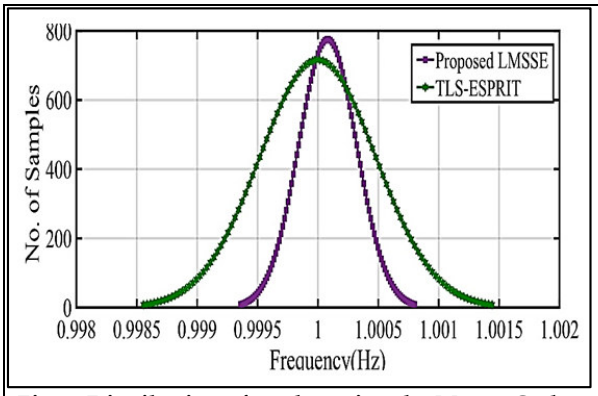

Fig. 7: Distribution of modes using the Monte-Carlo simulation at SNR=10dB

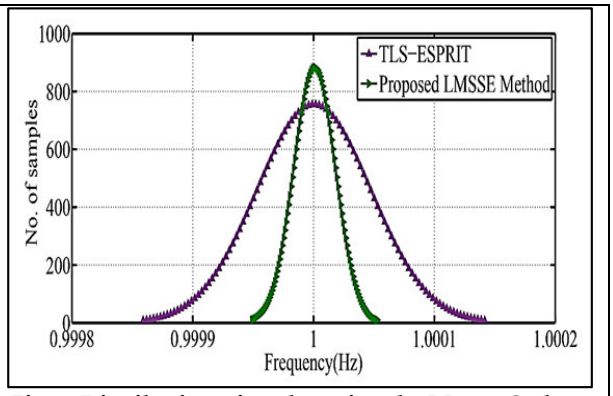

Fig. 8: Distribution of modes using the Monte-Carlo simulation at SNR=30dB

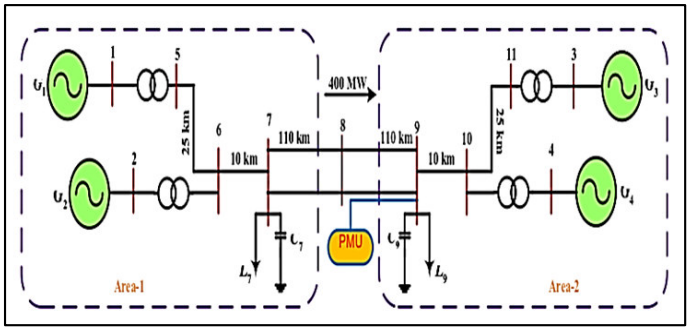

Fig 9.Single line schematic of two-area kundur's power system

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RESEARCH ARTICLE

Targeted Therapy for Cancer in Women

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ABSTRACT

Aloe vera is that the oldest healthful plant ever known and also the most applied healthful plant worldwide. Extracts of aloe could be a well-tried skin expert. aloe facilitate to assuage skin injuries full of burning, skin irritations, cuts and bug bites, and its disinfectant properties relieve itch and skin swellings. it's known to assist block the looks of wrinkles and actively repair the broken skin cells that cause the visible signs of aging. Succulent could be a powerful detoxifier, antiseptic and tonic for the nervous system. It conjointly has immune-boosting and anti-viral properties. Analysis has well-tried that adding aloe to one's diet improves digestion. As a general health tonic, Aloe could be a helpful supply of vitamins. aloe Gel contains an oversized vary of vitamins - even B complex, Vitamin A, contains B-Group vitamins, Vitamin C, fat-soluble vitamin and pteroylglutamic acid. Our aim is to determine the effect of effect of aloevera in different cancer in women. We have taken different cancer cell line and treated them with different concentration of the aloe vera. The effect of the extraction was measured by different spectroscopic analysis i.e Fluorescence Anisotropy, also confirmatory test has been done by the MTT assay Reactive Oxygen Species analysis (ROS) .

Key words: Cancer cell line, fluorescence anisotropy, MTT assay, Reactive Oxygen Species analysis.

INTRODUCTION

Aloe Gel contains vital ingredients as well as nineteen of the twenty amino acids required by the soma and 7 of the eight essential ones that simply can't be created (Vardy et al.1999). succulent contains 2 categories of Aloins: (1) nataloins, that yield picric and oxalic acids with acid, and don't provides a red coloration with nitrous acid; and (2) barbaloins, that yield aloetic acid (C7H2N3O5), chrysammic acid (C7H2N2O6), picric and oxalic acids with acid, being reddened by the acid. In our social and economic life we tend to hardly watch out of our food we tend to ar

taking. The uses of assorted pesticides, preservatives, etc. flip the foods into poison. Furthermore the aspect effects of those pesticides and preservatives, etc. is dangerous as a result of it ends up in initiation of various cancer. In these whole world, the amount of patients dying from cancer is increasing in an exceedingly} very threatening approach. We tend to found Alovera to be a possible drug because the term Aloes indicates the dried juice that flows from transversally cut bases of its leaves. it's the most effective flavouring answer to suppor the health and healing mechanisms of the body as a result of it doesn't heal, rather it feeds the body's own systems so as for them to operate optimally and be healthy. Pharmacologically it's Associate in Nursing immunity booster and detoxifies the system. It's counseled in adjuvant medical aid with antibiotics, NSAIDs (Nonsteroidal medicine Drugs) and therapy to eliminate drug induced redness and alternative adverse effects.

Aloe vera (Aloe barbadensis) is one among the seasoner remedies with a long history for its curative and therapeutic properties for numerous ailments. until date over seventy five active elements with healthful worth have been known in aloe and are steered to possess synergistic action in assuaging the pathological conditions (Scalbert and Williamson, 2000; Hamman, 2008; Nejatzadeh-Barandozi, 2013). Its numerous biological activities embrace rising the bioavailability of coadministered vitamins and absorption of poorly absorbed drugs, and conjointly possess purgative, anti-microbial, immunostimulatory, wound healing, anti-inflammatory drug, anti-tumor, and anti-diabetic activities (Azam et al., 2003; Nejatzadeh-Barandozi, 2013). Accumulating scientific proof suggests that aloe possesses outstanding preventive and therapeutic potential against numerous cancers (Niciforovic et al., 2007; Joseph and dominion, 2010). The bioactive constituents of aloe with chemopreventive potential like glycoprotein, aloin, barbaloin, aloe-emodin and aloesin have shown to possess immune-potentiating, antimutagenic, Many of the ANti-cancer agents presently used have an origin in natural sources together with plants. aloe is one such plant being studied extensively for its numerous health advantages, together with cancer interference. during this study, the cytotoxic potential of aloe crude extract (ACE) alone or together with cisplatin in human breast (MCF-7) and cervical (HeLa) cancer cells was studied by cell viability assay, nuclear morphological examination and cell cycle analysis. Effects were correlative with modulation of expression of genes concerned in cell cycle regulation, programmed cell death and drug metabolism by RT-PCR.

Exposure of cells to ACE resulted in significant loss of cell viability in a very dose- and time-dependent fashion, that was found to be mediate by through the apoptotic pathway as proved by changes within the nuclear morphology and therefore the distribution of cells within the completely different phases of the cell cycle. Apparently, ACE failed to have any important toxicity towards traditional cells, therefore putting it within the class of safe chemo preventive agent. Further, the consequences were correlative with the down regulation of cyclin D1, CYP 1A1, CYP 1A2 and accumulated expression of bax and p21 in MCF-7 and Norse deity cells. Additionally, low dose combination of ACE and cisplatin showed a mixture index but one, indicating synergistic growth inhibition compared to the agents applied severally. last, these results signify that aloe may be a good anti-neoplastic agent to inhibit neoplastic cell growth and increase the therapeutic effectualness of conventional medicine like cispolatin. therefore promoting the event of plant-derived therapeutic agents seems warranted for novel cancer treatment ways. The aforesaid activities of aloe (or its constituents) square measure mediate via targeting numerous effector molecules like ER-α, STAT3 super molecule, STAT3-regulated anti-apoptotic (Bcl-xL), MMP-2, peptidase plasmin activator (u-PA), VEGF receptor (VEGFR) a pair of, c-Myc, and VEGF (Chen et al., 2010; Huang et al., 2013; Pan et al., 2013). apparently, numerous studies have shown that the prophylactic use of aloe will scale back the intensity of radiation-induced inflammation (Ahmadi, 2012; Haddad et al., 2013). Moreover, the combined use of metastatic tumor agents, particularly at low concentrations, and succulent constituents potentiated the expansion repressive result of the previous on cancer cells (Fenig et al., 2004; Tabolacci et al., 2013). Aloe vera, because of its varied approach towards targeting cancer cells and fewer undesirable facet effects, could persuade be AN agent of selection for treatment of human carcinomas. Therefore, this study was designed to guage the potential of favorable interactions within the novel combination of cisplatin with aloe crude extract (ACE), with the aim of potentiating growth inhibition and apoptotic death by chemotherapeutical medicine at lower doses and reducing its facet effects on traditional cells. to boot these effects of aloe were correlative with the modulation of expression of assorted genes.

Cancer is that the second reason behind death when vas diseases. With due attention to fast progress within the phytochemical study of plants, they're turning into standard attributable to their malignant tumor effects. The aim of this study was to research the effective medicative plants and spice within the treatment of cancer and study their mechanism of action. the trouble for locating new malignant tumor agents with higher effectuality and lesser facet effects has been continued . Natural compounds area unit sensible sources for the event of recent remedies for various diseases. Through an experiment, many medicative plants and flavouring ingredients are rumored to possess malignant tumor effects. Also, varieties of phytochemicals isolated from medicative plants are shown to decrease cell proliferation, induce necrobiosis, retard metastasis and inhibit development.

MATERIAL AND METHODS

Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% heat inactivated fetal calf serum (Gibco™, Thermo Fisher Scientific), penicillin (100 U/mL) and streptomycin (100 μg/mL) (Merck, India), TMA-DPH (1-(4-Trimethylammoniumphenyl)-6-Phenyl-1,3,5-Hexatriene *p*-Toluenesulfonate) (Thermo Fisher Scientific), were used in this work. All the materials were used in the experiments without further purification.

CELL CULTURE

Human cervical epithelial malignant carcinoma cell lines (HeLa) were maintained in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% heat inactivated fetal calf serum (Gibco™, Thermo Fisher Scientific), penicillin (100 U/mL) and streptomycin (100 μg/mL) at 37°C in a humidified atmosphere containing 5% CO2. HeLa cells at a concentration of 1.5×105 cells/mL were grown in a 25 cm2 flask of complete culture medium. At 85 % confluency HeLa cells were and trypsinized, and seeded on a 96 well tissue culture plate for overnight according to the selection of experiments.

MTT ASSAY

Approximately 1×10^5 mL^{-1} HeLa cells in their exponential growth phase were seeded in a flat-bottomed 96-well Tissue culture plate for 24h at 37°C in a 5% CO_2 incubator. Series of concentrations (5, 25, 50, 100, and 250 μg/mL) of Aloevera in the medium were added to the plate in a triplicate manner. Cytotoxicity evaluation of Aloevera was performed using MTT assay and MTT was added to each well and the plates incubated for 3 h in a dark chamber. 100 μl of DMSO was added to dissolve the formazan crystals and the absorbance read at 540 nm using ELISA reader (EPOCH, BIOTEK) (Zhu et al., 2001).) The % of survival was calculated using untreated cells as 100 %.

$$\textbf{\% Cell Viability} = \frac{\textbf{(A) Control – (B) test}}{\textbf{(A) Control X 100}}$$

Where (A) test is the absorbance of the test sample and (B) control is the absorbance of the control sample. Non-treated cells were used as the control, and the samples were imaged using an inverted photomicroscope. The Values of MTT assay correspond to mean and standard deviations of three independent experiments.

FLUORESCENCE ANISOTROPY

The fluorescence anisotropy of HeLa was assessed by the determination of TMA-DPH steady-state fluorescence polarization after the cell membrane exterior phospholipid layer permeation of the probe (Dowell, 2002; Pearson, T.,1996; Pearson, T. et.al,2001, Shrivastava, et.al. 2007; Katona,2004; Lakowicz,2004; Hollan, 1996). For the measurement of the changes in the TMA-DPH fluorescent properties following the membrane permeation, we added 2.5μM TMA-DPH to a 2 ml of cell in the measuring cuvette. The cell suspension with the fluorescent probe

was incubated for 30 min at 37°C. The measurement has been done between excitation and emission state, 360 nm and 430 nm respectively.

ROS ANALYSIS

Membrane fluidity of cancer cells was shown to have a decisive role in the direct cell to cell contact and the modulation of the activity of membrane enzymes are to be affected by the increased release of reactive oxygen species (ROS) (Garden, 2001).

For the measurement of the intracellular ROS, DCF-DA was added to a 2 ml of HeLa suspensions. The cell suspension with DCF-DA was incubated for 60 min at 37^0 C in a dark condition. Cells without Aloevera were used as control. Fluorescence intensity was measured in a fluorescence spectrophotometer (model Hitachi, USA) at excitation and emission wavelengths of 504 and 529 nm, respectively.

ANTIOXIDANT ENZYMES ACTIVITIES

Superoxide dismutase (SOD) and Catalase (CAT) activities were measured by commercially available kits. The cells were seeded into 12- well plates at a concentration of 7×10^5 cells/well and all measurements were performed according to supplier's recommendations.

RESULT AND DISCUSSION

FLUORESCENCE ANISOTROPY

Fig 1 have shown the graph for the fluorescence anisotropy. These results have shown that the nanoparticles were interacted with the cellular membrane and dissociated the membrane proteins to enter into the cell and to interact with the cytoplasmic organelles. Thus these nanoparticles have interacted with the mitochondria and reduce the growth of the cancer cells.

MTT ASSAY

MTT assay was undertaken in order to evaluate the cell viability in cells stressed by Aloevera. First we evaluated the effects of Aloevera on HeLa cells viability. Incubation with 5µg/ml, 25µg/ml , 50µg/ml, 100µg/ml, 250µg/ml for 3, 6, 12 and 24 h resulted in a concentration dependent decrease in cell viability, the LC50 was 79.83 ± 0.856 µg/ml. Based on these results Aloevera at submaximal concentrations after 12 h, 50 and 100 µg/ml were selected in this study. The main findings of this assay are the LC50 of Aloevera was 79.83 µg/ml and submaximal concentrations of 80 and 100 µg/ml were selected in this study. Similar results were obtained in previous findings demonstrated a dose dependent reduction of MTT-value in HeLa cells treated with Aloevera, though cells were different (M. Ahamed ,2011, L. Capasso, et.al. 2014).

According to the National Cancer Institute (USA), vegetables crude extracts are cytotoxic considered when their IC50 values are less than 30 µg/ml (M. da, et.al. 2013). After a large screening, Aloevera (60 and 80 µg/ml) concentrations were selected due to their best actions. The present study agree with the results of Remila et al. (2015) who have demonstrated that pre-trearment of THP-1 cells with P. lentis Aloevera extracts for 24 h strongly inhibited H_2O_2 damage, with maximum protection at 100 µg/ml (S. Remila, et.al. 2015). The triplicate study of the cell culture has shown that the number of cells is decreasing by the increment of time and the concentration of the drugs respectively.

ROS production

In order to investigate the effect of Aloevera induced cytotoxicity mediated through ROS generation, HeLa cells were treated with the two selected concentrations of the Aloevera. We detected a significant decrease of ROS level in cells

treated with Aloevera (Fig: 7). Oxidative stress, which is an imbalance between ROS production and the antioxidant systems favouring a ROS excess, has been identified as a common mechanism for cell damage. During oxidative stress, ROS are produced mainly from the mitochondrial electron transport chain. To minimize the damage induced by ROS, free radicals can be transformed to other less toxic molecules, for example, the superoxide anion is enzymatically converted into hydrogen peroxide by superoxide dismutase (SOD) and hydrogen peroxide may be enzymatically converted into water by catalase or glutathione peroxidase enzymes (E. Huerta-García , et.al, 2014). Aloevera have been demonstrated to generate more free radicals and ROS than larger particles, likely due to their higher surface area (C. Sioutas, et.al, 2005). Aloevera have been reported to reduce cell viability and to induce oxidative stress by depletion of glutathione and induction of reactive oxygen species in HEp-2 and MCF-7 cells (M.A. Siddiqui, et.al, 2013), cell death via apoptotic pathway and ROS generation in HepG2 cells in dose-dependent manner (M. Ahamed, et.al, 2012), Aloevera also increased intracellular ROS, apoptosis and necrosis in BEAS-2B and A549 cells (L. Capasso, et.al, 2014), Our results confirmed that Aloevera is toxic to HeLa cells. In the Fig 6, ROS analysis has been shown in triplicate studies. These analyses showed that the requirement of the oxygen got low with the increase of time and concentration of the drug. These need of oxygen lead the cells to the apoptosis and thus the cell dies due to the treatment of the drugs. These have also coincided with the result of the MTT assay. With the increase of the concentration of the Aloevera, the number of viable cells decreased. The Aloevera showed the better result as the variation of the valance electron was increased as a result those reacted with the protein particles of the cells and dissociated it which leads the cells to destroy.

ANTIOXIDANT ENZYMES ACTIVITIES

Pre-incubation of cells with both concentrations 50 and 100 µg/ml of Aloevera led to enhance the antioxidant enzymes, SOD and CAT, activities shown in Figs. 5 and 6. Similarly, the Aloevera also induce a significant depletion of antioxidants. The accumulation of ROS, e.g. superoxide radicals (O2%) and hydroxyl free radicals (%OH) decrease the defensive effects of cellular antioxidant enzymes, e.g. SOD, CAT (A. Li, et.al. 2012). Exposure of HT22 hippocampal cells to Aloevera resulted decrease in the activity of SOD and the other detoxification enzymes which has been founded in this work (K. Niska, et.al. 2015).

CONCLUSION

Aloevera have exhibited promising biomedical applications based on its anticancer, antibacterial, anti-diabetic, anti-inflammatory, drug delivery, as well as bio-imaging activity. Due to inherent toxicity of Aloevera, they possess strong inhibition effects against cancerous cell and bacteria, by inducing intracellular ROS generation and activating apoptotic signalling pathway, which makes Aloevera a potential candidate as anticancer and antibacterial agents. In addition, Aloevera have also been well known to promote the bioavailability of therapeutic drugs or bio molecules when functioning as drug carriers to achieve enhanced therapy efficiency. Moreover, with the ability to decrease blood glucose and increase in insulin levels, Aloevera have shown the promising potential in treating diabetes and attenuating its complications, which can be further evaluated. Aloevera are listed as a kind of safe substance by the FDA. However, some critical issues of Aloevera still need to be further explored, which include the following: (1) lack of comparative analysis of its biological advantages with other Aloevera, (2) the limitations of Aloevera toxicity toward biological systems remain a controversial issue in recent researches, (3) lack of evidence-based randomized research specifically exploring therapeutic roles in improving anticancer, antibacterial, anti inflammatory, and anti diabetic activities, and (4) lack of insight into corresponding animals study about its anticancer, antibacterial, anti-inflammatory, and antidiabetic activities. Following studies focused on the above mentioned issues could further elucidate and comprehend the potential use of Aloevera in biomedical diagnostic and therapeutic fields. We believe that Aloevera would dramatically promote the development of medicine, and Aloevera are expected to make more exciting contributions in these fields.

Aloevera in medicine are a new and emerging topic of interest for researchers. With all their promising characteristics, the *in vivo* application of Aloevera is still rare and there is currently a serious lack of *in vivo* research

into Aloevera. Hence, a much better collaboration between clinicians, biologists and material scientists is required for the in-depth understanding of cancer biology and intelligent design of Aloevera extract for their better clinical use. A dynamic collaboration could lead to the development of smart Aloevera that show superior accuracy of selectivity and toxicity towards cancer cells while causing no harm to normal cells. This is in fact an achievable aim, considering the highly promising characteristics of Aloevera and their inherent nature of selectivity and toxicity towards cancer cells, making them unequivocally a key tool for next-generation cancer treatment.

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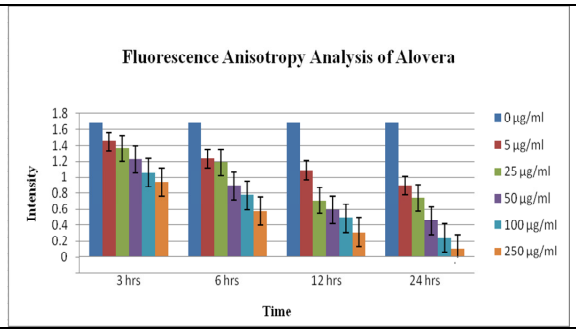

Fig: 1: Fluorescence Anisotropy of HeLa Cells treated with Aloevera. Data represented are mean ± SD of three independent experiments. *p < 0.05; **p < 0.01; ***p < 0.001 treatments compared to control.

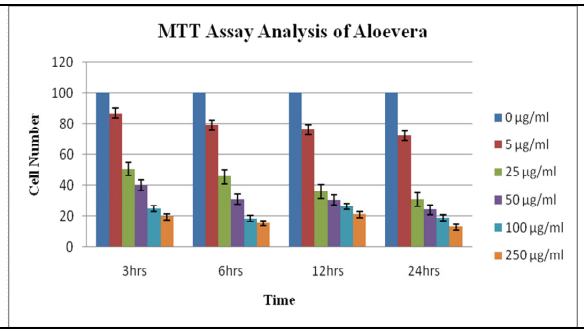

Fig 2: MTT Assay of HeLa Cells treated with Aloevera. Data represented are mean ± SD of three independent experiments. *p < 0.05; **p < 0.01; ***p < 0.001 treatments compared to control.

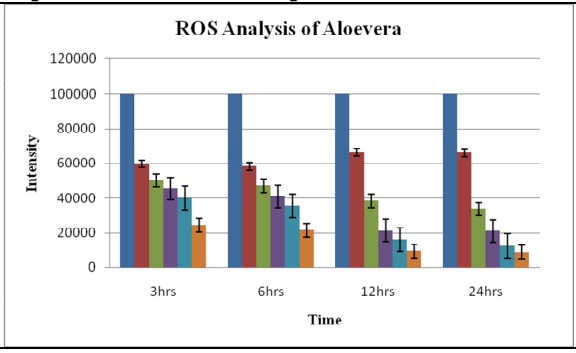

Fig 3: ROS of HeLa cells treated with Aloevera. Data represented are mean ± SD of three independent experiments. *p < 0.05; **p < 0.01; ***p < 0.001 treatments compared to control.

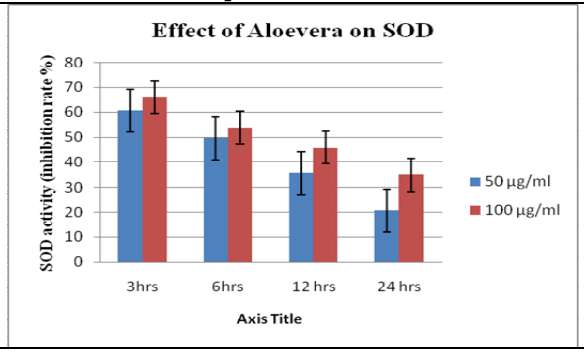

Fig 4: Effects of *Aloe vera* on SOD activity in HeLa cells. Cells were treated with different concentrations for 3, 6. 12 and 24 hours. Data represented are mean ± SD of three independent experiments. *p < 0.05; **p < 0.01; ***p < 0.001 treatments compared to control.

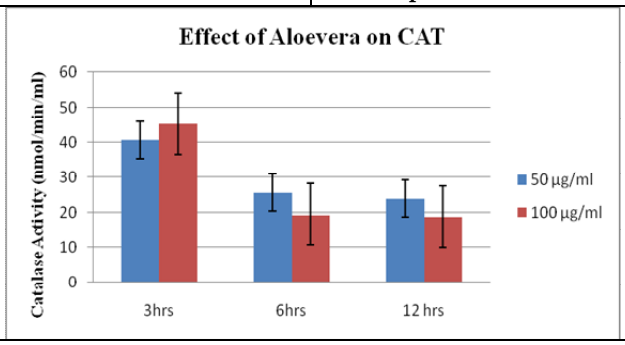

Fig 5: Effects of Aloevera on CAT activity in HeLa cells. Cells were treated with different concentrations for 3, 6. 12 and 24 hours. Data represented are mean ± SD of three independent experiments. *p < 0.05; **p < 0.01; ***p < 0.001 treatments compared to control.

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RESEARCH ARTICLE

An *In silico* Analysis of the Peppermint as Bio-Pesticide (No Side Effect)

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ABSTRACT

As aboriginal sources of medications, medicinal plants are used from the ancient times. Peppermint is one of the highly used potential medicinal plants in the world. This plant is traditionally used for the treatment of common cold, diarrhoea, fever due to several infective cause, jaundice, as a health tonic for the liver and cardiovascular health, and as an antioxidant. It is also used to improve sexual dysfunctions and serve as a contraceptive. All parts of this plant are used to extract the active phytochemicals, but the compositions of phytoconstituents widely differ from one part to another and with place, season, and time of harvest. We are using this property of Peppermint to get some new drugs for Graymold. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Graymold and pharmacophores from Peppermint and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others. From this we can deduce that these two pharmacophores can be a solution to Lung Cancer in near future. Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine. As cancer incidence rates and survival time increase, use of CAM will likely increase. However, little is known about the use of CAM in cancer patients, specifically in emerging countries.

Key Words: Peppermint, Docking, In Silico Analysis, Graymold, Pharmacophore

INTRODUCTION

Emergence and spread of antibiotic resistance among pathogenic bacteria represents a major obstacle in the treatment of infectious diseases. Antimicrobial resistance (AMR) is a global health problem associated with increased morbidity and mortality. Factors associated with it are well documented and known, but unfortunately the root causes of it continue to be ignored. There are several reasons for the development of AMR. One of the most important is antibiotic overuse/and or improper use of antimicro- bials that make the development and spread of resistance much more likely. Inadequate clinical diagnosis of an infection combined with the prescribing of improper antimicrobials contributes to selective pressure and accelerates AMR. Moreover, the practice of adding antibiotics to agricultural feed promotes drug resistance. More than half of the antibiotics produced in the United States are used for agricultural purposes (Hao et al., 2014; WHO, 2015a). Developing countries are inequitably affected by leading infectious disease killers. Not only do we blame emerging infectious disease organisms, but resistant ones affecting populations where public health infrastructure is fragmented, vaccines are not readily available, there is the existence of substandard and counterfeit drugs, a lack of access to health-care services, and poor health-care seeking behaviour (Sosa, 2004).

Many studies have reported that bacteria have developed resistance because of prolonged treatment with conventional antibiotics possessing a broad-range efficacy via toxic or growth- inhibitory effects on target organisms, rendering the traditional antibiotic treatment virtually ineffective (Xavier and Bassler, 2003). Therefore, there is increased demand for the development of alternative strategies to conventional antibiotic therapy (Zeng et al., 2008). Unfortunately, continuous increases in the global isolation rates of methicillin-resistant Staphylococcus aureus (MRSA), methicillin-resistant Staphylococcus epidermidis (MRSE) and carbapenem-resistant Gram-negative bacilli clinical isolates poses a serious therapeutic problem because no new antimicrobial agents are currently available for treatment of infected patients (WHO, 2015a; Elabd et al., 2015; Asaad et al., 2013). For medicinal purposes, the antimicrobial activity of substances derived from plant extracts has been recognized and widely studied for many years (Mohamed et al., 2015; Hamoud et al., 2012). Mentha piperita L., a medicinally important plant that belongs to the family Lamiaceae and is commonly known as peppermint, is a hybrid of Mentha spicata L. (spearmint) and Mentha aquatic. It was cultivated by the ancient Egyptians and documented in the Icelandic pharmacopoeia of the 13th Century. It is widely grown in temperate areas of the world, particularly in Europe, North America and North Africa, but is nowadays cultivated throughout all regions of the world (Singh et al., 2011).

It is primarily cultivated for its oil, which is extracted from the leaves of the flowering plant. Peppermint oil is used for flavouring pharmaceuticals and oral preparations, such as tooth- pastes, dental creams and mouth washes. Higher and aromatic plants have traditionally been used in folk medicine as well as to extend the shelf life of food, showing inhibition against bacteria, fungi and yeast. Most of their properties are due to essential oils produced as secondary metabolites (Saeed et al., 2006; Fabio et al., 2007; Bansod and Rai, 2008; Jeyakumar et al., 2011). *Mentha piperita* (Lamiaceae), the peppermint (mint) plant is an aromatic perennial herb cultivated in most part of the world, have traditionally been used in folk medicine. Leaves of mint plant are frequently used in herbal tea and for culinary purpose to add flavour and aroma. The distinctive smell and flavour, a characteristic feature of *Mentha spp*. is due to the naturally occurring cyclic terpene alcohol called menthol. Menthol is prescribed as a medication for gastrointestinal disorders, common cold and musculoskeletal pain (Patil et al., 2007). The mint plants are rich sources of iron and magnesium, which play important role in human nutrition (Arzani et al., 2007). A large volume of literature is available on the medicinal properties of essential oils present in *Mentha spp*. (Gulluce et al., 2007; Rasooli, 2008). However, no much study has been directed toward the antioxidant and antimicrobial properties of the mint leaves which are locally available.

***Botrytis cinerea* is a necrotrophic fungus that affects many plant** species, although its most notable hosts may be wine grapes. In viticulture, it is commonly known as "botrytis bunch rot"; in horticulture, it is usually called "grey

mould" or "graymold". The fungus gives rise to two different kinds of infections on grapes. The first, grey rot, is the result of consistently wet or humid conditions, and typically results in the loss of the affected bunches. The second, noble rot, occurs when drier conditions follow wetter, and can result in distinctive sweet dessert wines, such as Sauternes or the Aszú of Tokaji/Grasă de Cotnari. The species name *Botrytis cinerea* is derived from the Latin for "grapes like ashes"; although poetic, the "grapes" refers to the bunching of the fungal spores on their conidiophores, and "ashes" just refers to the greyish colour of the spores *en masse*. The fungus is usually referred to by its anamorph (asexual form) name, because the sexual phase is rarely observed. The teleomorph (sexual form) is an ascomycete, *Botryotiniafuckeliana*, also known as *Botryotiniacinerea.* The disease, graymold, affects more than 200 dicotyledonous plant species and a few monocotyledonous plants found in temperate and subtropical regions. Serious economic losses can be a result of this disease to both field and greenhouse grown crops. The causal agent, *Botrytis cinerea* can infect mature or senescent tissues, plants prior to harvest, or seedlings. There is a wide variety of hosts infected by this pathogen including protein crops, fiber crops, oil crops, and horticultural crops. Horticultural crops include vegetables (examples are chickpeas, lettuce, broccoli, and beans) and small fruit crops (examples are grape, strawberry, and raspberry), these are most severely affected and devastated by graymold. Plant organs affected include fruits, flowers, leaves, storage organs, and shoots.

MATERIAL AND METHODS

Phytochemicals of Peppermint have been listed with their structure data files which are taken from pubchem ChEBI. Genes has been taken randomly for Graymold using NCBI database. Table 1 has been showing the enlisted pharmacophores and the targeted genes. The PDB numbers of enzymes are taken from RCSB. The In-silico analysis has been done using BIOVIA –Discovery studio. We have performed various docking and used the Ramachandan plot and others.

Protein identification and preparation

The reported molecular targets responsible for Graymold are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Peppermint were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from Peppermint was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Peppermint with the selected targets of Gray Mold. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Peppermint to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Breast ly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandan Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

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4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Breast administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

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CONCLUSION

CSCs typically exhibit three key characteristics, which are not mutually exclusive. Firstly, CSCs are highly tumorigenic and can form tumours in immune-deficient mice through xenotransplantation, which is not possible for non-CSCs. Secondly, CSCs that survive chemotherapy and radiotherapy generate resistance to such therapies through regulating intracellular stress; for example, regulating reactive oxygen species, which non-CSCs cannot. Thirdly, CSCs possess metastatic potential, illustrated by a report that CSCs have the ability to metastasize. The identified pharmacophores can be isolated from the Peppermint and can be commercialized as the natural drug for the Graymold which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.

The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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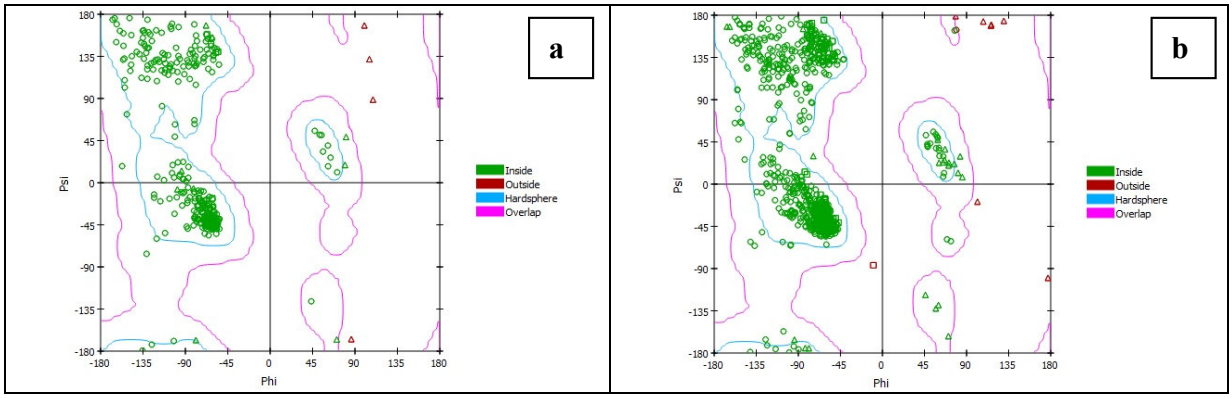
Table 1: The list of pharmacophores and the targeted genes from Graymold

Sl.No	Pharmacophores from Peppermint	Targeted Genes from Graymold	PDB No of the Genes
1	Menthone	Mannitol-1-phosphate 5-dehydrogenasE	5JNM
2	Beta Pinene	Deoxyribodipyrimidine photo-lyase	3UMV
3	Menthofuran	Mannitol-1-phosphate 5-dehydrogenase	3H2Z
4	1,8cineole	Deoxyribodipyrimidine Photo-Lyase	2J08



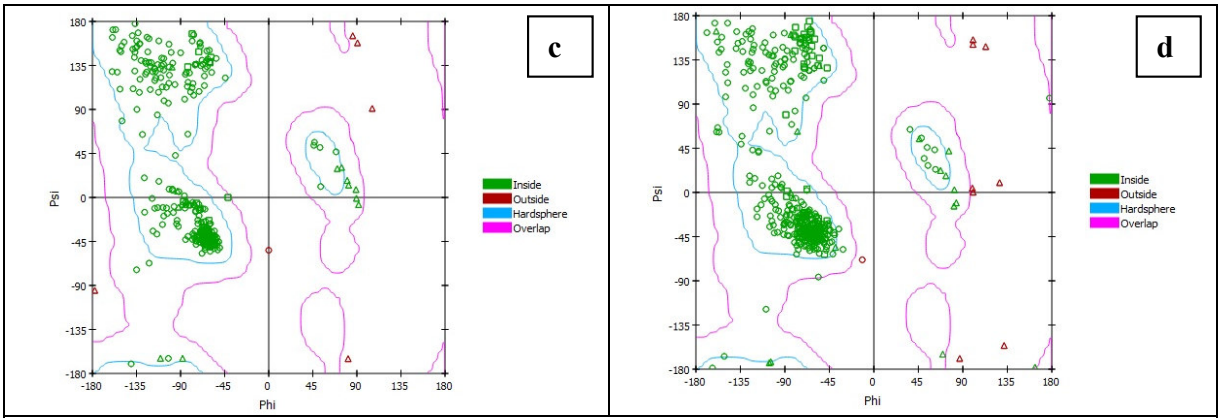


Figure 1: Ramachandan plot of (a) 5JNM (b) 3UMV (c) 3H2Z (d) 2J08

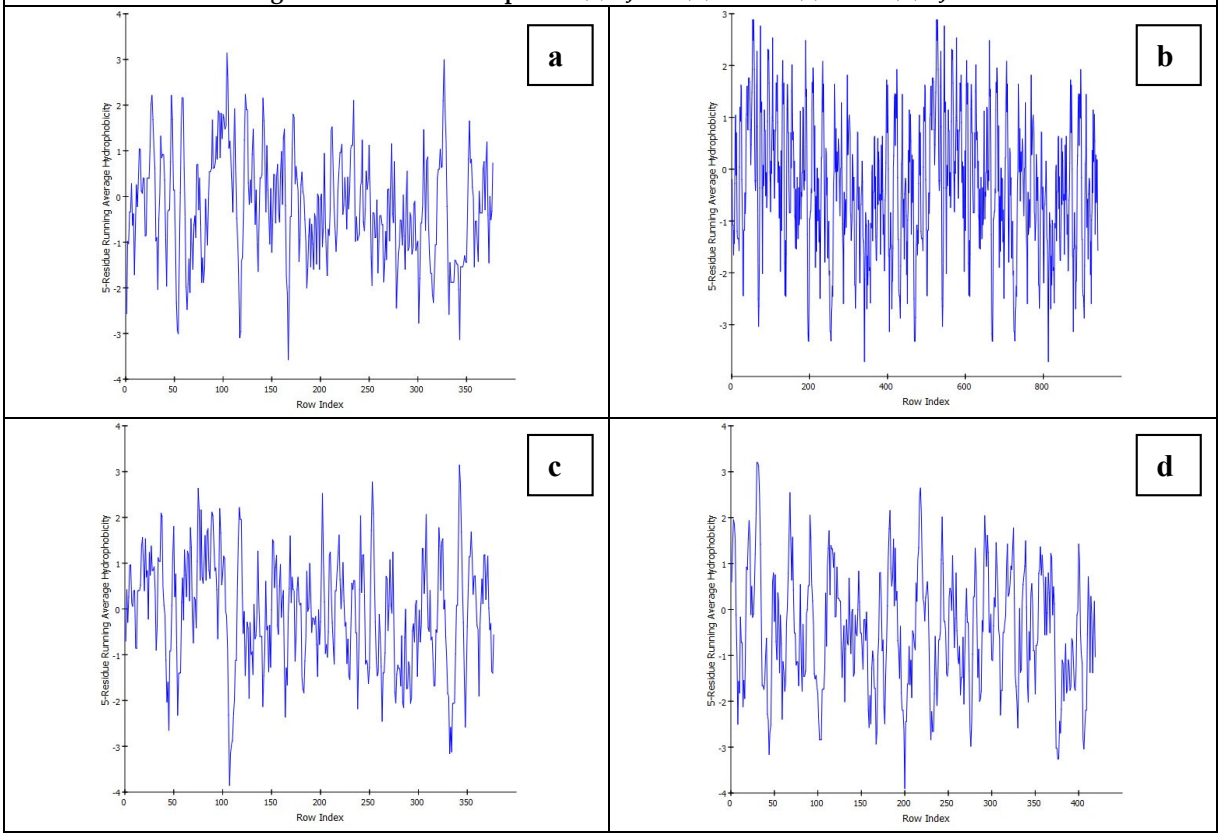


Figure 2: Hydrophobicity Plot of (a) 5JNM (b) 3UMV (c) 3H2Z (d) 2J08

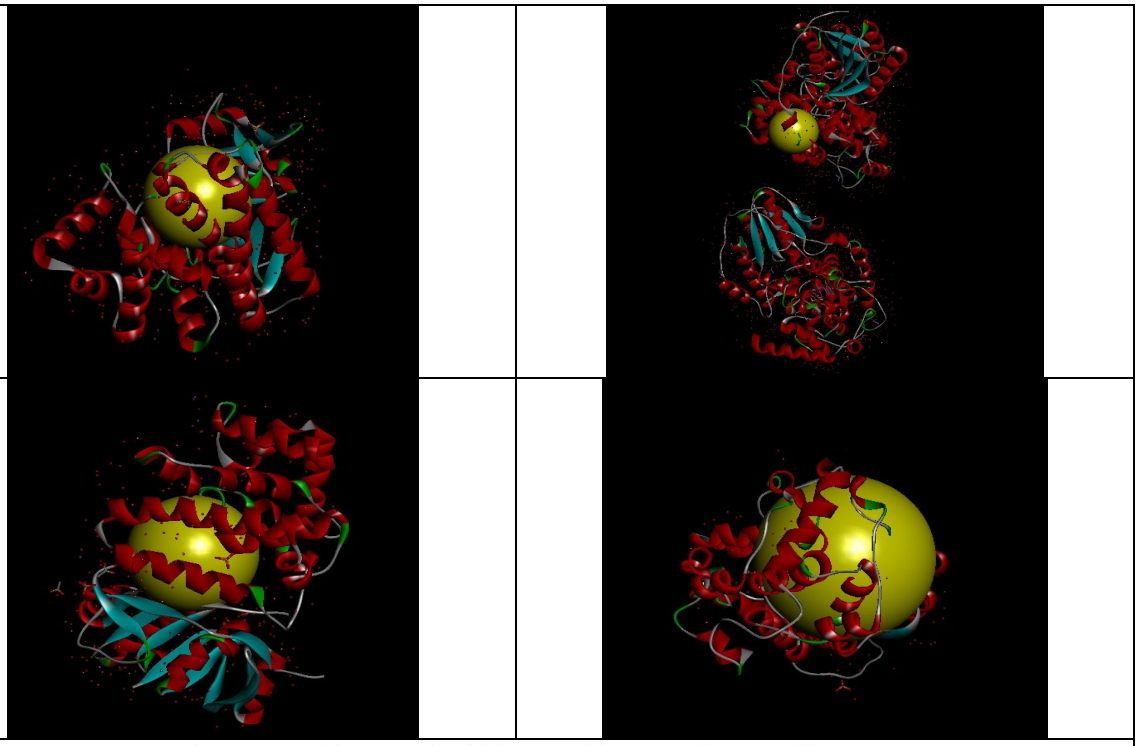


Figure 3: Docking Result of (a) 5JNM (b) 3UMV (c) 3H2Z (d) 2J08

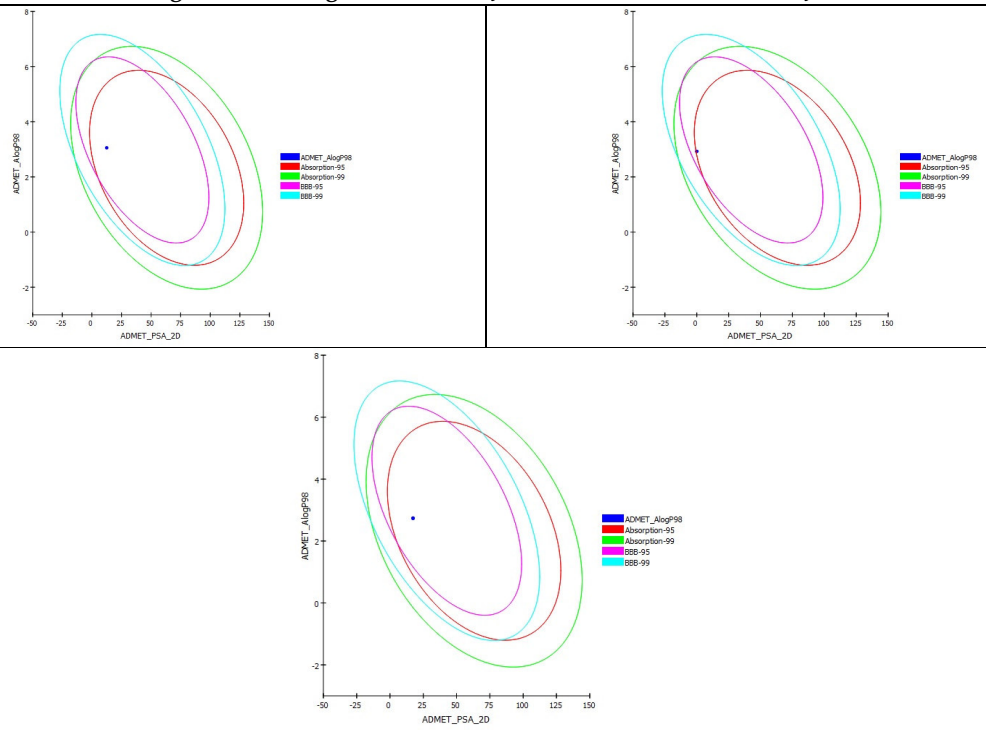


Figure 4: ADMET analysis report

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RESEARCH ARTICLE

Cinnamon: *In silico* Analysis as Targeted Bio-Pesticides

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is *Cinnamon* which has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. *Cinnamon* is full of antioxidants that are essential for living a healthy life. Antioxidants help in removing free radicals that can further mutate into cancer cells. We are using this property of *Cinnamon* to get some new drugs for Crown Gall. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Crown Gall and pharmacophores from *Cinnamon* and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others. From this we can deduce that these two pharmacophores can be a solution to Lung Cancer in near future.

Key Words: Cinnamon, Docking, *In silico* Analysis, Crown Gall, Pharmacophore

INTRODUCTION

From ancient many herbs and spices are being used as medicine for many diseases. *Cinnamon* is a spice, made from inner bark of trees known as Cinnamomum. Once it was to be rare and valuable so it was regarded as a gift for kings

but nowadays it is not only cheaper but also readily obtainable (Chen et.al, 2014). The medicinal use of this plant has been documented in Ayurveda (the Indian system of medicine), for over 6000 years. Cinnamomum comes from Greek word kinnamomon. W hich means 'sweet wood'.There are two types of cinnamon, true *Cinnamon* (*Cinnamomum zeylanicum, C. verum*) and cassia (*Cinnamomum aromaticum*) (Kayande et.al, 2014). The bark of *Cinnamon* is an important spices used all over the world for cooking and medicine proposes (Sangal, 2011). The characteristic odour and flavour of *Cinnamon* are due to the oils and other derivatives, like cinnamaldehyde, cinnamic acid and cinnamate. *Cinnamon* has some meditational properties (Torbati et.al, 2014). It contains polyphenols which act as antioxidants. From the study of antioxidant activity of 26 spices, *Cinnamon* was found out to be a clear winner (Shan et.al, 2005). *Cinnamon* is also used for natural food preserver (Nikos G. Tzortzakis, 2009). It can also helpful for lowering blood sugar level because of its antidiabetic effect (Kim et.al, 2006). In addition to that it act as anti microbial (Chan et.al, 2001), anticancer (Anderson et.al, 2010) anti-inflammatory (Tung et.al, 2010), antifungal (Wang et.al, 2010) and also has been reported to have activities against neurological disorder (Peterson et.al, 2009). From some research it has been found that it can also fight with HIV-1 (common strain of HIV virus in humans) (Filho et.al,2010). From a research it was found *Cinnamon* has most effective treatment on HIV-infected cells out of all 69 medicinal plants under research (Premanathan et.al, 2009).

Crown gall, plant disease, caused by the bacterium *Agrobacterium tumefaciens* (synonym *Rhizobium radiobacter*). Thousands of plant species are susceptible. They include especially grape, members of the rose family (Rosaceae), shade and nut trees, many shrubs and vines, and perennial garden plants. Symptoms include roundish rough-surfaced galls (woody tumourlike growths), several centimetres or more in diameter, usually at or near the soil line, on a graft site or bud union, or on roots and lower stems. The galls are at first cream-coloured or greenish and later turn brown or black. As the disease progresses, plants lose vigour and may eventually die. Crown gall can be avoided by using nursery stock free of suspicious bumps near the crown, former soil line, or graft union; practicing five-year rotation or avoiding replanting for that period; removing severely infected plants (including as many roots as possible); protecting against injury; keeping down weeds; controlling root-chewing insects and nematodes; cutting away large galls on trees; and disinfecting wounds. Rapid and accurate diagnosis of disease is necessary before proper control measures can be suggested. It is the first step in the study of any disease. Diagnosis is largely based on characteristic symptoms expressed by the diseased plant. Identification of the pathogen is also essential to diagnosis. Diagnosis is best done in the presence of the growing plant. Disease is suspected when, for example, part or all of a plant begins to die. Disease also is indicated when blossoms, leaves, stems, roots, or other plant parts appear abnormal—i.e., misshapen, curled, discoloured, overdeveloped, or underdeveloped. Diseased plants also often fail to respond normally to fertilizing, watering, pruning, insect and mite control, or other recommended practices.

MATERIAL AND METHODS

Phytochemicals of Cinnamon have been listed with their structure data files which are taken from pubchem ChEBI. Genes has been taken randomly for Crown Gall using NCBI database. Table 1 has been showing the enlisted pharmacophores and the targeted genes. The PDB numbers of enzymes are taken from RCSB. The *In-silico* analysis has been done using BIOVIA –Discovery studio. We have performed various docking and used the Ramachandan plot and others.

Protein identification and preparation

The reported molecular targets responsible for Crown Gall are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy

their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from *Cinnamon* were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from *Cinnamon* was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of *Cinnamon* with the selected targets of Crown Gall. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from *Cinnamon* to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

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Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the *Cinnamon* and can be commercialized as the natural drug for the Crown Gall which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Crown Gall

Sl.No	Pharmacophores from Cinnamon	Targeted Genes from Crown Gall	PDB No of the Genes
1	Cinnamic Aldehyde	Agrobacterium Tumefaciens D-Psicose 3-Epimerase	2hk1
2	2′-Hydroxycinnamaldehyde	Protein-Secreting Atpase	4gzi
3	Polyphenol Type-A	Agrobacterium Tumefaciens D-Psicose 3-Epimerase	6j17
4	Cinnamic Acid		

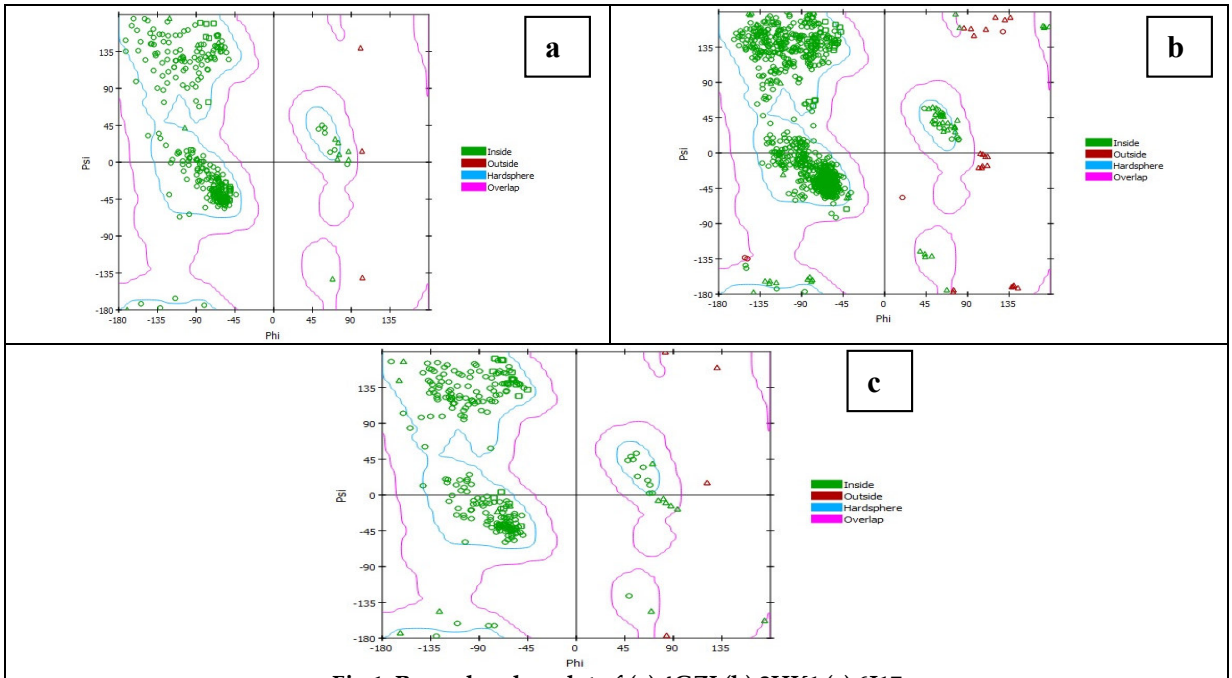
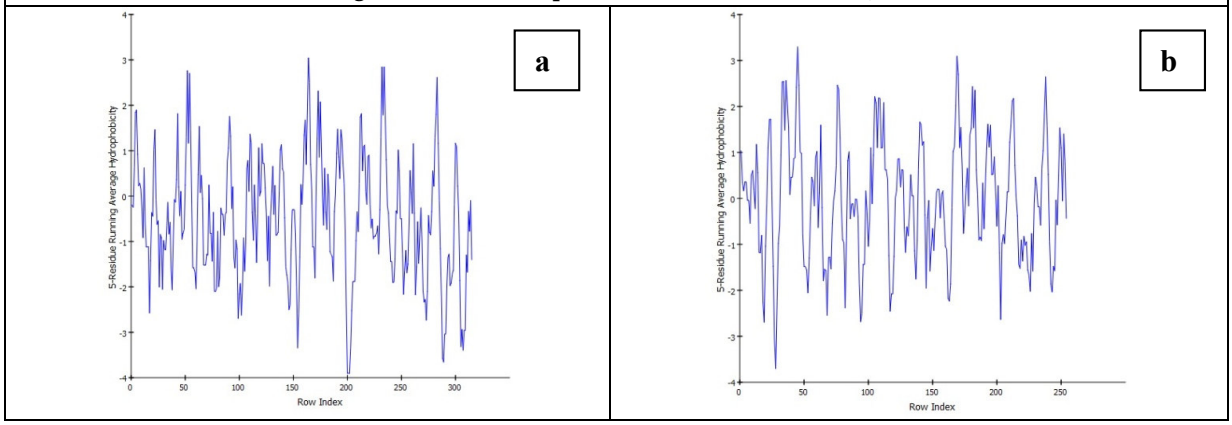


Fig 1: Ramachandan plot of (a) 4GZI (b) 2HK1 (c) 6J17



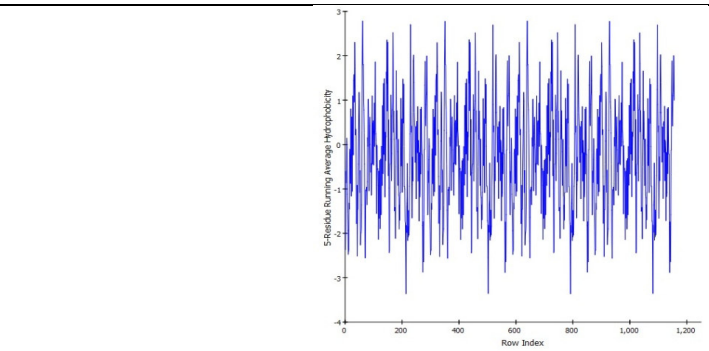
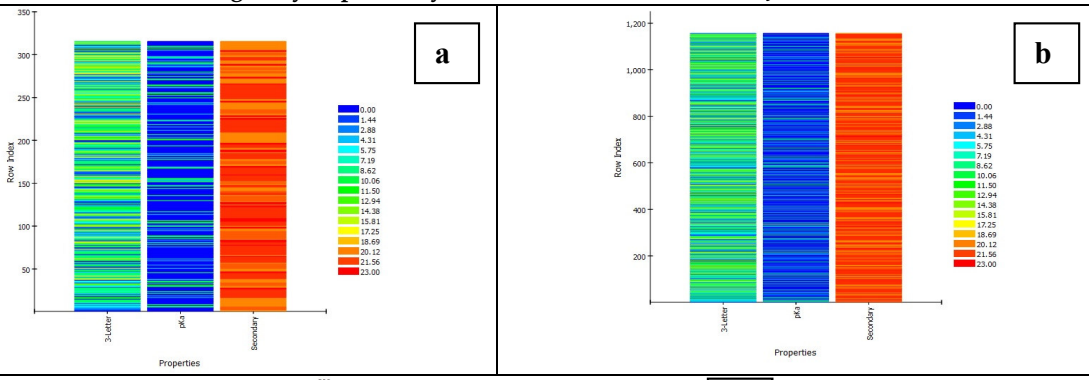


Fig 2: Hydrophobicity Plot of (a) 4GZI (b) 2HK1 (c) 6J17



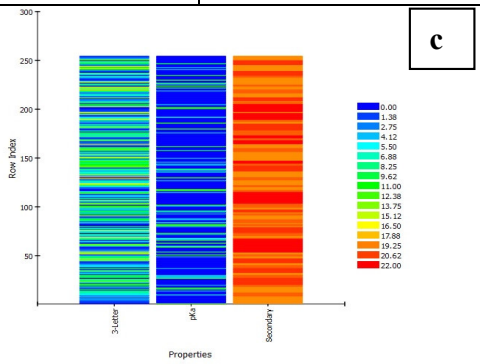
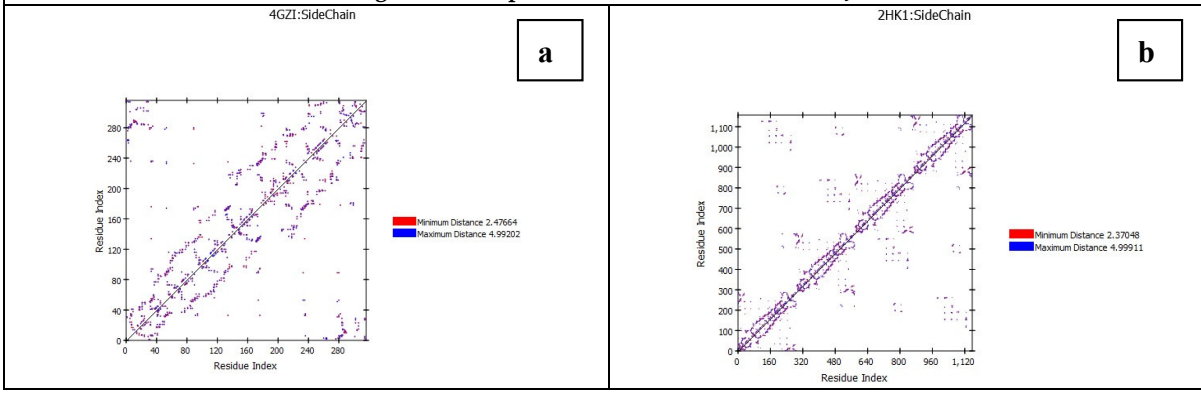


Fig 3: Heat Map Plot of (a) 4GZI (b) 2HK1 (c) 6J17



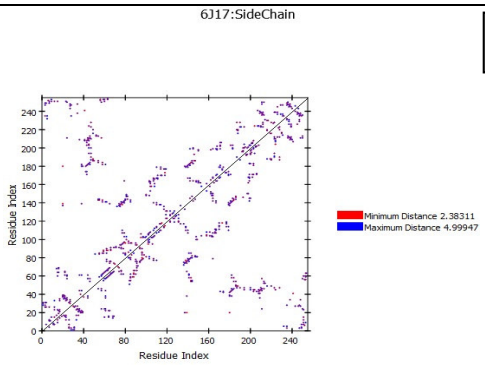


Fig 4: Side chain Plot of (a) 4GZI (b) 2HK1 (c) 6J17

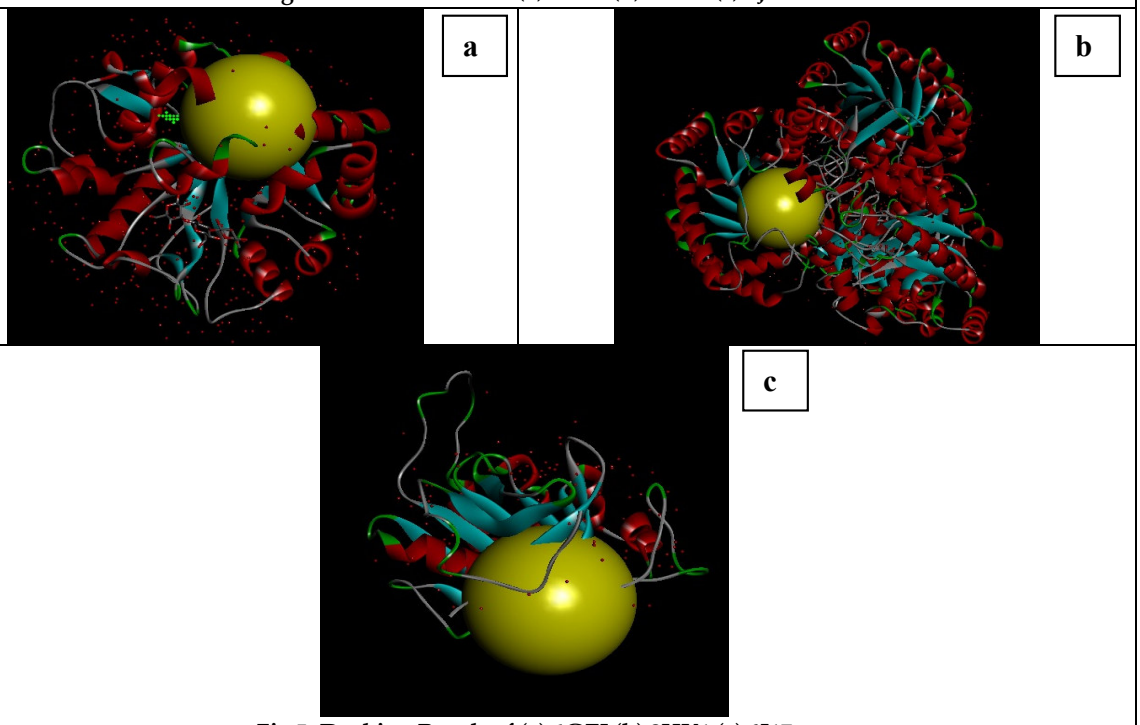
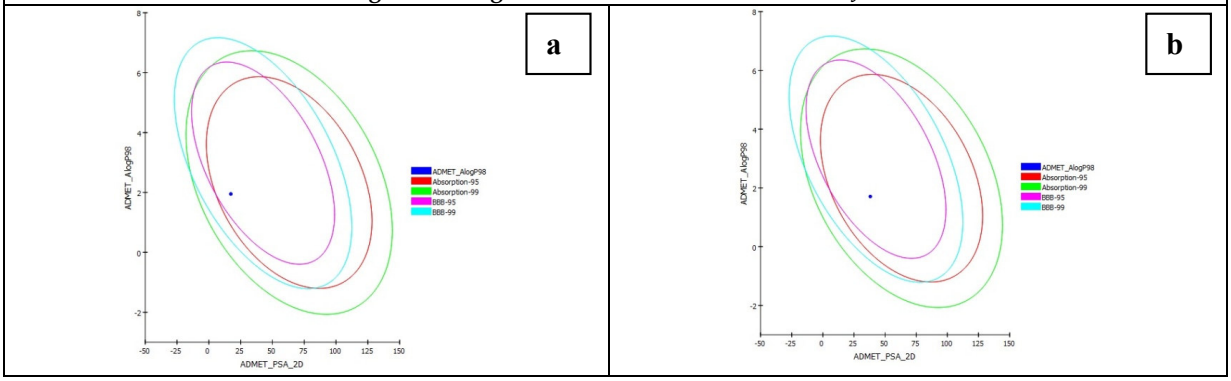


Fig 5: Docking Result of (a) 4GZI (b) 2HK1 (c) 6J17



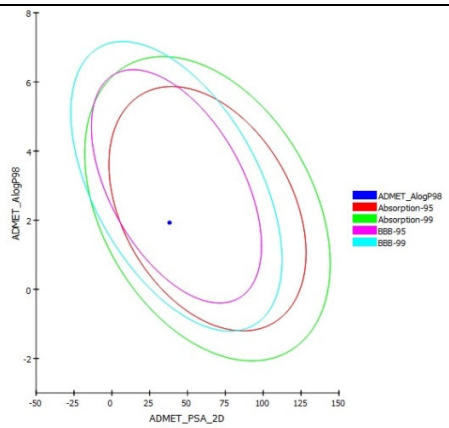


Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

An *In silico* Analysis of the Peppermint as Therapy for Typhoid

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ABSTRACT

As aboriginal sources of medications, medicinal plants are used from the ancient times. Peppermint is one of the highly used potential medicinal plants in the world. This plant is traditionally used for the treatment of common cold, diarrhoea, fever due to several infective cause, jaundice, as a health tonic for the liver and cardiovascular health, and as an antioxidant. It is also used to improve sexual dysfunctions and serve as a contraceptive. All parts of this plant are used to extract the active phytochemicals, but the compositions of phytoconstituents widely differ from one part to another and with place, season, and time of harvest. *Salmonella enterica* subspecies enterica serovar Typhi (*Salmonella typhi*) is the cause of typhoid fever and a human host–restricted organism. Our understanding of the global burden of typhoid fever has improved in recent decades, with both an increase in the number and geographic representation of high-quality typhoid fever incidence studies, and greater sophistication of modeling approaches. The 2017 World Health Organization Strategic Advisory Group of Experts on Immunization recommendation for the introduction of typhoid conjugate vaccines for infants and children aged >6 months in typhoid-endemic countries is likely to require further improvements in our understanding of typhoid burden at the global and national levels. Furthermore, the recognition of the critical and synergistic role of water and sanitation improvements in concert with vaccine introduction emphasize the importance of improving our understanding of the sources, patterns, and modes of transmission of *Salmonella typhi* in diverse settings.

Key Words: Peppermint, Docking, In Silico Analysis, Typhoid, Pharmacophore

INTRODUCTION

Emergence and spread of antibiotic resistance among pathogenic bacteria represents a major obstacle in the treatment of infectious diseases. Antimicrobial resistance (AMR) is a global health problem associated with increased morbidity and mortality. Factors associated with it are well documented and known, but unfortunately the root causes of it continue to be ignored. There are several reasons for the development of AMR. One of the most important is antibiotic overuse/and or improper use of antimicro- bials that make the development and spread of resistance much more likely. Inadequate clinical diagnosis of an infection combined with the prescribing of improper antimicrobials contributes to selective pressure and accelerates AMR. Moreover, the practice of adding antibiotics to agricultural feed promotes drug resistance. More than half of the antibiotics produced in the United States are used for agricultural purposes (Hao et al., 2014; WHO, 2015a). Developing countries are inequitably affected by leading infectious disease killers. Not only do we blame emerging infectious disease organisms, but resistant ones affecting populations where public health infrastructure is fragmented, vaccines are not readily available, there is the existence of substandard and counterfeit drugs, a lack of access to health-care services, and poor health-care seeking behaviour (Sosa, 2004).

Many studies have reported that bacteria have developed resistance because of prolonged treatment with conventional antibiotics possessing a broad-range efficacy via toxic or growth- inhibitory effects on target organisms, rendering the traditional antibiotic treatment virtually ineffective (Xavier and Bassler, 2003). Therefore, there is increased demand for the development of alternative strategies to conventional antibiotic therapy (Zeng et al., 2008). Unfortunately, continuous increases in the global isolation rates of methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant *Staphylococcus epidermidis* (MRSE) and carbapenem-resistant Gram-negative bacilli clinical isolates poses a serious therapeutic problem because no new antimicrobial agents are currently available for treatment of infected patients (WHO, 2015a; Elabd et al., 2015; Asaad et al., 2013). For medicinal purposes, the antimicrobial activity of substances derived from plant extracts has been recognized and widely studied for many years (Mohamed et al., 2015; Hamoud et al., 2012). *Mentha piperita* L., a medicinally important plant that belongs to the family Lamiaceae and is commonly known as peppermint, is a hybrid of *Mentha spicata* L. (spearmint) and Mentha aquatic. It was cultivated by the ancient Egyptians and documented in the Icelandic pharmacopoeia of the 13th Century. It is widely grown in temperate areas of the world, particularly in Europe, North America and North Africa, but is nowadays cultivated throughout all regions of the world (Singh et al., 2011). It is primarily cultivated for its oil, which is extracted from the leaves of the flowering plant. Peppermint oil is used for flavouring pharmaceuticals and oral preparations, such as tooth- pastes, dental creams and mouth washes.

Higher and aromatic plants have traditionally been used in folk medicine as well as to extend the shelf life of food, showing inhibition against bacteria, fungi and yeast. Most of their properties are due to essential oils produced as secondary metabolites (Saeed et al., 2006; Fabio et al., 2007; Bansod and Rai, 2008; Jeyakumar et al., 2011). *Mentha piperita* (Lamiaceae), the peppermint (mint) plant is an aromatic perennial herb cultivated in most part of the world, have traditionally been used in folk medicine. Leaves of mint plant are frequently used in herbal tea and for culinary purpose to add flavour and aroma. The distinctive smell and flavour, a characteristic feature of *Mentha spp.* is due to the naturally occurring cyclic terpene alcohol called menthol. Menthol is prescribed as a medication for gastrointestinal disorders, common cold and musculoskeletal pain (Patil et al., 2007). The mint plants are rich sources of iron and magnesium, which play important role in human nutrition (Arzani et al., 2007). A large volume of literature is available on the medicinal properties of essential oils present in *Mentha spp*. (Gulluce et al., 2007; Rasooli, 2008). However, no much study has been directed toward the antioxidant and antimicrobial properties of the mint leaves which are locally available.

Salmonella enterica subspecies enterica serovar *typhi (Salmonella typhi*) is the cause of typhoid fever. Together, *Salmonella typhi* and *Salmonella serovar Paratyphi* A are the major agents of enteric fever. Like other typhoidal

Salmonella serovars, Salmonella typhi is a human host–restricted organism. The role of water as a vehicle for typhoid fever has been appreciated since the late 1800s (Newton 2014, CDC 2016) and the role of food not long after (Wain et.al, 2015). Our understanding of the global burden of typhoid fever has improved in recent decades, with an increase in both the number and geographic representation of high-quality typhoid fever incidence studies, and greater sophistication of modeling approaches. The 2017 World Health Organization (WHO) Strategic Advisory Group of Experts on Immunization (SAGE) recommendation for the introduction of typhoid conjugate vaccines (TCVs) for infants and children aged >6 months in typhoid-endemic countries (WHO 2008) is likely to require further improvements in our understanding of typhoid burden not only at the global level, but also at the national and subnational levels. Furthermore, the recognition of the critical and synergistic role of water and sanitation improvements in concert with vaccine introduction (Crump and Mintz 2015, Theo et.al, 2016) emphasizes the need to improve our understanding of the sources, patterns, and modes of transmission of *Salmonella typhi* in diverse local settings. The Gram-negative bacterium that causes typhoid fever is *Salmonella enterica* sub sp. *Enterica serovar typhi.* Based on MLST subtyping scheme, the two main sequence types of the *S.* Typhi are ST1 and ST2, which are currently wide spread globally (Stephens et.al, 2019, Wang et.al,2016, Magill 2017). The global phylogeographical analysis showed dominance of a haplotype 58 (H58) which probably originated in India during late 1980s and now spreading through the world carrying multidrug resistance. (Jackson et.al, 2015, Yap et.al, 2016, Kumar and Kumar 2017) A recently proposed and more detailed genotyping scheme has been reported in 2016 and is being used widely since. This scheme re-classified the nomemclature of H58 to genotype.

MATERIALS AND METHODS

Phytochemicals of Peppermint have been listed with their structure data files which are taken from pubchem ChEBI. Genes has been taken randomly for Typhoid using NCBI database. Table 1 has been showing the enlisted pharmacophores and the targeted genes. The PDB numbers of enzymes are taken from RCSB. The In-silico analysis has been done using BIOVIA –Discovery studio. We have performed various docking and used the Ramachandan plot and others.

Protein identification and preparation

The reported molecular targets responsible for Typhoid are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Peppermint were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which

focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from Peppermint was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Peppermint with the selected targets of typhoid. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Peppermint to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Breast ly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Breast administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

CSCs typically exhibit three key characteristics, which are not mutually exclusive. Firstly, CSCs are highly tumorigenic and can form tumours in immune-deficient mice through xenotransplantation, which is not possible for non-CSCs. Secondly, CSCs that survive chemotherapy and radiotherapy generate resistance to such therapies through regulating intracellular stress; for example, regulating reactive oxygen species, which non-CSCs cannot. Thirdly, CSCs possess metastatic potential, illustrated by a report that CSCs have the ability to metastasize. The identified pharmacophores can be isolated from the Peppermint and can be commercialized as the natural drug for the Typhoid which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.

The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Typhoid

Sl.No	Pharmacophores from Peppermint	Targeted Genes from Typhoid	PDB No of the Genes
1	Menthone	L-lactate dehydrogenase A chain	5ZJD
2	Beta Pinene	Retinal dehydrogenase	6DUM
3	Menthofuran	lactate dehydrogenase	6MV8
4	1,8cineole	NADPH-dependent methylglyoxal reductase GRE2	4PVD

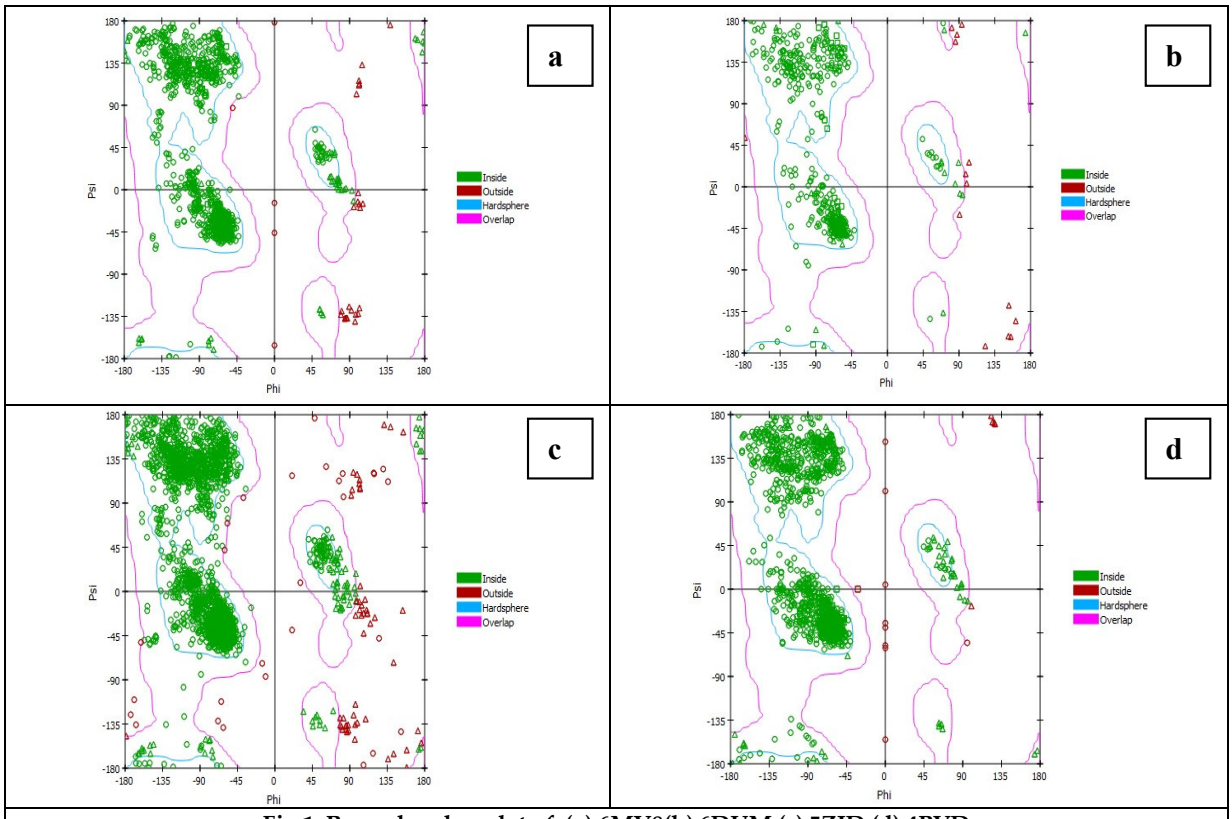

Fig 1: Ramachandan plot of (a) 6MV8(b) 6DUM (c) 5ZJD (d) 4PVD

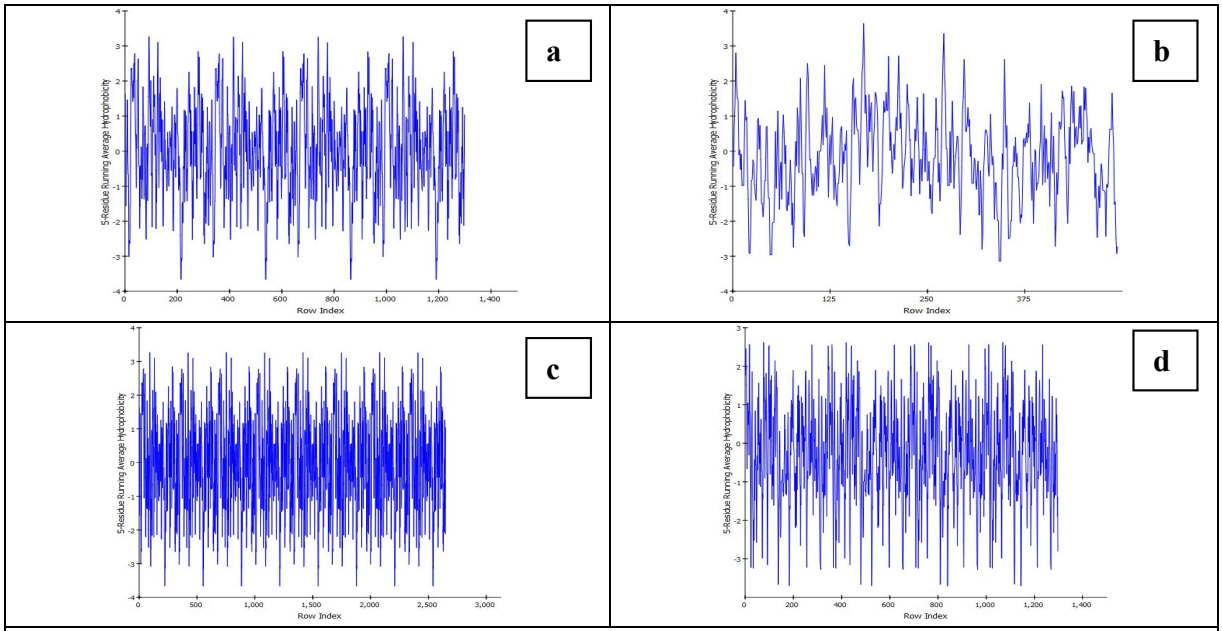

Fig 2: Hydrophobicity Plot of (a) 6MV8(b) 6DUM (c) 5ZJD (d) 4PVD

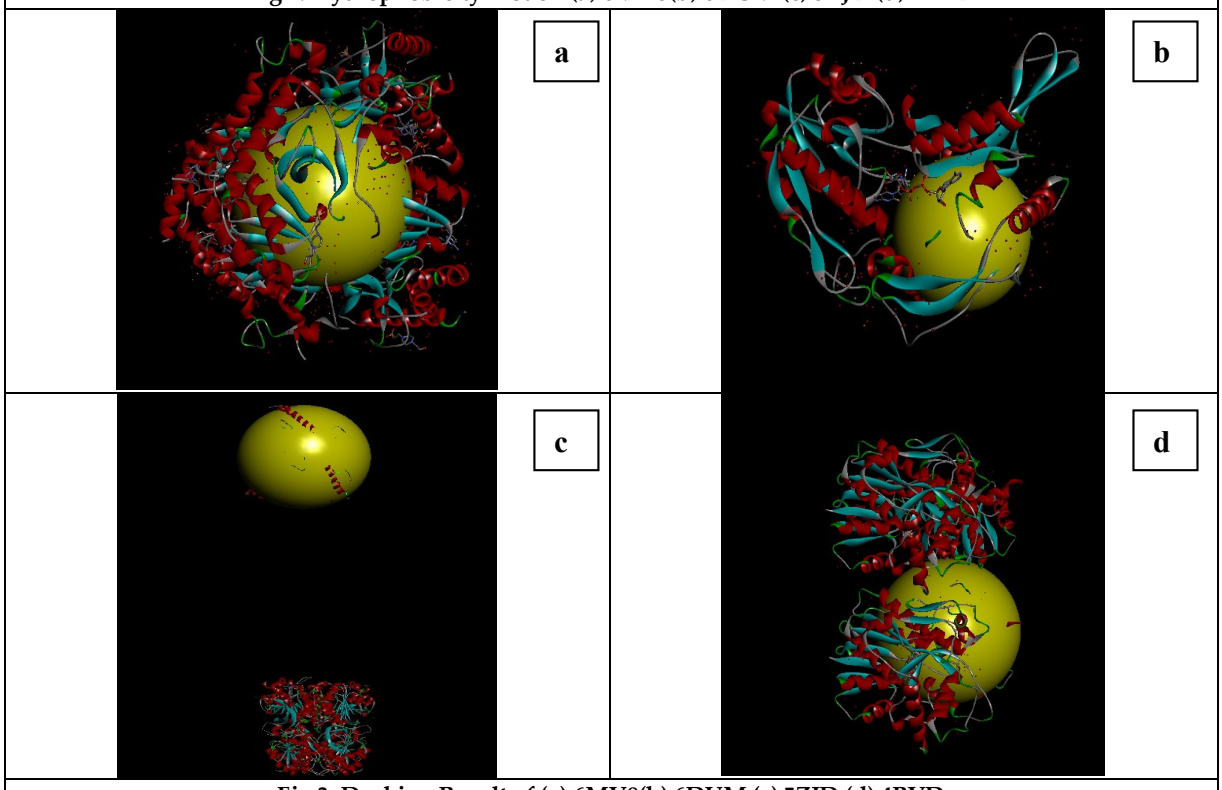

Fig 3: Docking Result of (a) 6MV8(b) 6DUM (c) 5ZJD (d) 4PVD

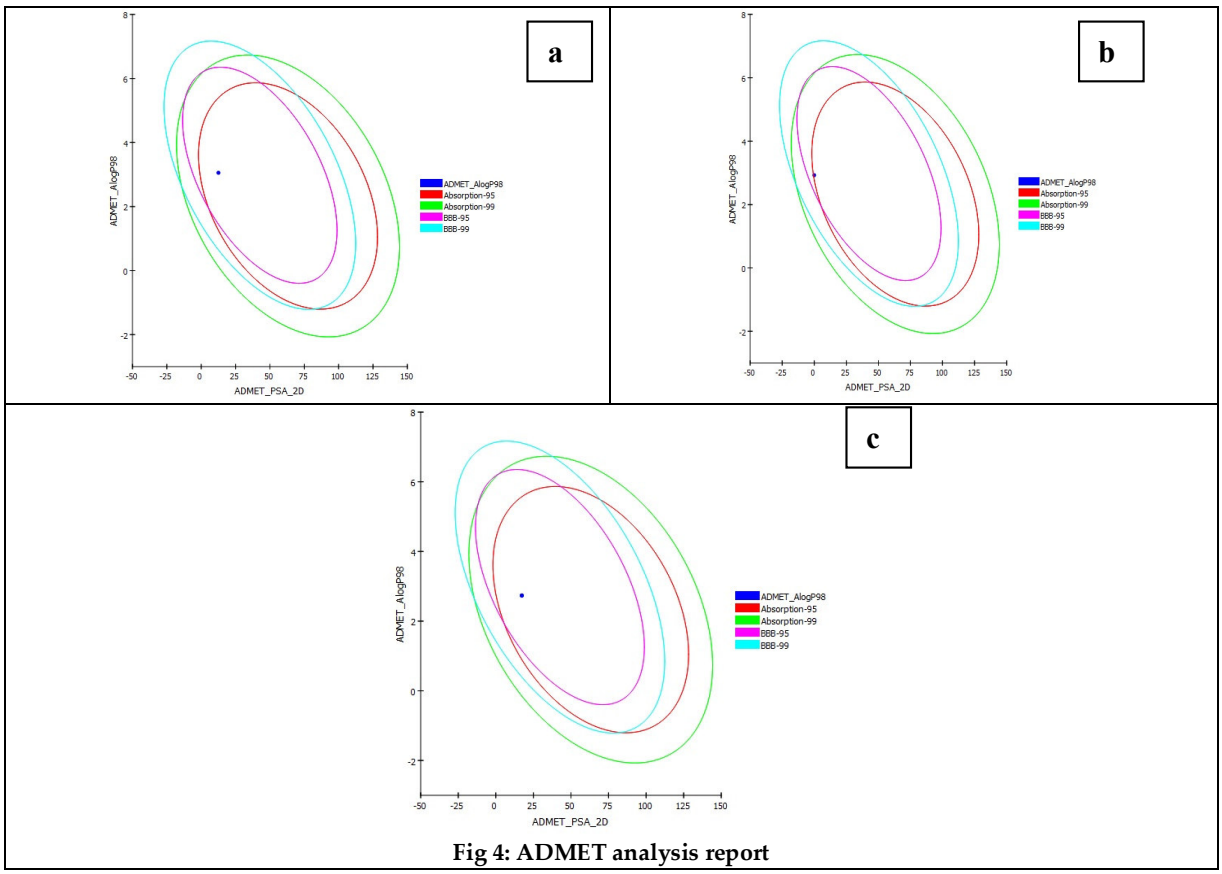

Fig 4: ADMET analysis report

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RESEARCH ARTICLE

Green Chiretta (*Andrographis paniculata): In silico* Analysis of Therapy for Breast Cancer

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ABSTRACT

As aboriginal sources of medications, medicinal plants are used from the ancient times. *Andrographis paniculata* is one of the highly used potential medicinal plants in the world. This plant is traditionally used for the treatment of common cold, diarrhoea, fever due to several infective cause, jaundice, as a health tonic for the liver and cardiovascular health, and as an antioxidant. It is also used to improve sexual dysfunctions and serve as a contraceptive. All parts of this plant are used to extract the active phytochemicals, but the compositions of phytoconstituents widely differ from one part to another and with place, season, and time of harvest. We are using this property of Green Chiretta to get some new drugs for Breast Cancer. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Breast Cancer and pharmacophores from Green Chiretta and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others. From this we can deduce that these two pharmacophores can be a solution to Lung Cancer in near future. Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine. As cancer incidence rates and survival time increase, use of CAM will likely increase. However, little is known about the use of CAM in cancer patients, specifically in emerging countries.

Key Words: Green Chiretta , Docking, In Silico Analysis, Breast Cancer, Pharmacophore

INTRODUCTION

Andrographis paniculata (Burm. F) Nees, commonly known as the "king of bitters," is an herbaceous plant belonging to the *A.canthaceae* and is found throughout tropical and subtropical Asia, Southeast Asia, and India. In India, *A.paniculata* is known as "Kalmegh"; in China it is known as "Chuan-Xin-Lian"; in Thailand it is known as "Fah Tha Lai"; in Malaysia it is known as "Hempedu bumi"; in Japan it is known as "Senshinren"; and in Scandinavian countries it is known as "green chiretta" (Chaudhary et. al, 2010). Extracts of this plant and andrographolide exhibit pharmacological activities such as those that are immunostimulatory (Joy et.al, 1998, Chaudhary et. Al, 2010), antiviral (Burkill et.al,1966), and antibacterial (Kavishankar et.al, 2011). As major active constituent, andrographolide exhibits a broad range of biological activities, such as anti-inflammatory, antibacterial, antitumor, antidiabetic, antimalarial, and hepatoprotective (Hajiaghaee and Akhondzadeh, 2012) Because of the impressive variety of these biological activities, researchers propose obtaining various leads by structurally modifying andrographolide.In recent decades, numerous andrographolide derivatives have emerged and their pharmacological activities have also been evaluated. However, studies that have comprehensively summarized or analyzed *A. paniculata* and its derivatives have been minimal. Therefore, to contribute to the advanced trends of research on andrographolide, this paper provides thorough information regarding the pharmacological activities of *A. paniculata* and its major compound andrographolide. Andrographolide is a major bioactive phytoconstituent found in various parts of *A. paniculata*, but particularly in the leaves.

The chemical name of andrographolide is 3α, 14, 15, 18-tetrahydroxy-5β,9βH, 10α-labda-8, 12-dien-16-oic acid γ-lactone, and its molecular formula and weight are C20H30O5 and 350.4 (C 68.54%, H 8.63%, and O 22.83%), respectively. The structure of andrographolide has been analyzed by using X-ray, 1H,13 C-NMR, and ESI-MS (Jarukamjorn and Nemoto 2008, Akbar 2011, Kabir et.al. 2014, Urbi et al. 2014, Duke 2017). Although andrographolide is not very soluble in water, it is soluble in acetone, chloroform, ether, and hot ethanol. Crystalline andrographolide was reported to be highly stable, over a period of three months (Kumar et.al 2008). Some scientists reported a simple and rapid method for isolating andrographolide from the leaf of *A. paniculata*. Andrographolide has been reported to have a wide range of biological activities, such as those that are anti-inflammatory (Rajagopal et.al 2003), antiallergic (Cheung et al. 2005), antiplatelet aggregation (Liet al.v2007, Harjotaruno et.al 2008), hepatoprotective (Zhou et.al 2006). In addition to these activities, the ability of ethanol or an aqueous extract of *A. paniculata* to decrease bloodglucose levels innormal rats or streptozotocin diabetic rats has been documented.In biological systems, andrographolide can interact withmany inter- and intracellular constituents as a bipolar compound, thus ensuing inmany biological responses. A recent study demonstrated that *A. paniculata* polysaccharides combined with andrographolide can ease the recovery of diabetic nephropathy.

As per WHO (2018) Cancer starts when cells begin to grow out of control. Breast cancer cells usually form a tumor that can often be seen on an x-ray or felt as a lump. It's important to understand that most breast lumps are benign and not cancer (malignant). Non-cancerous breast tumors are abnormal growths, but they do not spread outside of the breast. They are not life threatening, but some types of benign breast lumps can increase a woman's risk of getting breast cancer (NCI,2018). Any breast lump or change needs to be checked by a health care professional to determine if it is benign or malignant (cancer) and if it might affect your future cancer risk. Most breast cancers begin in the ducts that carry milk to the nipple (ductal cancers).Some start in the glands that make breast milk (lobular cancers) (Kayande et.al 2014).There are also other types of breast cancer that are less common like phyllodes tumor and angiosarcoma.A small number of cancers start in other tissues in the breast. These cancers are called sarcomas and lymphomas and are not really thought of as breast cancers.

Although many types of breast cancer can cause a lump in the breast, not all do. See Breast Cancer Signs and Symptoms to learn what you should watch for and report to a health care provider. Many breast cancers are also found on screening mammograms, which can detect cancers at an earlier stage, often before they can be felt, and

before symptoms develop (WHO, 2018). Breast cancer is cancer that forms in the cells of the breasts. Doctors know that breast cancer occurs when some breast cells begin to grow abnormally. These cells divide more rapidly than healthy cells do and continue to accumulate, forming a lump or mass. Cells may spread (metastasize) through your breast to your lymph nodes or to other parts of your body. Breast cancer most often begins with cells in the milk-producing ducts (invasive ductal carcinoma). Breast cancer may also begin in the glandular tissue called lobules (invasive lobular carcinoma) or in other cells or tissue within the breast. Researchers have identified hormonal, lifestyle and environmental factors that may increase your risk of breast cancer. But it's not clear why some people who have no risk factors develop cancer, yet other people with risk factors never do. It's likely that breast cancer is caused by a complex interaction of your genetic makeup and your environment (NCI,2019). Doctors estimate that about 5 to 10 percent of breast cancers are linked to gene mutations passed through generations of a family.A number of inherited mutated genes that can increase the likelihood of breast cancer have been identified. The most well-known are breast cancer gene 1 (BRCA1) and breast cancer gene 2 (BRCA2), both of which significantly increase the risk of both breast and ovarian cancer.

MATERIAL AND METHODS

Phytochemicals of Ashwagandha have been listed with their structure data files which are taken from pubchem ChEBI. Genes has been taken randomly for Breast Cancer using NCBI database. Table 1 has been showing the enlisted pharmacophores and the targeted genes. The PDB numbers of enzymes are taken from RCSB. The In-silico analysis has been done using BIOVIA –Discovery studio. We have performed various docking and used the Ramachandran plot and others.

Protein identification and preparation

The reported molecular targets responsible for Breast cancer are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Green Chiretta were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from Green Chiretta was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Green Chiretta with the selected targets of Breast Cancer. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Green Chiretta to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Breast ly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the

evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Breast administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

CSCs typically exhibit three key characteristics, which are not mutually exclusive. Firstly, CSCs are highly tumorigenic and can form tumours in immune-deficient mice through xenotransplantation, which is not possible for non-CSCs. Secondly, CSCs that survive chemotherapy and radiotherapy generate resistance to such therapies through regulating intracellular stress; for example, regulating reactive oxygen species, which non-CSCs cannot. Thirdly, CSCs possess metastatic potential, illustrated by a report that CSCs have the ability to metastasize. The identified pharmacophores can be isolated from the Green Chiretta and can be commercialized as the natural drug for the Breast Cancer which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.

The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Breast Cancer

Sl.No	Pharmacophores from Green Chiretta	Targeted Genes from Breast Cancer	PDB No of the Genes
1	Andrographolide	Transcription	6vpk
2	Neoandrographolide	Cell Adhesion	6xvt
3	14-Deoxy-11,12-Didehydroandrographolide	Lyase/Lyase Inhibitor	6vj3
4	5,7,2′,3′-Tetramethoxyflavanone	Oxidoreductase	6qgv

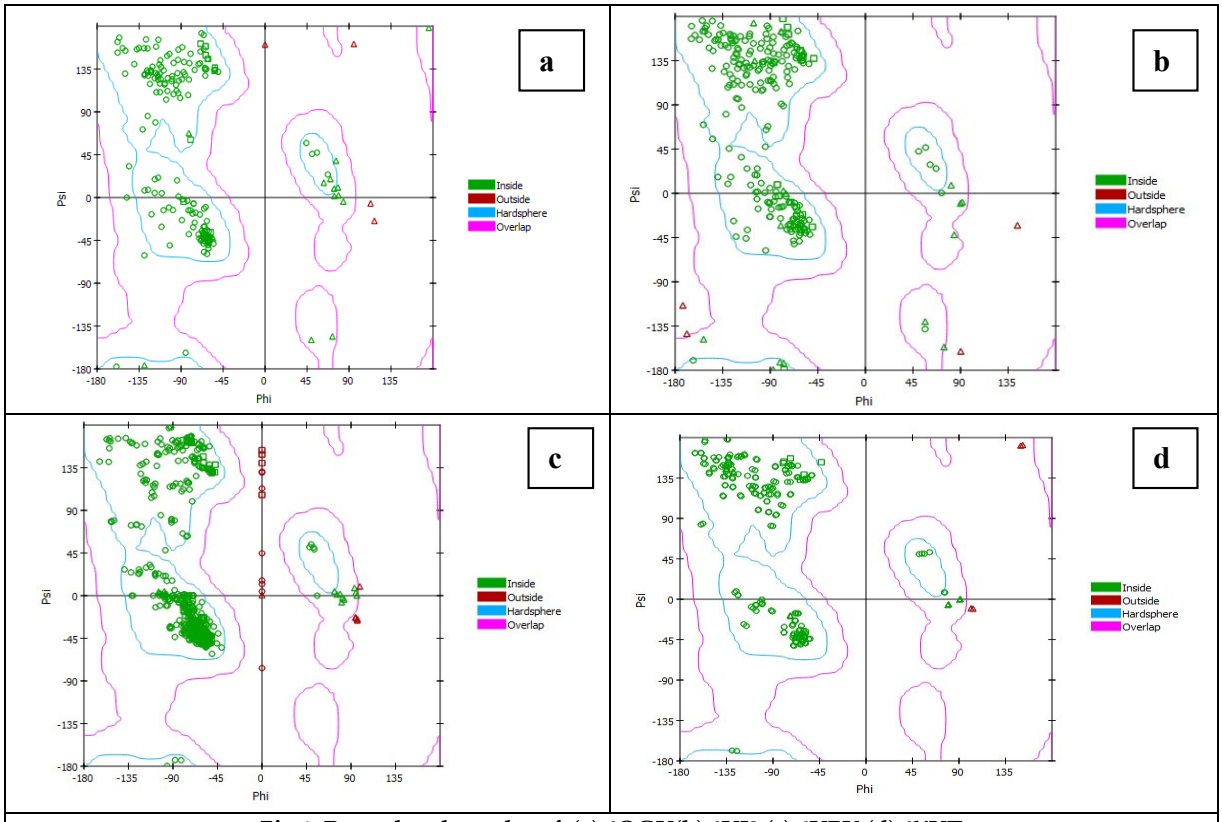
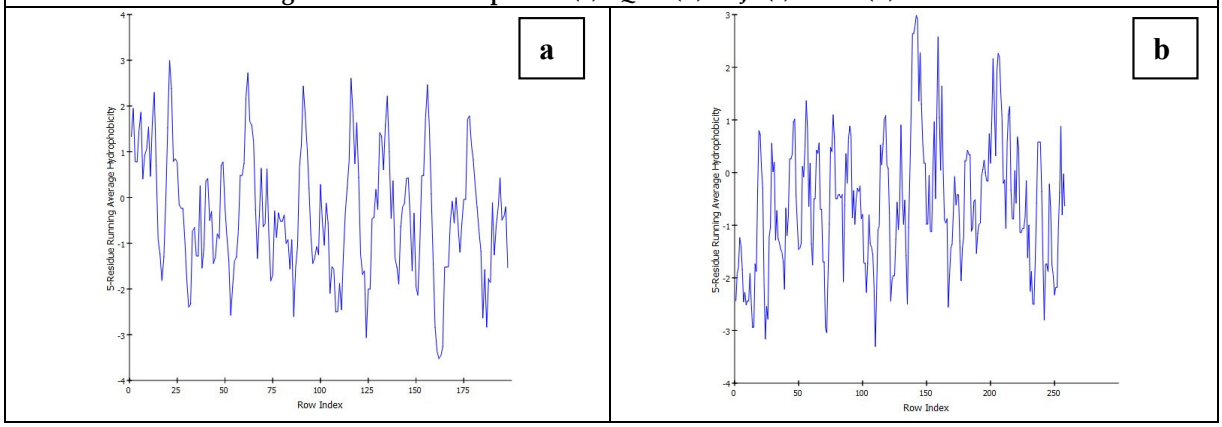


Fig 1: Ramachandran plot of (a) 6QGV(b) 6VJ3 (c) 6VPK (d) 6XVT



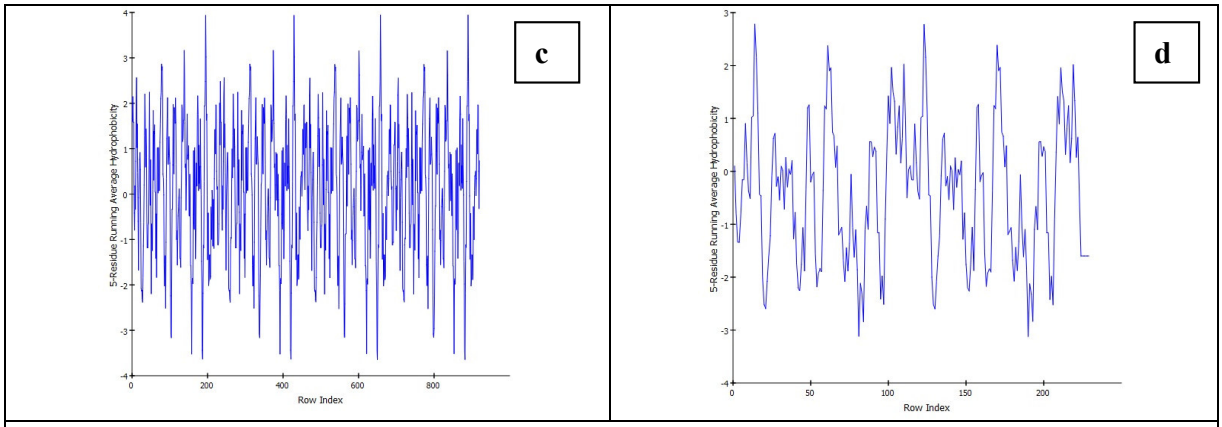


Fig 2: Hydrophobicity Plot of (a) 6QGV(b) 6VJ3 (c) 6VPK (d) 6XVT

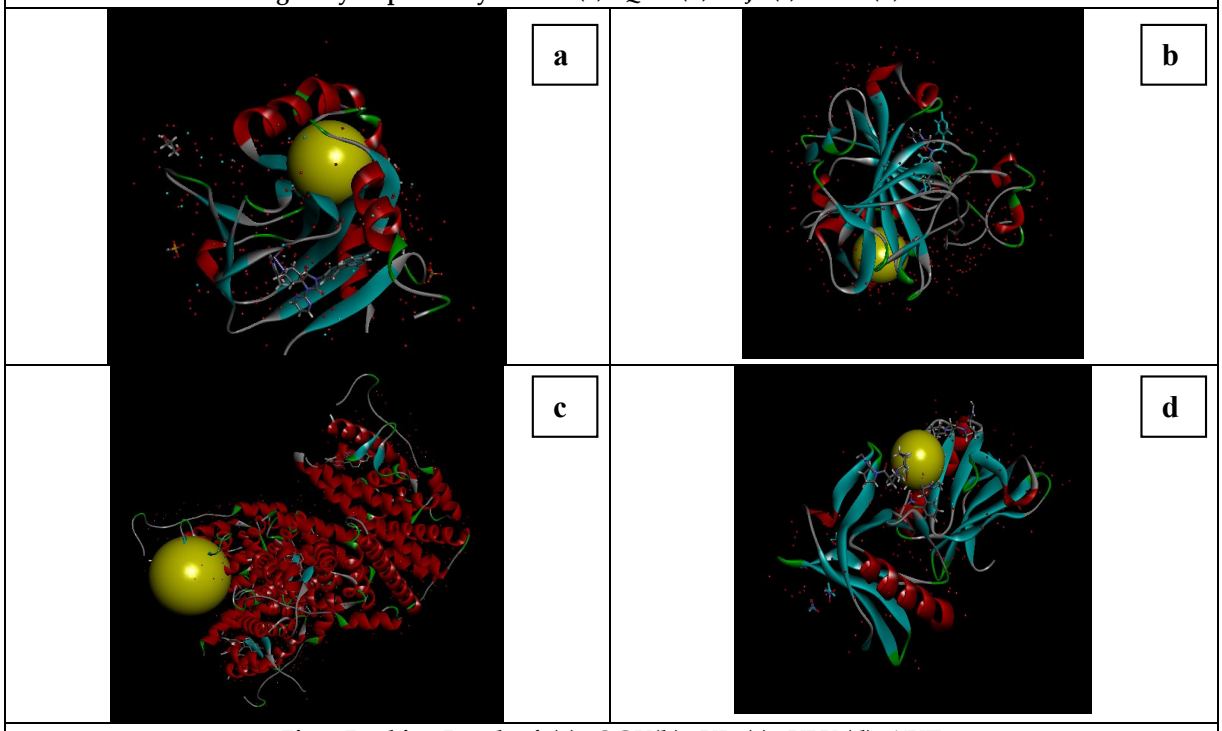


Fig 3: Docking Result of (a) 6QGV(b) 6VJ3 (c) 6VPK (d) 6XVT

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RESEARCH ARTICLE

Cumin: *In silico* Analysis as of Targeted Therapy for Diarrhoea

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. Cumin (*Cuminum cyminum* Linn.) is an important seed spice and one of the earliest known minor spices used by mankind. It is believed to be native of Egypt and Syria, Turkestan and the Eastern Mediterranean region. The typical pleasant aroma of the seeds is due to their volatile oil content, the principal constituent of which is cuminol (cuminaldehyde). Antioxidants help in removing free radicals that can further mutate into cancer cells. We are using this property of Cumin to get some new drugs for Diarrhoea. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Diarrhoea and pharmacophores from Cumin and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Cumin, Docking, *In silico* Analysis, Diarrhoea, Pharmacophore

INTRODUCTION

Ayurveda, the science of life, which is the ancient traditional system of Indian medicine, is believed to be well over 5,000 years old. Ayurveda has particularly emphasized the subtle yet incredible healing properties of herbs and spices, and among these cumin plays an important part, which is used both as an ayurvedic medicine and as well as

the main spice in Indian food recipes. Cumin *(Cuminum cyminum)* is one of the most valuable medicinal herbs and spice in the world. This plant belongs to the *Apiaceae* family and is geographically distributed in south Mediterranean and West Asia (latitudes 20-38° N and longitudes 30°- 80° E) (Zargari 1988, Balandary, 1992, katzer).There are different theories about the origin of cumin. However, based on documented evidences, it either originated in northern Egypt, in the south Mediterranean climate or in the Middle East (Wu et.al,1982, Chaudhari, 1992, Heravi 1962, Heravi 1977). The presence of wild cumin plants in vast areas of south Mediterranean, Saudi Arabia, Iran, Central Asia, Sahara and south Pakistan indicate that these areas could be the origin of domestication of cumin. Based on the background of cultivation, variation of wild types, particularly other species of cumin *(Cuminum setifolium*) and wide distribution of semi-wild races of cumin, the Iranian plateau and Middle East could also be the center of evolution of cumin. Cumin, as one of these medicinal plants, contains more than 100 different chemicals, including essential fatty acids and volatile oils (Mohiti et al, 2011). In recent years, herbal supplements have been used instead of chemical applications in aquaculture because they are more consumer acceptance and ecofriendly approach in disease management (Raa, 1996). Medicinal herbs or spices are able to enhance immunity and generate more pathogen resistance (Harikrishnan et al., 2011a). Several studies have also reported that the spices like garlic, ginger, thyme, rosemary and fenugreek improved health status, growth performance and/or disease resistance in *Dicentrarchus labrax* and *O. mossambicus* (Yılmaz & Ergün, 2012; Yılmaz et al., 2012; Yılmaz et al., 2013). Varieties of spices have been used traditionally to prevent and treat diseases and are known to improve the immune system (Chauhan et al., 2010). Allspice (*Cuminum cyminum, Apiaceae*) has been used as a spice since ancient times (Azeez, 2008). It is cultivated in the Mediterranean countries (Amin, 2001), especially in India, the world's largest producer and consumer of cumin, with annual production ranging between 0.1 and 0.2 million tonnes (Azeez, 2008). It has been used in medicines as a stimulant of the immune system, tyrosinase inhibitor activity and also as a hypoglycaemic, hypolipidaemic, chemoprotective and relaxant compound in animals and human beings (Boskabady et al., 2005; Azeez, 2008).

Diarrhea poses a diagnostic and therapeutic challenge to clinicians, in part, because it has diverse etiologies. Diagnostic tests may be difficult or not readily available, a specific diagnosis may be elusive, and targeted treatment may be unavailable, leading to the need for trials of empiric therapy. Although diarrhea may be obvious to the patient, it is important to define the basic characteristics of the diarrhea: frequency and consistency. A more quantitative approach is to determine stool weight/24 hrs in a timed collection. A rational classification for evaluation of diarrhea considers acute and chronic (more than 4 weeks) forms. This approach emphasizes the likelihood of an infectious etiology for acute conditions, whereas chronic diarrhea is much less likely to be infectious, and other causes should be considered. An alternative classification for diarrhea is based on the appearance of the stool: fatty, inflammatory (associated with blood in the stool) or watery, as detailed elsewhere.

MATERIALS AND METHODS

Phytochemicals of Cumin have been listed with their structure data files which are taken from pubchem ChEBI. Genes has been taken randomly for Diarrhoea using NCBI database. Table 1 has been showing the enlisted pharmacophores and the targeted genes. The PDB numbers of enzymes are taken from RCSB. The *In-silico* analysis has been done using BIOVIA –Discovery studio. We have performed various docking and used the Ramachandan plot and others.

Protein identification and preparation

The reported molecular targets responsible for Diarrhoea are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water

molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Cumin were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from Cumin was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Cumin with the selected targets of Diarrhoea. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Cumin to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

CSCs typically exhibit three key characteristics, which are not mutually exclusive. Firstly, CSCs are highly tumorigenic and can form tumours in immune-deficient mice through xenotransplantation, which is not possible for non-CSCs. Secondly, CSCs that survive chemotherapy and radiotherapy generate resistance to such therapies through regulating intracellular stress; for example, regulating reactive oxygen species, which non-CSCs cannot. Thirdly, CSCs possess metastatic potential, illustrated by a report that CSCs have the ability to metastasize. The identified pharmacophores can be isolated from the Cumin and can be commercialized as the natural drug for the Diarrhoea which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.

The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Diarrhoea

Sl.No	Pharmacophores from Cumin	Targeted Genes from Diarrhoea	PDB No of the Genes
1	Berberine	Forkhead Box P3	4WK8
2	P-Coumaric	Guanylate Cyclase 2c	6JT2
3	Saponins	Apolipoprotein E	6V7M
4	4-Isopropylbenzoic Acid	Guanylate Cyclase 2c	6JT0

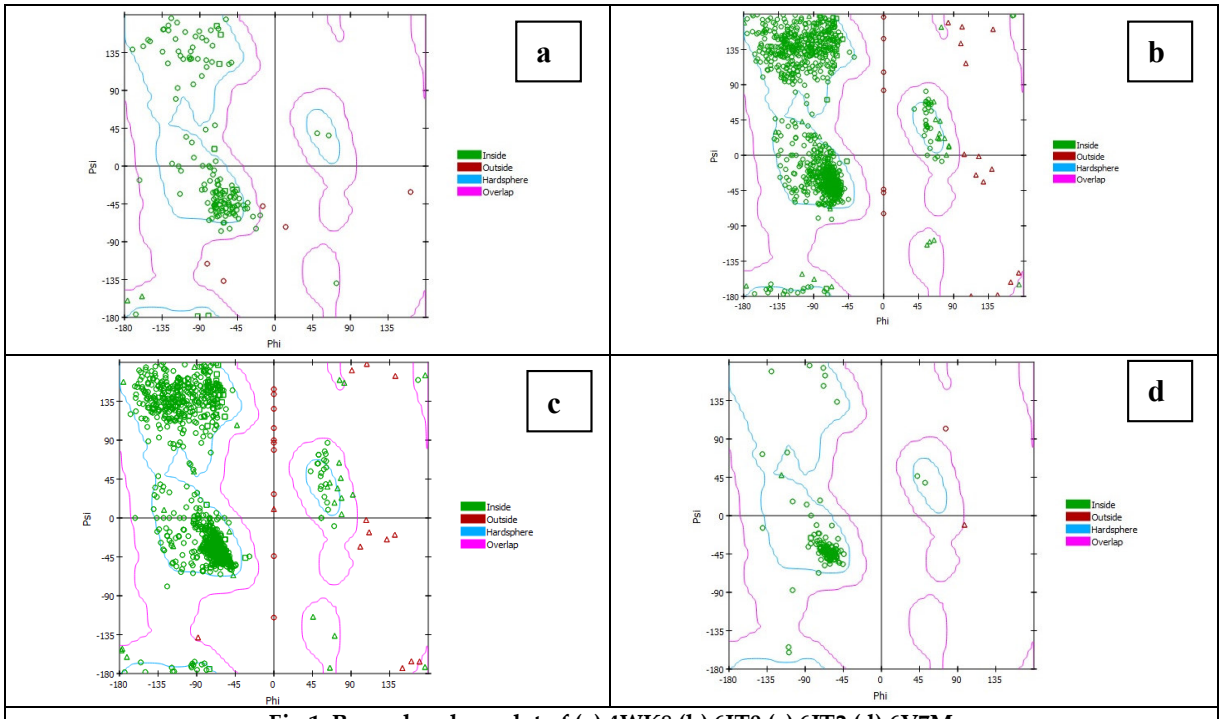

Fig 1: Ramachandran plot of (a) 4WK8 (b) 6JT0 (c) 6JT2 (d) 6V7M

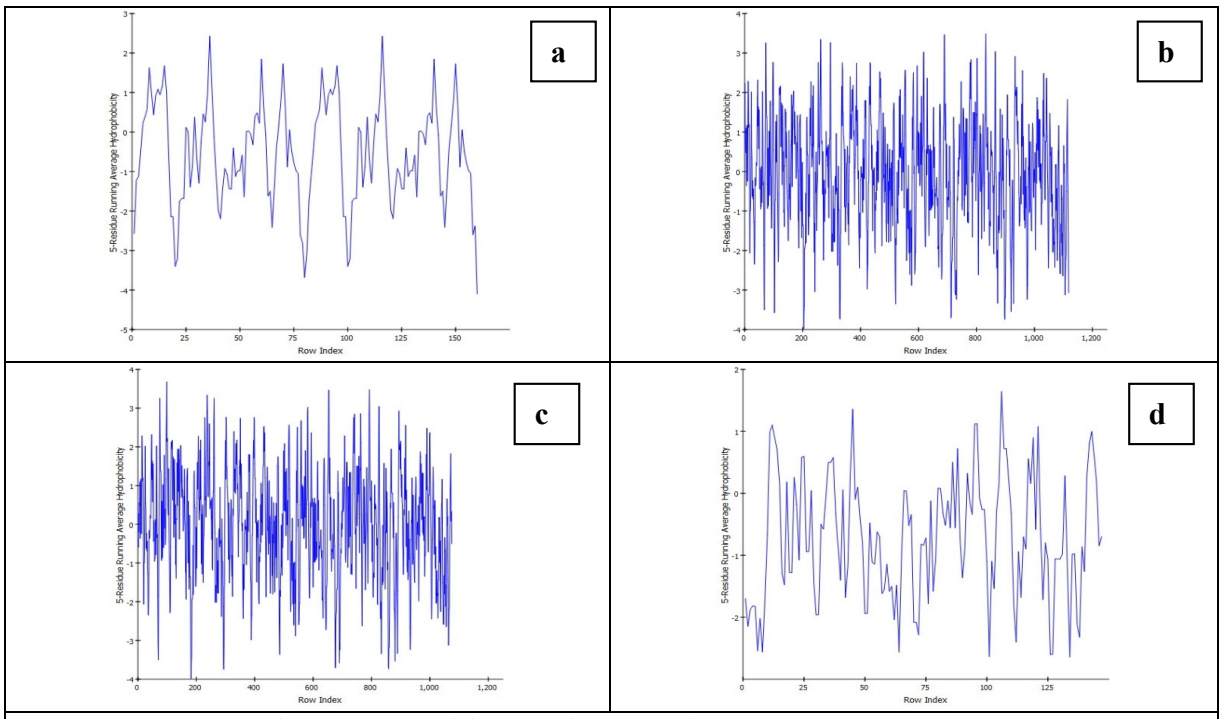

Fig 2: Hydrophobicity Plot of (a) 4WK8 (b) 6JT0 (c) 6JT2 (d) 6V7M

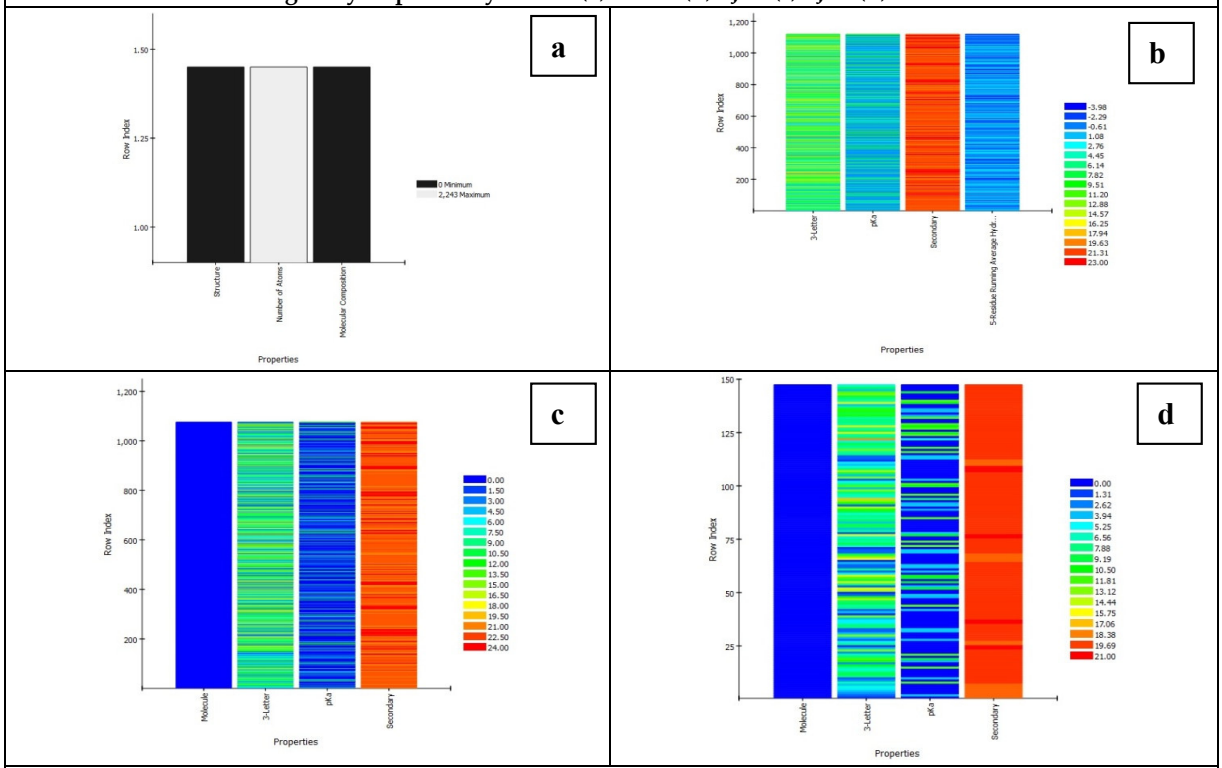

Fig 3: Heat Map Plot of (a) 4WK8 (b) 6JT0 (c) 6JT2 (d) 6V7M

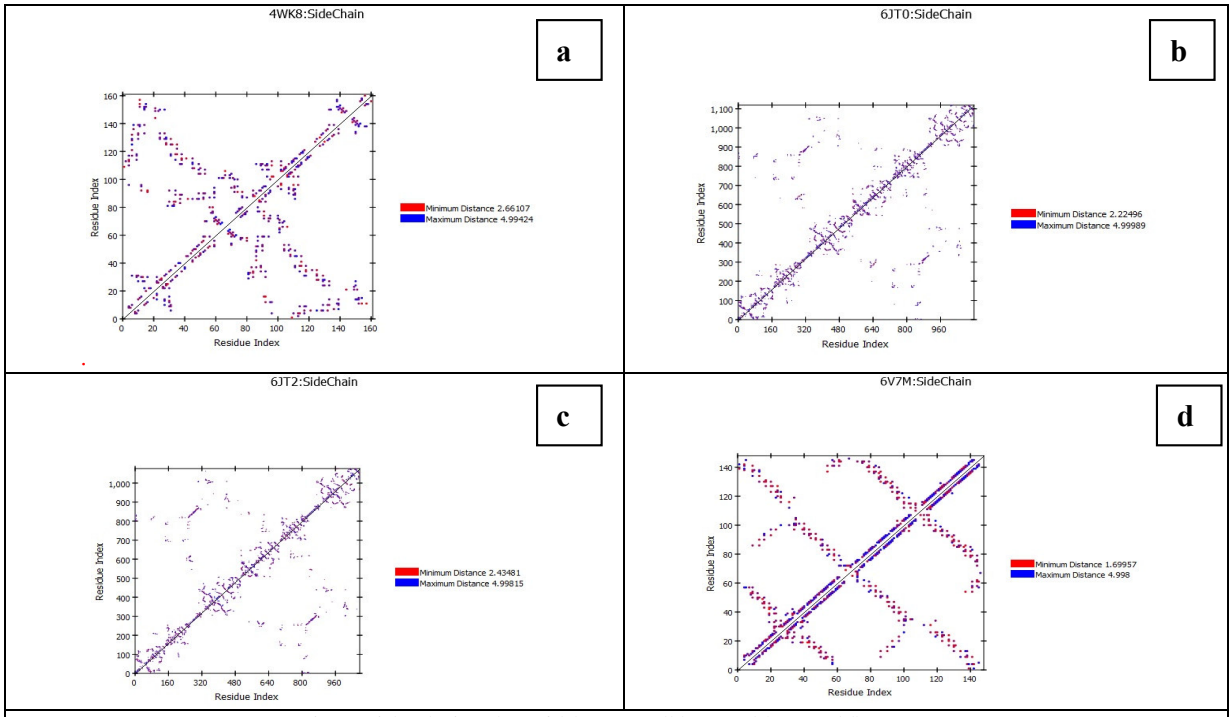

Fig 4: Side chain Plot of (a) 4WK8 (b) 6JT0 (c) 6JT2 (d) 6V7M

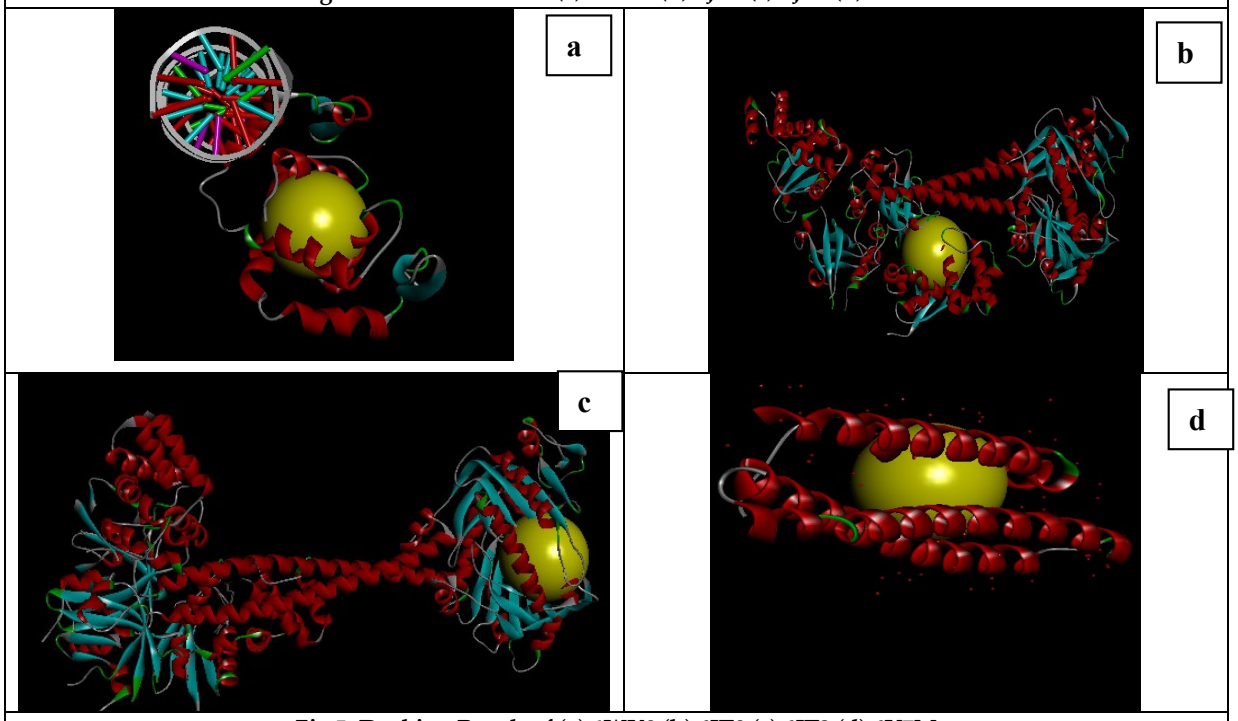

Fig 5: Docking Result of (a) 4WK8 (b) 6JT0 (c) 6JT2 (d) 6V7M

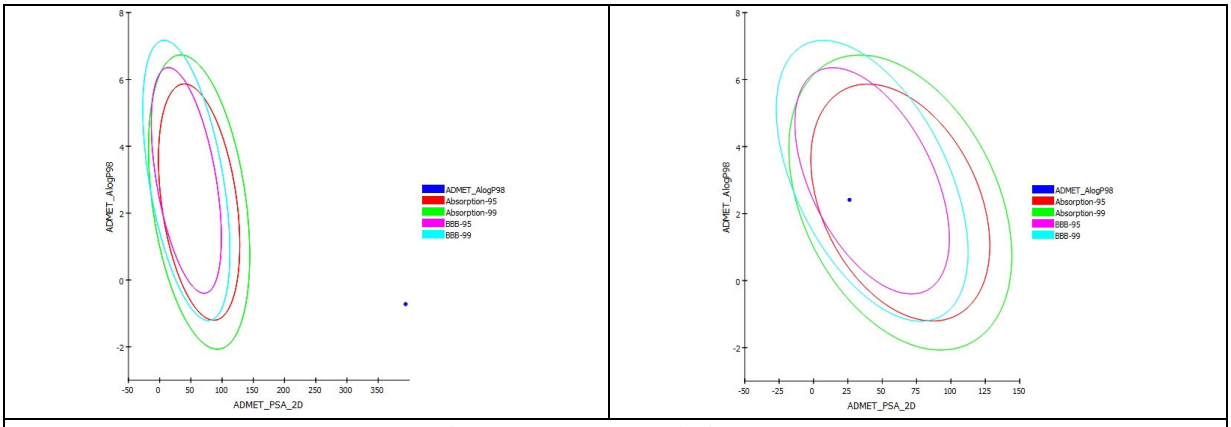

Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

Cinnamon: *In silico* Analysis as Targeted Therapy for Gastric Cancer

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is Cinnamon which has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. Cinnamon is full of antioxidants that are essential for living a healthy life. Antioxidants help in removing free radicals that can further mutate into cancer cells. We are using this property of Cinnamon to get some new drugs for Gastric Cancer. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Gastric Cancer and pharmacophores from Cinnamon and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others. From this we can deduce that these two pharmacophores can be a solution to Lung Cancer in near future. Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine. As cancer incidence rates and survival time increase, use of CAM will likely increase. However, little is known about the use of CAM in cancer patients, specifically in emerging countries.

Key Words: Cinnamon, Docking, *In silico* Analysis, Gastric Cancer, Pharmacophore

INTRODUCTION

From ancient many herbs and spices are being used as medicine for many diseases. Cinnamon is a spice, made from inner bark of trees known as Cinnamomum. Once it was to be rare and valuable so it was regarded as a gift for kings but nowadays it is not only cheaper but also readily obtainable (Chen et.al, 2014). The medicinal use of this plant has been documented in Ayurveda (the Indian system of medicine), for over 6000 years. *Cinnamomum* comes from Greek word kinnamomon. W hich means 'sweet wood'.There are two types of cinnamon, true cinnamon (*Cinnamomum zeylanicum, C. verum*) and cassia (*Cinnamomum aromaticum*) (Kayande et.al, 2014). The bark of Cinnamon is an important spices used all over the world for cooking and medicine proposes (Sangal, 2011). The characteristic odour and flavour of cinnamon are due to the oils and other derivatives, like cinnamaldehyde, cinnamic acid and cinnamate. Cinnamon has some meditational properties (Torbati et.al, 2014). It contains polyphenols which act as antioxidants. From the study of antioxidant activity of 26 spices, Cinnamon was found out to be a clear winner (Shan et.al, 2005). Cinnamon is also used for natural food preserver (Nikos G. Tzortzakis, 2009). It can also helpful for lowering blood sugar level because of its antidiabetic effect (Kim et.al, 2006). In addition to that it act as anti microbial (Chan et.al, 2001), anticancer (Anderson et.al, 2010) anti-inflammatory (Tung et.al, 2010), antifungal (Wang et.al, 2010) and also has been reported to have activities against neurological disorder (Peterson et.al, 2009). From some research it has been found that it can also fight with HIV-1 (common strain of HIV virus in humans) (Filho et.al,2010). From a research it was found cinnamon has most effective treatment on HIV-infected cells out of all 69 medicinal plants under research (Premanathan et.al, 2009).

Cancer is the most notorious disease. Cancer is mainly due to abnormal growth of cell in our body. Cancer is not a single disease [15]. There are many types of Cancer, distinguished according to which cell it occurs. Most common cancers are Lung cancer, breast cancer, colorectal cancer, prostate cancer, skin cancer, gastric / stomach cancer. Stomach cancer is the second most common cancer worldwide (Derakhshan et.al, 2004). The carcinogenesis of Gastric cancer refers to accumulation of genetic alteration of multiple genes such as oncogenes, tumour suppressor and mismatch repair genes (Holian et.al, 2002). From the GLOBOCAN 2018 data, stomach cancer is found in 1.03 million people and 783000 people are death due to this Gastric cancer. Gastric cancer is caused due to many reasons. The most important factors responsible for gastric cancer are *Helicobacter pylori,* alcohol, smoking, redmeat, obesity (Rawla and Barsouk, 2019), (Lindblad et.al, 2005), (Merry et.al, 2007).

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RESULT AND DISCUSSION

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The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

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ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

CSCs typically exhibit three key characteristics, which are not mutually exclusive. Firstly, CSCs are highly tumorigenic and can form tumours in immune-deficient mice through xenotransplantation, which is not possible for non-CSCs. Secondly, CSCs that survive chemotherapy and radiotherapy generate resistance to such therapies through regulating intracellular stress; for example, regulating reactive oxygen species, which non-CSCs cannot. Thirdly, CSCs possess metastatic potential, illustrated by a report that CSCs have the ability to metastasize. The

identified pharmacophores can be isolated from the Cinnamon and can be commercialized as the natural drug for the Gastric Cancer which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.

The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Gastric Cancer

Sl.No	Pharmacophores from Cinnamon	Targeted Genes from Gastric Cancer	PDB No of the Genes
1	Cinnamic Aldehyde	lymphoid myeloid leukaemia protein	1HFA
2	2′-Hydroxycinnamaldehyde	Oxidoreductase	2J5W
3	Polyphenol Type-A	NF-kappa B binding site	2KBD
4	Cinnamic Acid	Porcine Pepsinogen	3PSG

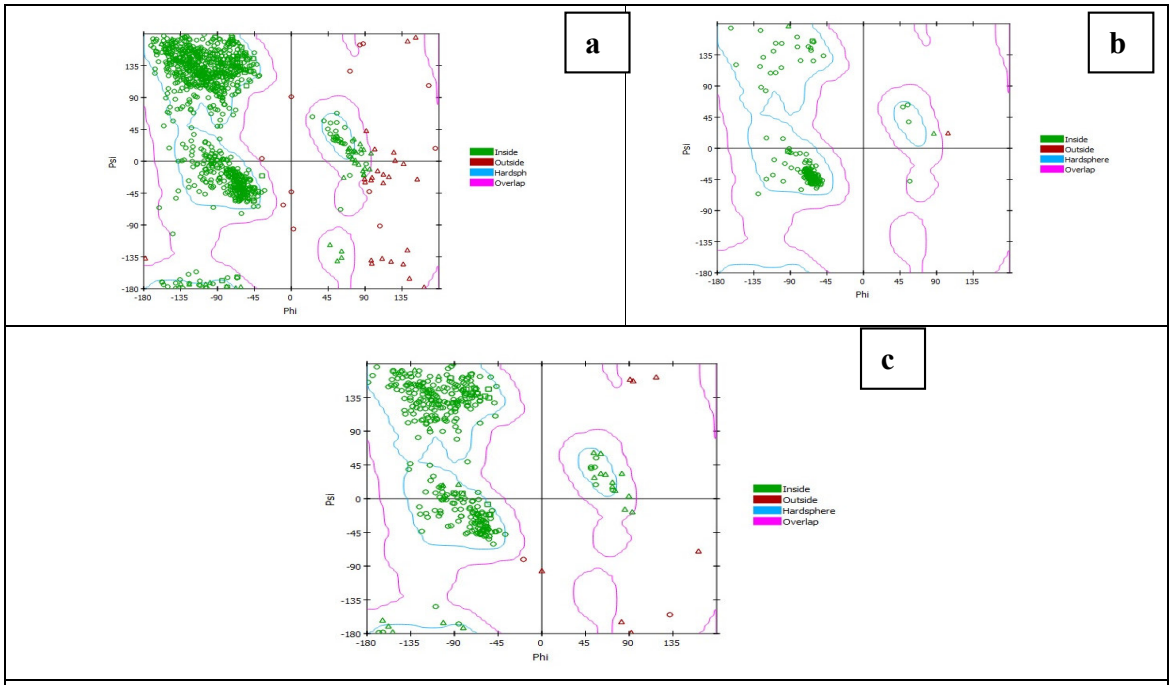

Fig 1: Ramachandan plot of (a) 2J5W (b) 1FHA (c) 2PSG

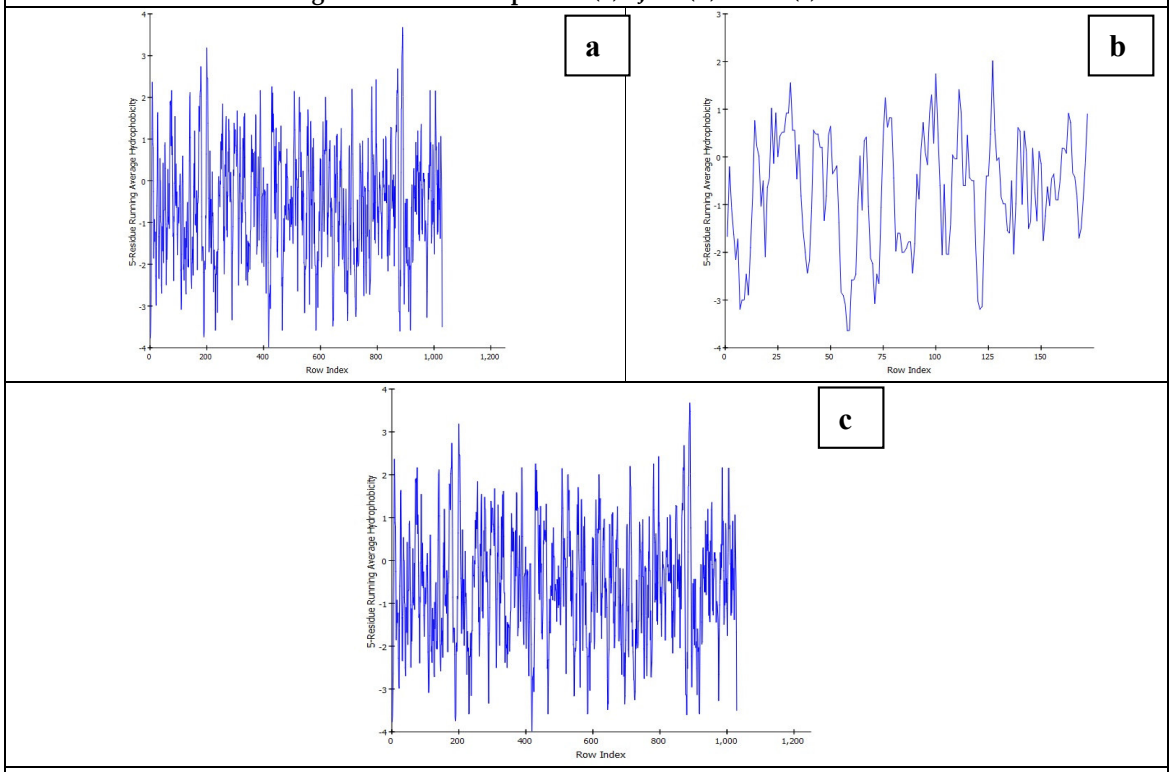

Fig 2: Hydrophobicity Plot of (a) 2J5W (b) 1FHA (c) 2PSG

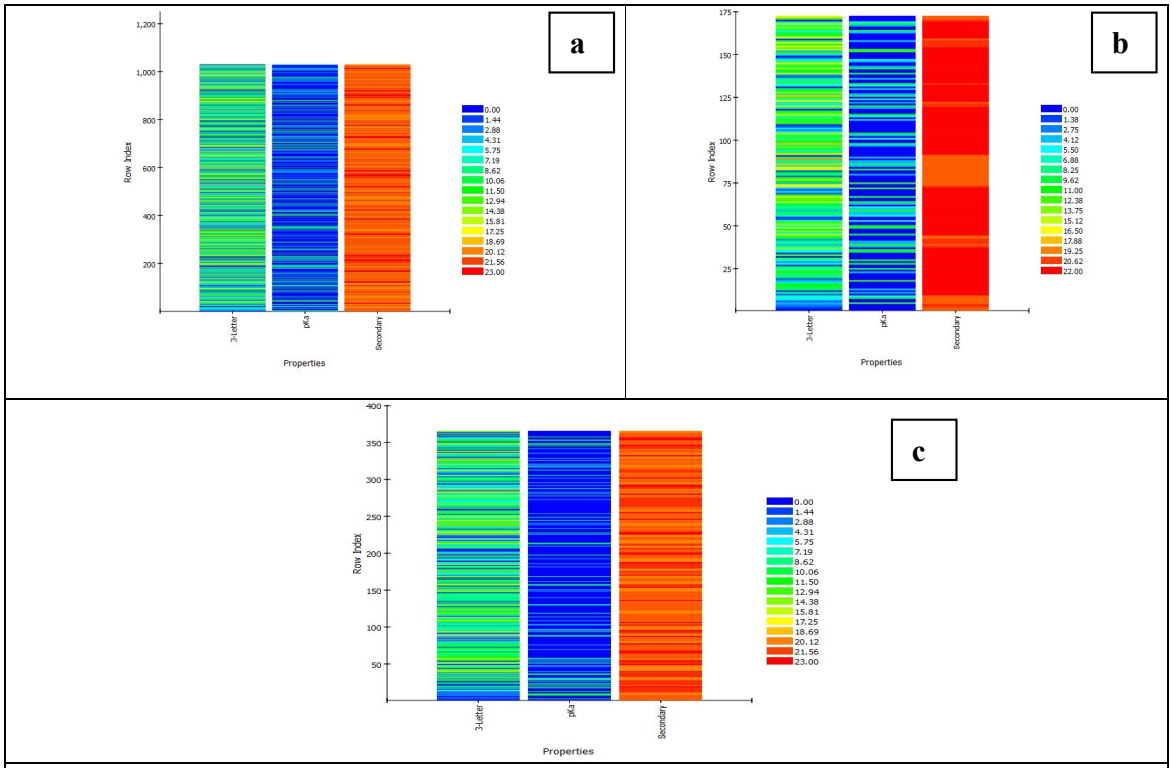

Fig 3: Heat Map Plot of (a) 2J5W (b) 1FHA (c) 2PSG

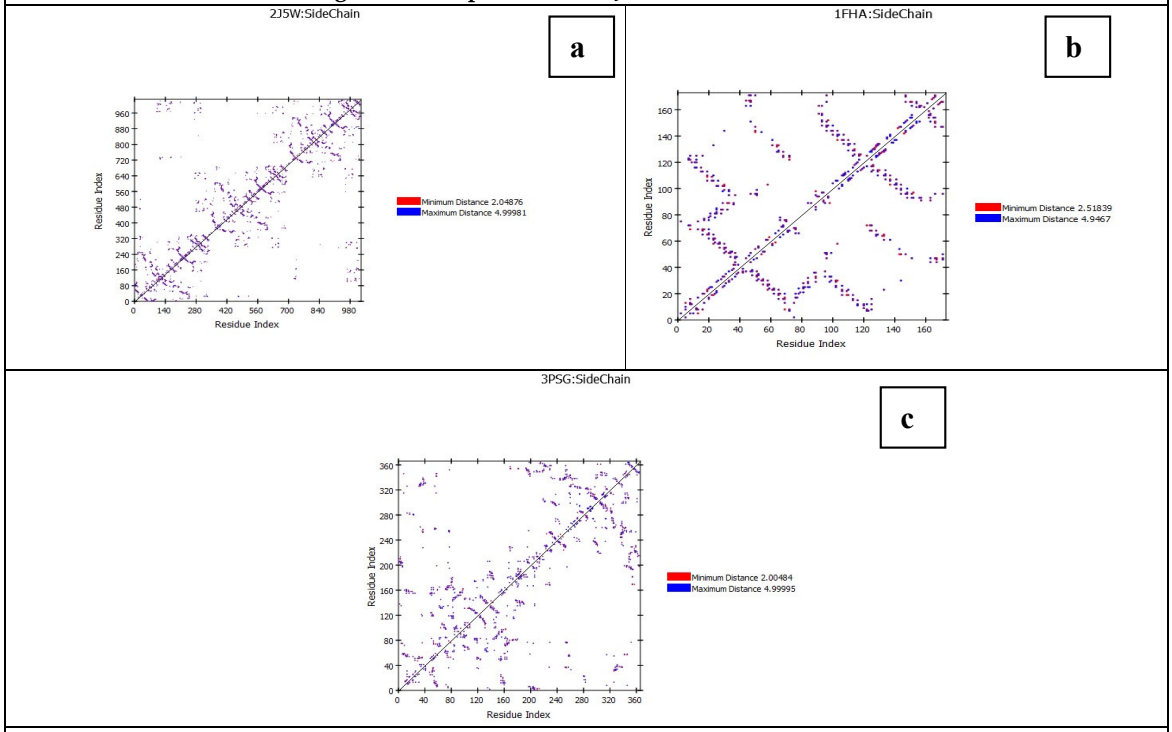

Fig 4: Side chain Plot of (a) 2J5W (b) 1FHA (c) 2PSG

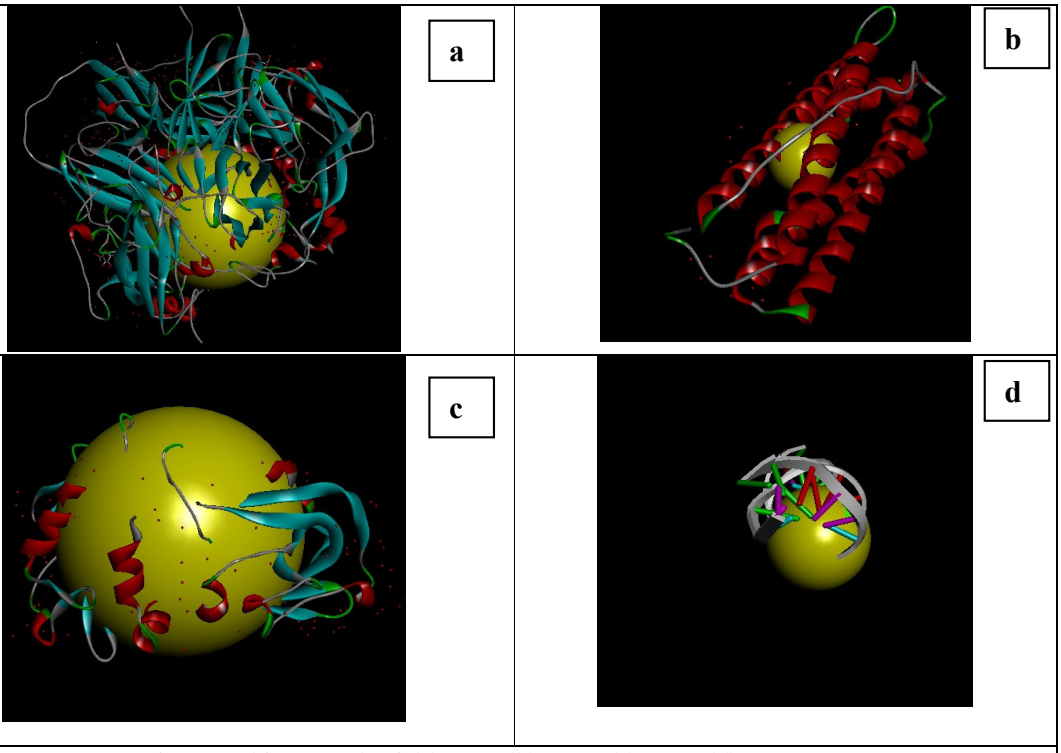

Fig 5: Docking Result of (a) 2J5W (b) 1FHA (c) 2PSG (d) 2KBD

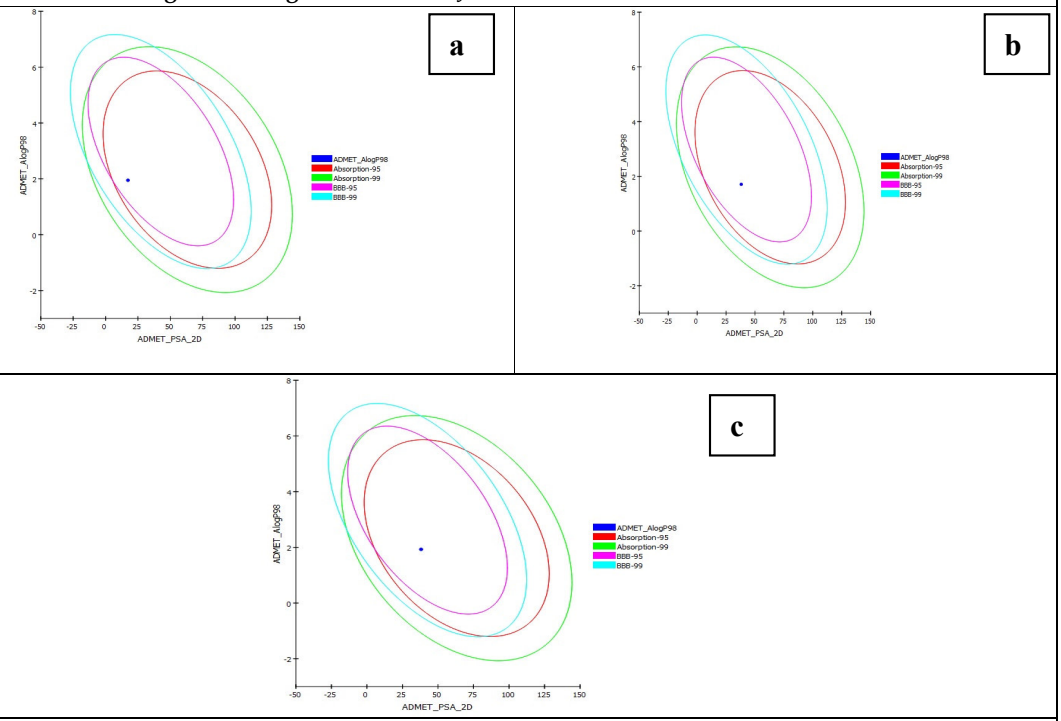

Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

In silico Analysis of the Cumin as Targeted Biopesticides

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is Cumin which has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. Cumin is full of antioxidants that are essential for living a healthy life. We are using this property of Cumin to get some new drugs for Rice Tungro Gene. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Rice Tungro Gene and pharmacophores from Cumin and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Cumin, Docking, *In silico* Analysis, Rice Tungro Gene, Pharmacophore

INTRODUCTION

Ayurveda, the science of life, which is the ancient traditional system of Indian medicine, is believed to be well over 5,000 years old. Ayurveda has particularly emphasized the subtle yet incredible healing properties of herbs and spices, and among these cumin plays an important part, which is used both as an ayurvedic medicine and as well as

the main spice in Indian food recipes. Cumin *(Cuminum cyminum)* is one of the most valuable medicinal herbs and spice in the world. This plant belongs to the *Apiaceae* family and is geographically distributed in south Mediterranean and West Asia (latitudes 20-38° N and longitudes 30°- 80° E) (Zargari 1988, Balandary, 1992, katzer).There are different theories about the origin of cumin. However, based on documented evidences, it either originated in northern Egypt, in the south Mediterranean climate or in the Middle East (Wu et.al,1982, Chaudhari, 1992, Heravi 1962, Heravi 1977). The presence of wild cumin plants in vast areas of south Mediterranean, Saudi Arabia, Iran, Central Asia, Sahara and south Pakistan indicate that these areas could be the origin of domestication of cumin. Based on the background of cultivation, variation of wild types, particularly other species of cumin *(Cuminum setifolium*) and wide distribution of semi-wild races of cumin, the Iranian plateau and Middle East could also be the center of evolution of cumin. Cumin, as one of these medicinal plants, contains more than 100 different chemicals, including essential fatty acids and volatile oils (Mohiti et al, 2011). In recent years, herbal supplements have been used instead of chemical applications in aquaculture because they are more consumer acceptance and ecofriendly approach in disease management (Raa, 1996). Medicinal herbs or spices are able to enhance immunity and generate more pathogen resistance (Harikrishnan et al., 2011a). Several studies have also reported that the spices like garlic, ginger, thyme, rosemary and fenugreek improved health status, growth performance and/or disease resistance in *Dicentrarchus labrax* and *O. mossambicus* (Yılmaz & Ergün, 2012; Yılmaz et al., 2012; Yılmaz et al., 2013). Varieties of spices have been used traditionally to prevent and treat diseases and are known to improve the immune system (Chauhan et al., 2010). Allspice (*Cuminum cyminum, Apiaceae*) has been used as a spice since ancient times (Azeez, 2008). It is cultivated in the Mediterranean countries (Amin, 2001), especially in India, the world's largest producer and consumer of cumin, with annual production ranging between 0.1 and 0.2 million tonnes (Azeez, 2008). It has been used in medicines as a stimulant of the immune system, tyrosinase inhibitor activity and also as a hypoglycaemic, hypolipidaemic, chemoprotective and relaxant compound in animals and human beings (Boskabady et al., 2005; Azeez, 2008).

As the most important of the 14 rice viral diseases, tungro was first recognized as a leafhopper-transmitted virus disease in 1963. However, tungro, which means "degenerated growth" in a Filipino dialect, has a much longer history. It is almost certain that tungro was responsible for a disease outbreak that occurred in 1859 in Indonesia, which was referred to at the time as mentek. In the past, a variety of names has been given to tungro, including *accep na pula* in the Philippines, penyakit merah in Malaysia, and yellow-orange leaf in Thailand. The difficulty in forecasting outbreaks and the rapidity of disease spread as epidemics developed created a problem of alarming dimensions. The development of appropriate methods to manage tungro was constrained for a long time by a limited knowledge of the epidemiology of the disease and the ecology of its leafhopper vectors.

MATERIALS AND METHODS

Phytochemicals of Cumin have been listed with their structure data files which are taken from pubchem ChEBI. Genes has been taken randomly for Rice Tungro Gene using NCBI database. Table 1 has been showing the enlisted pharmacophores and the targeted genes. The PDB numbers of enzymes are taken from RCSB. The *In-silico* analysis has been done using BIOVIA –Discovery studio. We have performed various docking and used the Ramachandan plot and others.

Protein identification and preparation

The reported molecular targets responsible for Rice Tungro Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy

their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

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The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

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Table 1: The list of pharmacophores and the targeted genes from Rice Tungro Gene

Sl.No	Pharmacophores from Cumin	Targeted Genes from Rice Tungro Gene	PDB No of the Genes
1	Berberine	Oxidoreductase,	6H08
2	P-Coumaric	L-Ornithine,	6JKI
3	Saponins	N5-Monooxygenase	6FOQ
4	4-Isopropylbenzoic Acid		

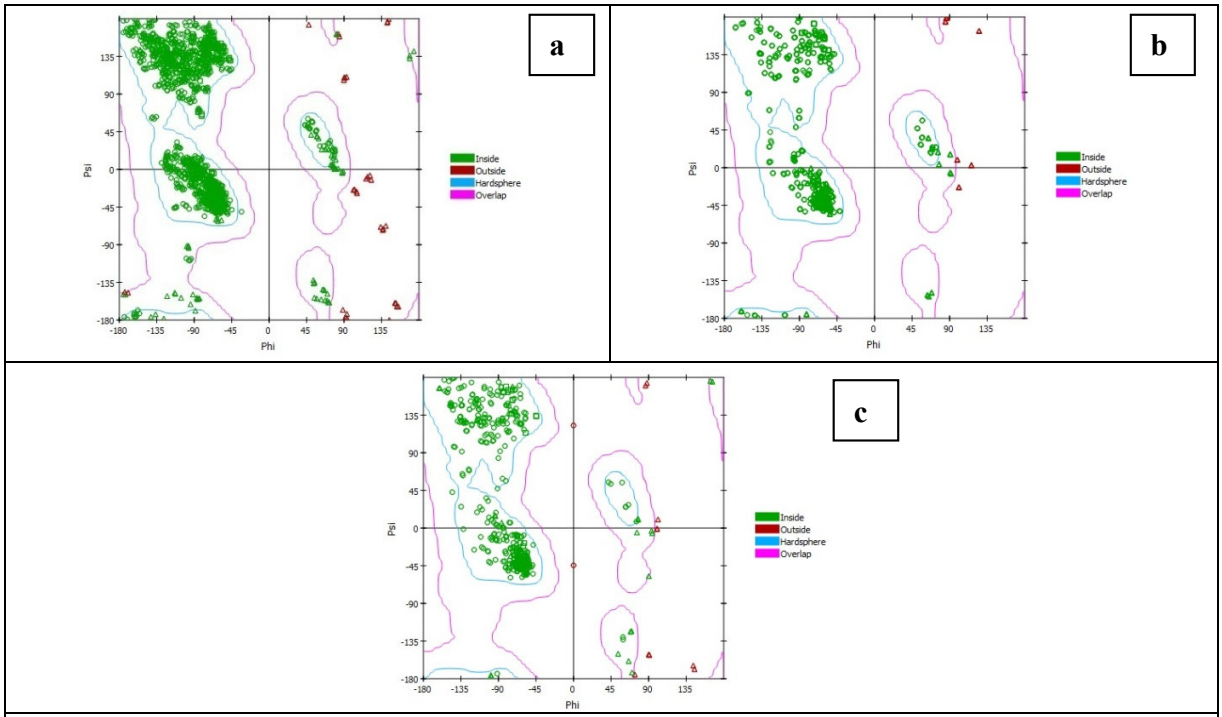

Fig 1: Ramachandran plot of (a) 6FOQ (b) 6H08 (c) 6JKI

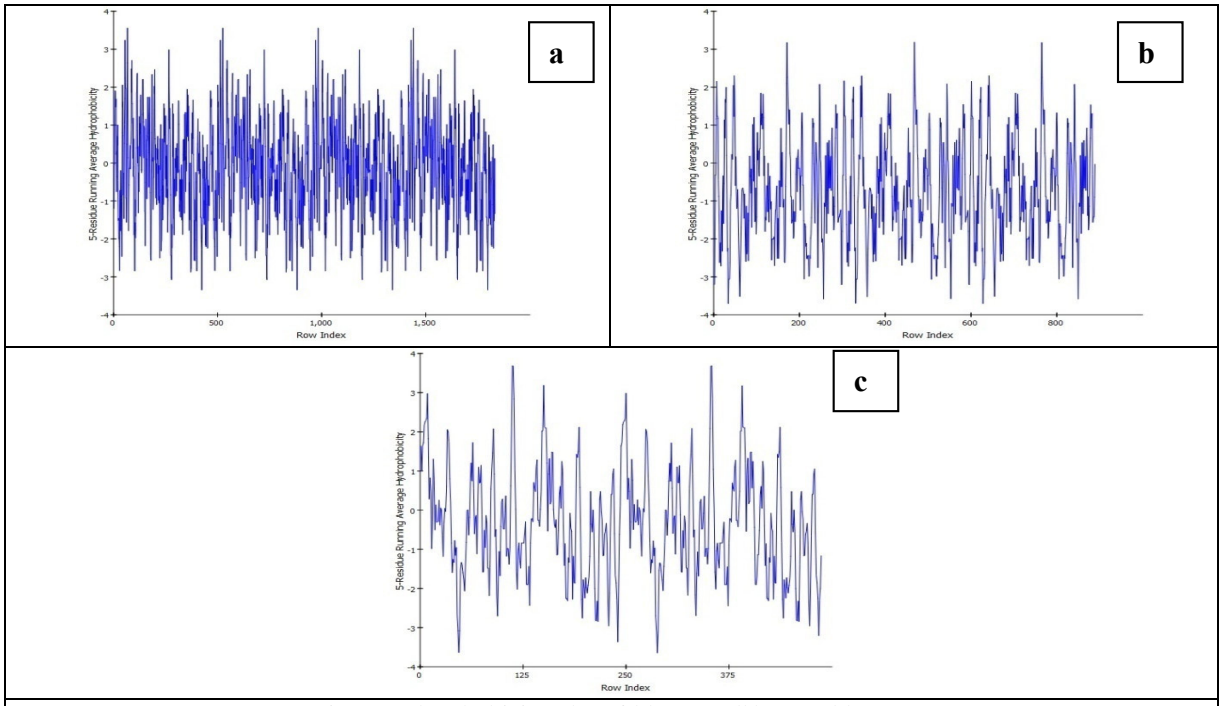

Fig 2: Hydrophobicity Plot of (a) 6FOQ (b) 6H08 (c) 6JKI

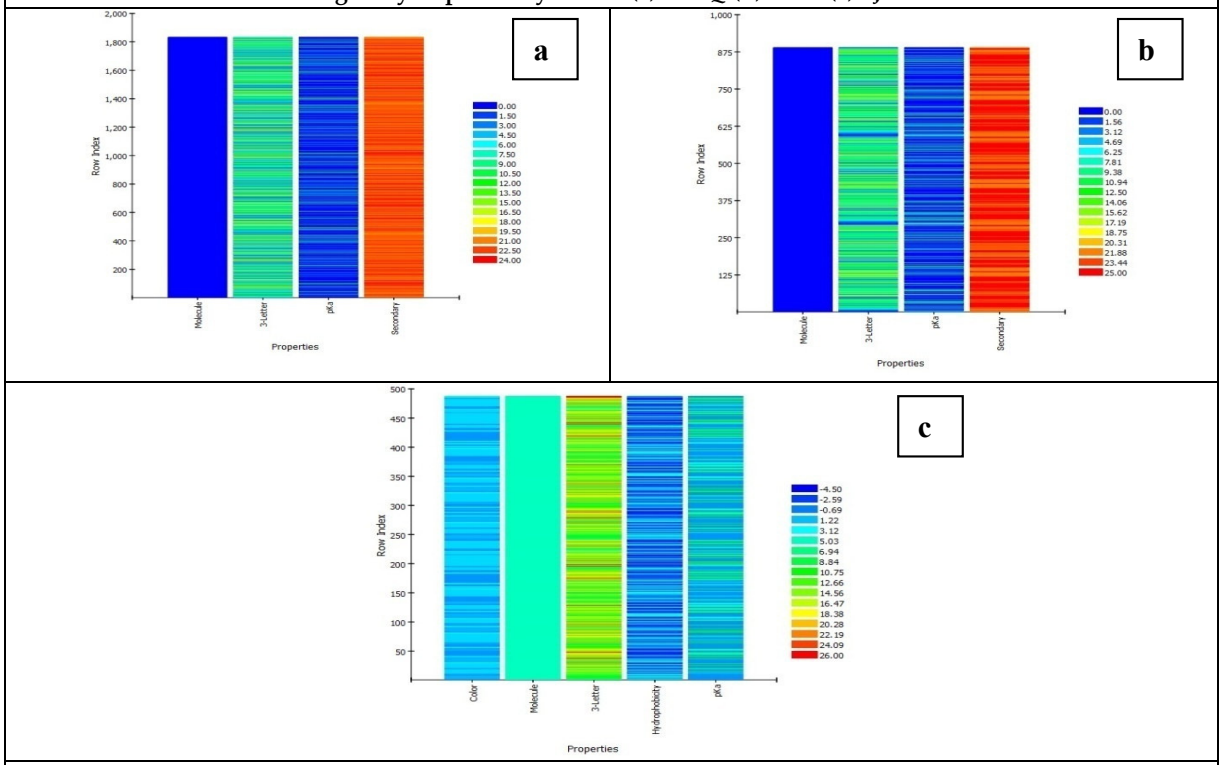

Fig 3: Heat Map Plot of (a) 6FOQ (b) 6H08 (c) 6JKI

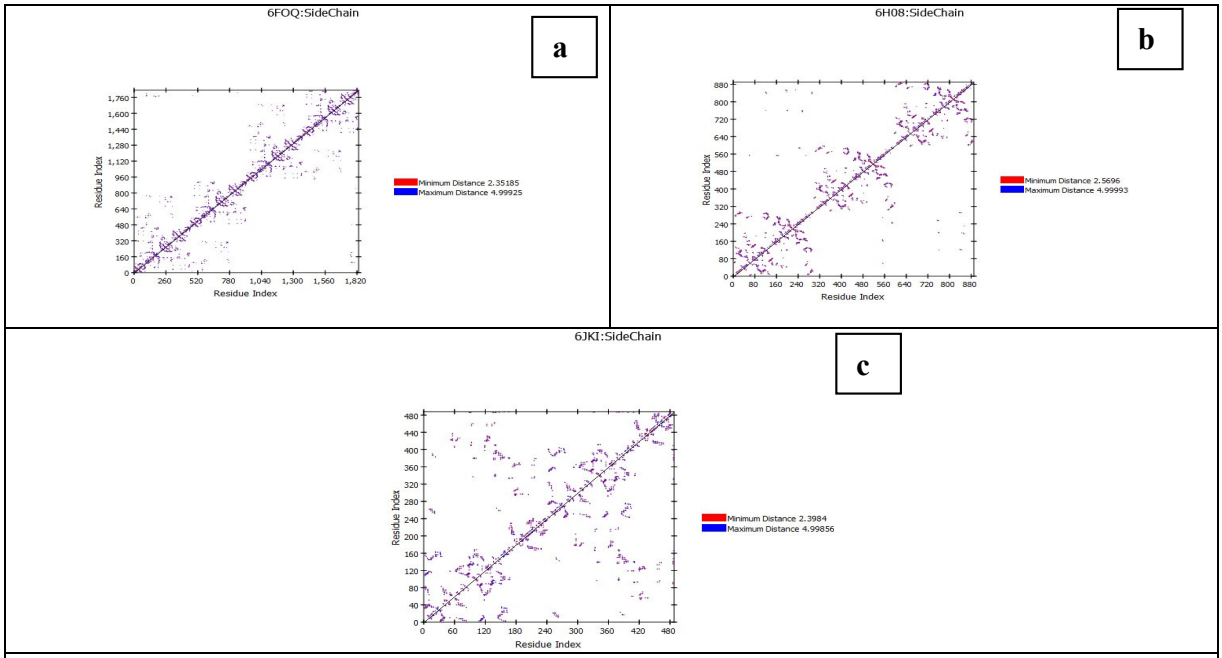

Fig 4: Side chain Plot of (a) 6FOQ (b) 6H08 (c) 6JKI

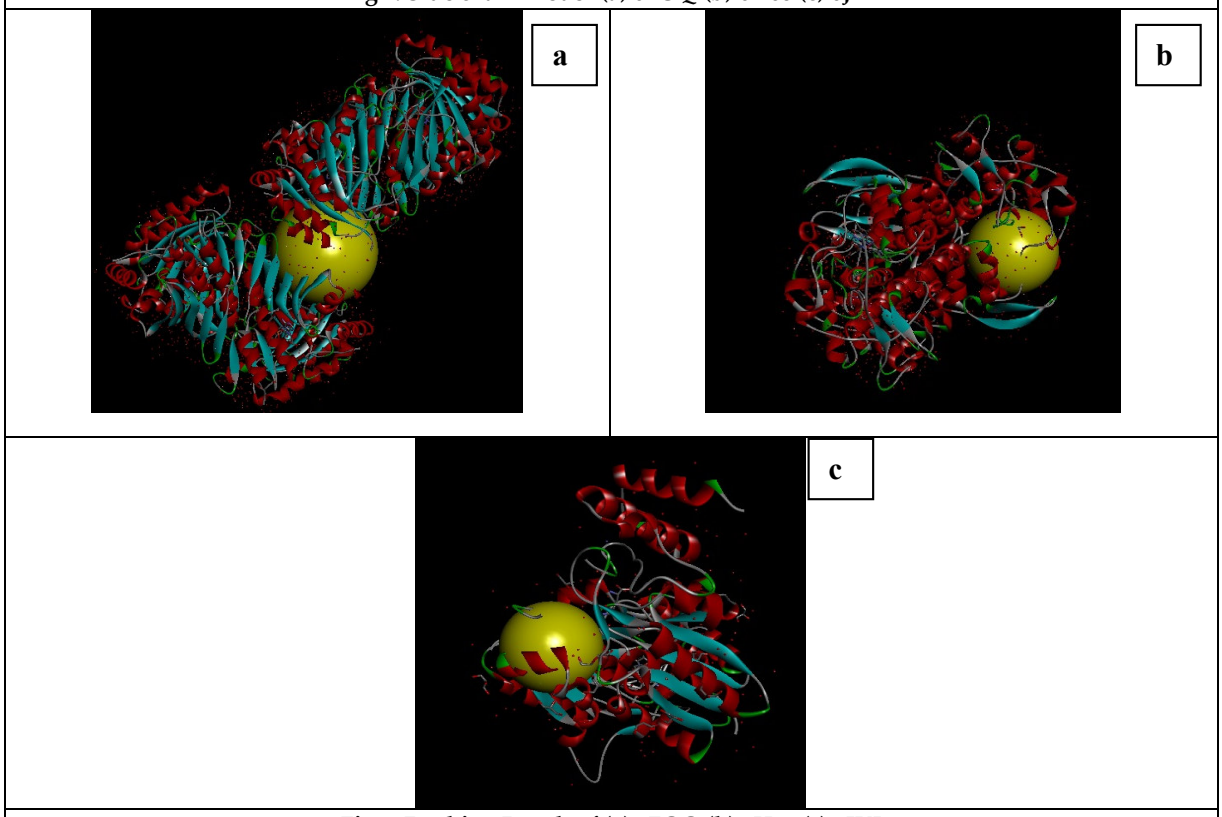

Fig 5: Docking Result of (a) 6FOQ (b) 6H08 (c) 6JKI

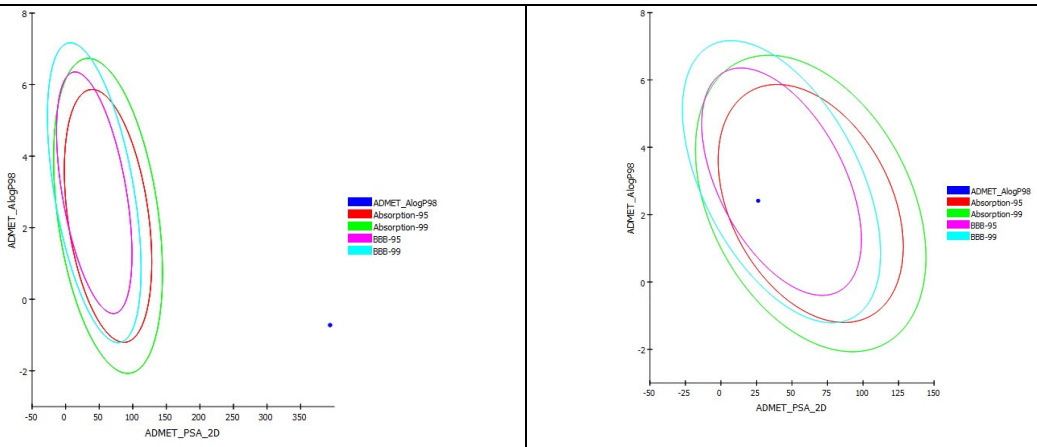

Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

In silico Analysis of the Ashwagandhaas Targeted Therapy for Oral Cancer

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is Ashwagandhawhich has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. Ashwagandhais full of antioxidants that are essential for living a healthy life. Antioxidants help in removing free radicals that can further mutate into cancer cells. We are using this property of Ashwagandhato get some new drugs for Oral Cancer. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Oral Cancer and pharmacophores from Ashwagandhaand did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others. From this we can deduce that these two pharmacophores can be a solution to Lung Cancer in near future. Complementary and alternative medicine (CAM) is a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine. As cancer incidence rates and survival time increase, use of CAM will likely increase. However, little is known about the use of CAM in cancer patients, specifically in emerging countries.

Key Words: Aswagandha, Docking, *In Silico* Analysis, Oral Cancer, Pharmacophore

INTRODUCTION

Ayurvedic medicines are largely based upon herbal and herbomineral preparations (Shivraj et al,2019) and have specific diagnostic and therapeutic principles (Patwardhan and Hopper, 1992). Modulation of immune responses (Abhijit Deshpande et.al, 2020, Devereaux and Tewelde, 2017, Idrose 2015,) to alleviate the diseases has been of interest for many years and the concept of 'Rasayana' in Ayurveda is based on related principles. Immunostimulation in a drug-induced immunosuppression model and immunosuppression in an experimental hyper- reactivity model by the same preparation can be said to be true immunomodulation (Patwardhan et al., 1990). Ashwagandha is a plant belongs to the Solanaceae or nightshade family.The binomial name of Ashwagandha is "*Withania somnifera*" (Nilambari et al2020, Charak, Samhita, 1949). It is also known as Indian ginseng (Amritha et.al, 2020, Khanchandani et. al, 2019, Singh et al, 2019), poison gooseberry,or winter cherry. It is used as a medicinal herb in Ayurvedic medicine.Ayurveda is one of the traditional systems of medicine practiced in India (National Cancer Institute , 2020, Nagendraprasad et.al, 2020, Lopresti et.al, 2019, Gannon et.al, 2014) This plant is a small erect, woody, perennial, much branched shrub that grows upto about 1.5 m in height. Leaves are dull green, elliptic, usually up to 10–12 cm long. The flowers are small, green and bell-shaped. The ripe fruit is orange-red. It is cultivated now in wet and irrigated areas of Rajasthan, Maharashtra, Gujarat, Haryana, Punjab, Himachal Pradesh , Karnataka and in Odisha (Tripathi et.al, 2020).

The plant, particularly its root powder, has been used for centuries in traditional Indian medicine. It's root contains so many phytochemicals such as Anahygrine, Anaferine, Isopelletierine, Cuscohygrine, Withaferin A ,Vinblastine ,Steroidal Lactones, withanolide etc (Subramanya et al, 2019, Edwards et.al, 2015). Among these sitoindoside and withanolide are the biologically active compounds that containing glucose molecules at carbon 27 are derived (Kelgane et.al, 2020). Mainly due to the poor quality of clinical research with the plant, there is no high-quality evidence that it provides any medicinal benefit (Vassou et.al, 2016, MedlinePlus. 2017) and may cause adverse effects if taken together with prescription drugs (Vineet et.al,2019). As every herbal plant has their own significance (GRIN, 2011) and still now there is no strong evidence has been found against the use of *Withania somnifera* (Missouri Botanical Garden, 2012).

Cancer causes when there occur an altertion in the unusual gene mutation (Kylee et.al, 2020, Abrahamse, 2019). As a consequence, the cells stop following the instructions of genes.It starts to grow and divide uncontrollably instead of dying when it should (Durai et.al, 2019, Li et.al, 2017). Cancer cells continue to grow because they behave differently than normal cells (Bahn et al, 2011). India Is the 2nd largest populated country after China having 1.37 billion people. Indian people are suffering alot by different kind of diseases such as heart attack, cancer,Dengue, Malaria , AIDS, hepatitis, tuberculosis etc. Among these cancer is leading the 2nd position after Heart disease which is the cause of death. Cancers are of different types such as oral cancer, breast cancer, prostate cancer,lung cancer,blood cancer etc.Being knowing that tobacco is a cancer causing agent we people fond of eating these as a Sauk. So by seeing these passionate among the people, I liked to work on oral cancer.

Oral cancer includes the cancer of tongue,lips, cheeks etc.It appears as a sore in the mouth that doesn't go away. It causes due to smoking cigarettes, chewing tobacco products,Consuming excessive amount of alcohols etc.Fusobacterium nucleatum is ubiquitous in the oral cavity, absent or infrequently detected elsewhere in the body under normal conditions.It is a Gram-negative anaerobe. In India, 20 per 1,00,000 population are affected by oral cancer which accounts for about 30% of all types of cancer. Our *In silico* analysis of the targeted genes in Oral cancer and the pharmacophores are successfully done using BIOVIA software and this studies has shown a hopeful result of the targeted therapy for oral cancer with Ashwagandha.

MATERIALS AND METHODS

Phytochemicals of Ashwagandha have been listed with their structure data files which are taken from pubchem. Genes has been taken randomly for Oral cancer using NCBI database. Table 1 has been showing the enlisted pharmacophores and the targeted genes. The PDB numbers of enzymes are taken from RCSB. The *In-silico* analysis has been done using BIOVIA –Discovery studio. We have performed various docking and used the Ramachandran plot and others.

Protein identification and preparation

The reported molecular targets responsible for oral cancer are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARMm force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using
Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Ashwagandhawere taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 5 phytochemicals reported from Ashwagandha was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Ashwagandhawith the selected targets of Oral Cancer. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Ashwagandhato find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy

structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily orally absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran (1). The power of this approach was readily apparent and its use quickly became widespread (2–3). Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the “simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures.” In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

Ligand preparation

5 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after oral administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic

energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

CSCs typically exhibit three key characteristics, which are not mutually exclusive. Firstly, CSCs are highly tumorigenic and can form tumours in immune-deficient mice through xenotransplantation, which is not possible for non-CSCs. Secondly, CSCs that survive chemotherapy and radiotherapy generate resistance to such therapies through regulating intracellular stress; for example, regulating reactive oxygen species, which non-CSCs cannot. Thirdly, CSCs possess metastatic potential, illustrated by a report that CSCs have the ability to metastasize. The identified pharmacophores can be isolated from the Ashwagandhaand can be commercialized as the natural drug for the Oral Cancer which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.

The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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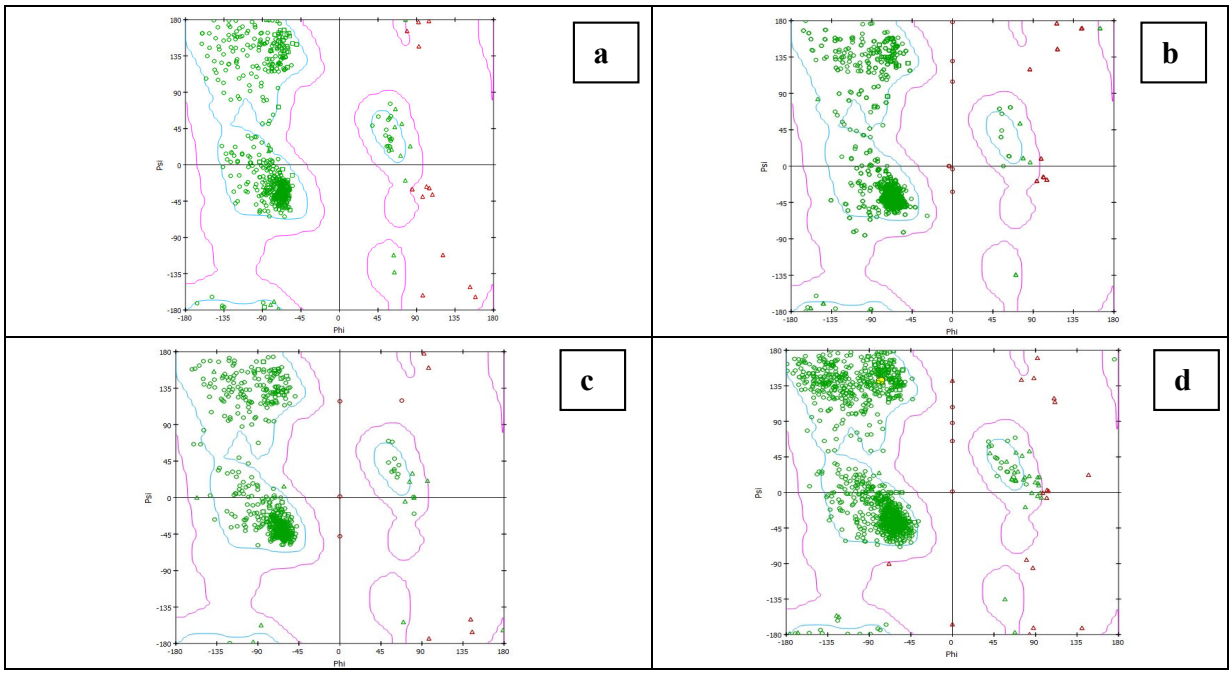
Table 1: The list of pharmacophores and the targeted genes from Oral Cancer.3

Sl.No	Pharmacophores from Ashwagandha	Targeted Genes from Oral Cancer	PDB No of the Genes
1	Anahygrine	anoctamin 1	6R65
2	Anaferine	cyclin dependent kinase 2	6QTG
3	Isopelletierine	methylenetetrahydrofolate reductase	6FCX
4	Cuscohygrine	prostaglandin-endoperoxide synthase 2	6Y3C
5	Withaferin A	glutathione S-transferase theta 1	4MPF



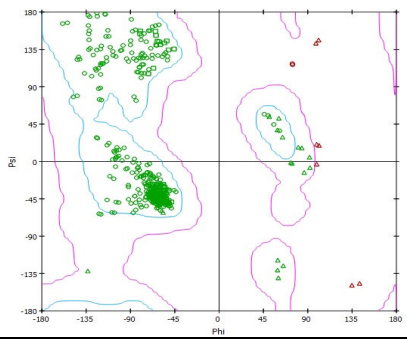


Fig 1: Ramachandran plot of (a) 6Y3C (b) 6R65 (c) 6QTG (d) 6FCX (e) 4MPF

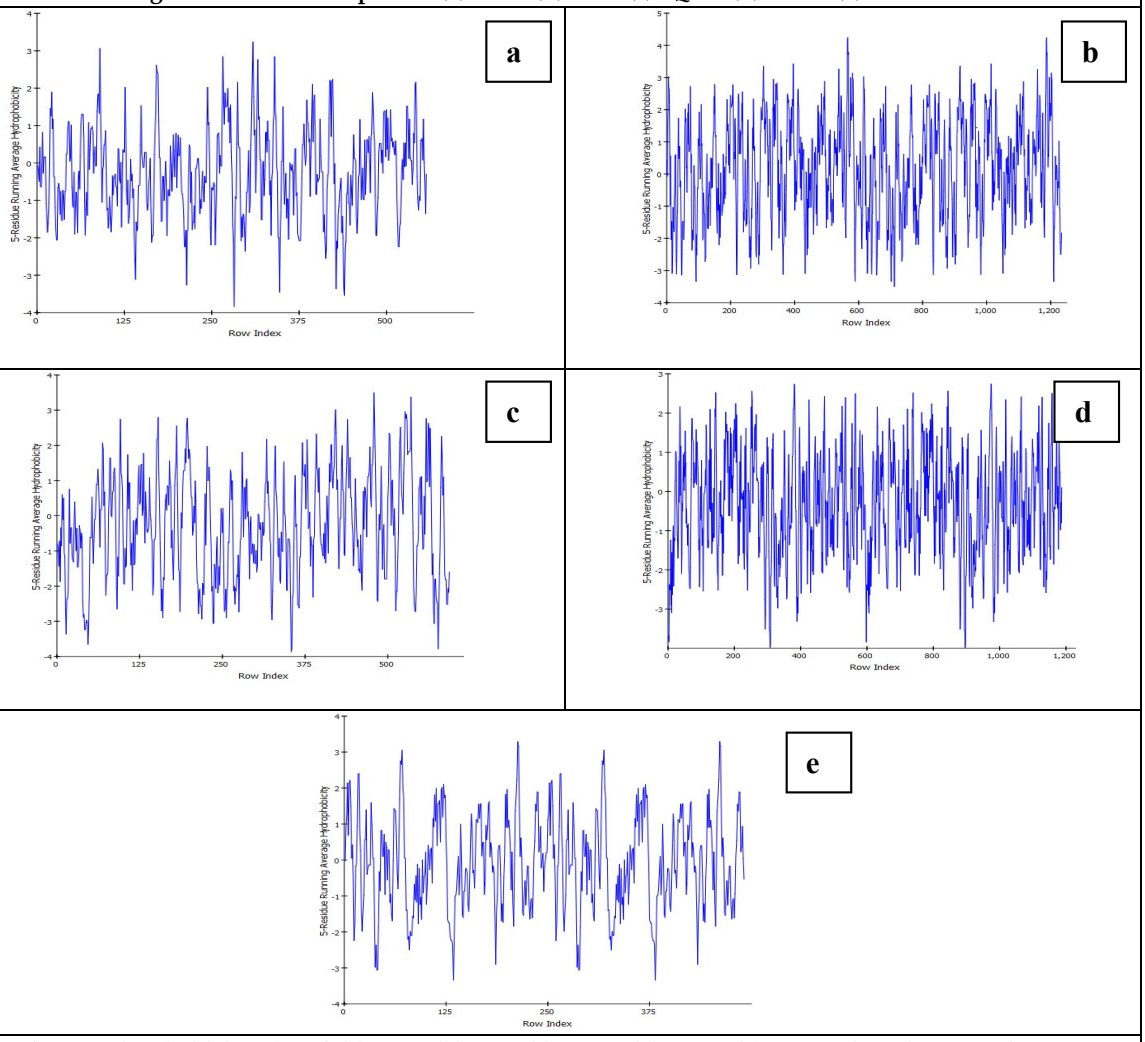


Fig 2: Hydrophobicity Plot of (a) 6Y3C (b) 6R65 (c) 6QTG (d) 6FCX (e) 4MPF Ligand preparation

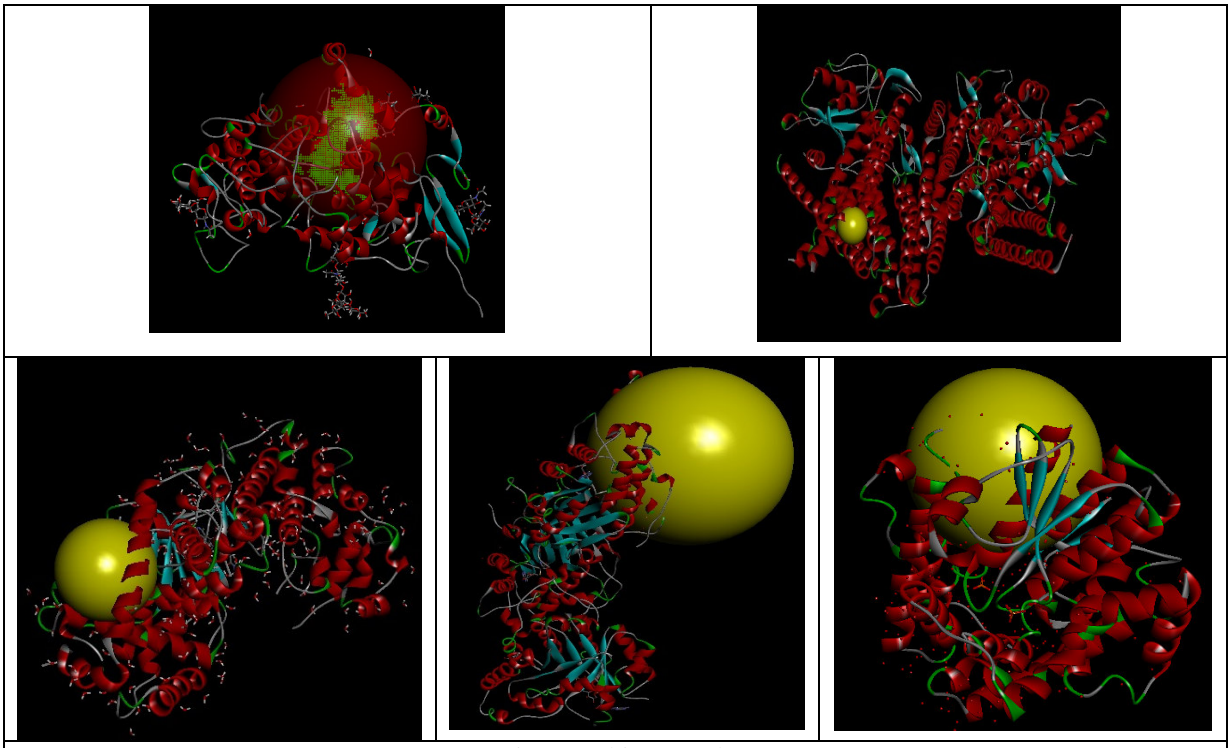


Fig: 3 Docking Result

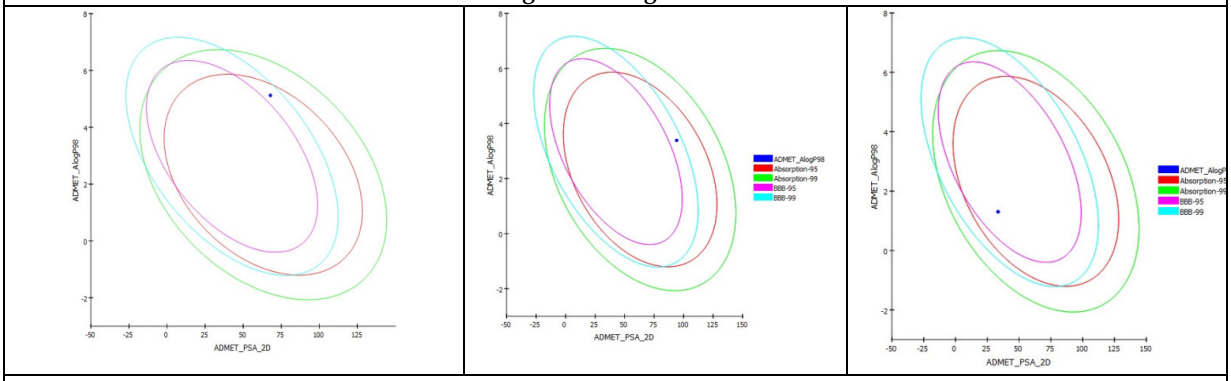


Fig 4: ADMET test analysis report

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RESEARCH ARTICLE

In-silico Analysis of Compounds Characterized from *Murraya koenigii* against Cancer

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ABSTRACT

Murraya koenigii is a culinary important plant of Indian origin, and also been a component of many formulations used in the Ayurvedic system of medicine since many centuries. A scrutiny of literature reveals some notable pharmacological activities of the plant. Carbazole alkaloids which are abundantly present in the leaves, fruits, roots and bark of this plant, have been reported for their antidiabetic, anticancer, antibacterial, anti-nociceptive and antioxidant activities. Besides these activities, the plant is described to have a wide array of therapeutic activities. Phytochemistry and pharmacology of this plant necessitates a comprehensive review of its prospects as an important therapeutic agent focusing on its anti carcinogenic activities. The current review provides a detailed report of the phytochemical, pharmacological, clinical and pre-clinical works carried out on this culinary plant and also throws light on its therapeutic prospects.

Keywords: culinary, anti-nociceptive, phytochemistry, therapeutic, pharmacology, carcinogenic

INTRODUCTION

Murraya koenigii commonly known as curry leaves or curry patta in Indian dialects which represesns more than 150 genera and 1600 species. Curry leaves belongs to the family rutaceae. *M. koinigii* is a highly valued plant for its aroma and medicinbal value. *M. koinigii* contaims a number of chemical constituents that interact to elicit their pharmacodynamic response. It grows through the Indian subcontinent and has wide culinary effect and is one of the main components of formulations in the traditional ayurvedic system [1] . There are different forms of *Murraya*

koenigii due to which they are found as the useful plant such as extract, essential oil, or directly used due to the presence of following active constituent bismahanine, murrayanine, murrayafoline-A, bi-koeniquinone-A, bismurrayaquinone, mukoenine-A, mukoenine-B, mukoenine-C, murrastifoline, Murrayazolinol, murrayacine, murrayazolidine, murrayazoline, mahanimbine, girinimbine, koenioline, xynthyletin, koenigineQuinone A and koenigine-Quinone B for therapeutic purpose by folk people[2-5] .These natural products have been shown to have antioxidant properties and are capable of scavenging free superoxide radicals, thus providing antiaging benefits as well as reducing the risk of cancer. It has been found that flavonoids reduce the lipid and glucose levels in blood and support the human immune system [6,7] . The health-promoting effects of flavonoids are the result of their ability to induce the activity of protective enzyme systems [8] . Several studies have suggested that flavonoids such as catechin and quercetin are able to control the growth of cancer cells in human body .

Chemical constituent

Murraya koenigii is very rich source of organic compounds with different chemical composition such as alkaloids, flavonoids carbohydrates, and sterol is present in the plant extract prepared in solvents such as petroleum ether, ethyl acetate, chloroform, ethanol and water [10,11-14] .For the confirmation of the phyto-constituents in the plant extract, various numbers of tests were performed: The presence of alkaloids was confirmed by using Mayer's reagent, which shows formation of white or cream colored precipitates in the extract of *Murraya koenigii*. [15] Phenolic compounds were confirmed by formation of white precipitate by the addition of few drops of 5% lead acetate solution to alcoholic extracts of *Murraya koenigii*. [15] The presence of flavonoids is detected by Yellow coloration of filter paper by dipping in ammoniated alcoholic upon the extract. [15] Presence of Saponins is considered when the extract showed honey comb like frothing formation after giving a shake with sodium bicarbonate. [15] The presence of proteins and free amino acids is indicated by the conducting the following tests i.e., Millons, Biurets and Ninhydrins test. vi. Presence of sterol and triterpenes are indicated by alcoholic extract which was shaken with chloroform and few drops of acetic anhydride along with few drops of concentrated sulphuric acid from the side of the tube form the blue to brick red coloration. [16] The essential oil composition of *Murraya koenigii* was studied and then presence of D-Sabinene, D-α-Terpinol, di-α-phellendrene, D-αpinene, caryophyllene and dipentene [17] and the property of *Murraya koenigii* oil is explained in the following table. [15]

Sl. no	Property	Value
1.	Specific Gravity (25°C)	0.9748
2.	Refractive Index (25°C)	1.5021
3.	Optical Rotation (25°C)	+ 4.8
4.	Saponification Value	5.2
5.	Saponification after Acetylation	54.6
6.	Moisture	66.3%
7.	Protein	6.1%
8.	Fat (Ether Extract)	1.0%
9.	Carbohydrate	18.7%
10.	Fibre	6.4%
11.	Mineral Matter	4.2%
12.	Calcium	810Mg/100 G
13.	Phosphorus	600Mg/100 G
14.	Iron Of Edible Portion	3.1Mg/100 G
15.	Carotene (As Vitamin A)	12 600Iμ/100 G
16.	Nicotinic Acid	2.3Mg/100 G
17.	Vitamin C	4 Mg/100 G
18.	Thiamine And Riboflavin	Absent

Determination of Anticancer Activity

MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium Bromide) Assay

The assay was conducted as follows: cancer cells were seeded in 96-well plates at a density of 1 × 104 cells/well in 100 μL RPMI. At 24 h after seeding, the medium was removed and the cells were incubated for 3 days with RPMI in the absence or presence of various concentrations of curry leaf extracts. Extracts concentrations used ranged between 20, 40, 80, 160, 320, and 640 μg/mL. After incubation, 20 μL of MTT reagent was added into each well. The plate was incubated again in a CO2 incubator at 37°C for 4 h. The resulting MTT-products were determined by measuring the absorbance at 570 nm using ELISA reader. [19] Each point represents the mean of triplicate experiments. The cell viability was determined using the formula.

Statistical Analysis

All analytical values shown represent the means of three replicates. Data were analysed using analysis of variance by Statistical Analysis System (SAS 9.0). Mean separation test between treatments was performed using Duncan multiple range test and a P value ≤ 0.05 was regarded as significant. [18]

Other studies related to anti-carcenogenic properties

Girinimbine, acarbazole isolated from the bark of *Murrya koenigii* significantly induced programmed cell death in HepG2 cells suggesting the necessity for further evaluations in preclinical human hepatocellular carcinoma models. [20] The results from the study conducted by Bhattacharya *et al.* 2010 provides evidence for the involvement of death receptor mediated extrinsic pathway of apoptosis in mahanine-induced anticancer activity in MOLT-3 cells, but not in K562 cells which are deficient in Fas/FasL. [21] Furthermore, 3 carbazole alkaloids mahanine, pyrayafoline and murrafoline, showed significant activity against HL-60 cells by inducing apoptosis through of capsase-9/capsase-3 pathway, through mitochondrial dysfunction. [22] Down regulation of cell survival factors by activation of capsase-3 through mitochondrial dependent pathways and disruption of cell cycle progression could be an additional mechanism. [23] The mean number of neoplasms in the colon and intestines were significantly low as demonstrated by morphological and histological studies in the *Murrya koenigii* treated animals. [24] The methanolic extract of *Murrya koenigii* leaves demonstrated a significant increase in the phagocytic index by the rapid removal of carbon particles from blood stream. It also demonstrated an increase in the antibody titer against ovalbumin and protection against cyclophosphamide-induces myelosuppression.

Some major chemicals specifically showing anti-carcinogenic effects.

CONCLUSION

Murraya koenigii is a leafy medicinal as well as green leafy plant that belongs to family Rutaceae. The various pharmacological activities of the plant has been seen such as such as activity on Anti diabetic, cholesterol reducing property, antimicrobial activity, antiulcer activity, Antioxidative property, cytotoxic activity, antidiarrhoea activity, anti-cancer activity with many other phagocytic activity.In this study we specifically took intrest over the anti-carcinogenic properties. The chemical composition of the *Murraya koenigii* consists of certain alkaloids which are proved to express certain anti-cancerous activities upon in-vitro exposure to cancer cells. Thus Curry leaves merits further phytochemical, pharmacological and clinical investigations for development of an effective natural plant.

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RESEARCH ARTICLE

Study on Temperature Dependence of NQR Frequency and Internal Motions in Potassium Chloroacetate Rare Combination of Plant Nutrient Potassium and Monochloroacetic acid Constituent of Herbicide

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ABSTRACT

Sodium chloroacetate and monochloro acetic acid are significant herbicides, plays important role in controlling weeds. There are several studies related to biological implications of sodium chloroacetate, monochloro acetic acid and potassium independently. Keeping in view the importance of potassium in plant growth and metabolism as well as herbicidal properties of monochloroacetic acid, we have combined potassium with monochloroacetic acid and carried out study on temperature dependence of ^{35}Cl NQR frequencies in potassium salt of monochloroacetic acid in the temperature range 77K to room temperature. Single resonance line has been observed throughout the temperature range studied. Using Bayer's theory and Brown's approximation torsional frequencies and their temperature dependence have been analysed. The estimated values of torsional frequencies lie in the range 75cm^{-1} to 39cm^{-1}. Study on biological implications of potassium chloroacetate gives wide scope.

Key words: Herbicide, Metabolism, Nuclear quadrupole resonance (NQR), potassium salt of monochloroacetic acid

INTRODUCTION

Potassium salt is one of the macro nutrients. Nitrogen helps in vegetative growth of the plants, phosphorous helps in maintaining cell structure and potassium helps in flowering.Seed germination to fruit production, plants need various macro and micro nutrients. Among the nutrients Potassium is called policeman nutrient it is one of the most important macronutrients, together with nitrogen(N) and phosphorous (P). Potassium is required for various biochemicals, physiological functions and intrinsically playing a key role in plant growth and development processes. It has also some interactive regulatory functions with other biomolecules [21, 12, 13, 14].

Potassium plays an imperative role in the photosynthesis process and the subsequent carbohydrate translocation and metabolism, which eventually increase the crop yield and improve the grain quality [15, 16, 17]. Stomatal regulation during photosynthesis is a vital event that governs the continual photosynthesis operation, and it is significantly moderated by the amount of K retained in the plant [20]. Potassium deficiency resulting in reduced stomatal conductance increased the mesophyll resistance and lowered the ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisCO) activity in plants, which eventually decreased the total photosynthesis rate [18]. The photosynthesis rate in plants increased with the higher utilization and export of photoassimilates. Evidence showed that the sucrose level in the leaves was increased by several folds when the plants were supplied with a sufficient level of K [18].K plays in regulating the stomatal aperture is in balancing CO_2 entry and H_2O vapor removal from intercellularspaces. However, the amount of CO_2 entry into the intercellular spaces represents the amount ofphotosynthate production in the leaf. Potassium plays an essential role in activating the ATP synthaseenzyme, thus assisting in the photosynthesis process. Shingles and McCarty [19] suggested that the ATPase performance is best when the K content in the plant is at an optimum level.

Present study was to conduct an inclusive bio-physical study on potassium chloroacetate. Monochloro acetic acid and sodium salt of chloroacetic acid is significant herbicides and plays important role in controlling weeds. There are several studies on biological implication of monochloro acetic acid, sodium chloroacetate and potassium having this broad bio-physical perspective we had decided to study temperature dependence of NQR frequency and internal motions in Potassium Chloroacetate. The NQR frequency of ^{35}Cl in monochloro acetic acid and sodium chloroacetate was reported first by Negita [1] and Allen [2]. Later Chandramani et al [3] measured NQR frequency in the temperature range 77K to 300K in both the compounds and they also evaluated torsional frequencies at different temperatures from 77K to room temperature using Bayer's, Kushida and Brown theory [4]. Keeping in view the importance of monochloroacetic acid and potassium in plant growth, metabolism and to explore the biological uses of potassium chloroacetate we have studied the temperature dependence of ^{35}Cl NQR frequency and torsional vibrations in potassium chloroacetate in the temperature range 77K to 300K.

MATERIALS AND METHODS

Potassium salt of monochloro acetic acid was prepared by neutralization of monochloro acetic acid with the base potassium hydroxide using phenolpthalene indicator. The precipitated salt was then dried in the oven. NQR signal of this sample has been measured at different temperature from 77 K to300 K. A homemade frequency modulated, self-quenched superegenerative spectrometer working in the range 20MHz to 40MHz has been used for detecting the resonances. The resonance frequencies were measured with a signal generator with an accuracy of ±1kHz and the temperatures were measured with a Pt-100 temperature sensor with an accuracy of ± 0.5K.

Method of Calculation

The temperature dependence of NQR interaction is mostly due to low frequency torsional vibrations. According to Bayer's and Kushida theory[4], the temperature dependence of NQRfrequency for the case $I = 3/2$ and $\eta = 0$ is given by

$$\nu_T = \nu_0\left[1 - \frac{3h}{8\pi^2}\sum_{i=x,y}\frac{1}{A_i f_i}\left(\frac{1}{2} + \frac{1}{\exp(hf_i/kT)-1}\right)\right] \text{.....(1)}$$

Where i = x, y, z denote the principal EFG axis, the z-axis is taken along the C-Cl direction.

Under high temperature approximation $hf_i / kT << 1$ and when $A_x = A_y \equiv A_i$, we have $f_x = f_Y \equiv f_i$ then equation (1) reduces to

$$\nu_T = \nu_0\left[1 - \frac{3h}{4\pi^2 A_i f_i^2}\right] \text{.....(2)}$$

Torsional frequency f_i in the potassium chloroacetate molecule was calculated at each temperature using equation (2). The procedure followed for the actual calculation of f_i is the same as that used by Chandramani et al [3]. Assuming linear temperature dependence for f_i as

$$f_i = f_i^o\left[1 - gT'\right] \text{.....(3)}$$

where T' is the temperature measured from any reference temperature T_o. g is the corresponding temperature coefficient and f_i is the lattice frequency at T' = 0K.Using high temperature approximation [4] we get

$$(d\nu/dT')_{T'=0}/(d^2\nu/dT'^2)_{T'=0} = (1 + 2T_o g)/(4g + 6T_o g^2) \text{ .....(4)}$$

where

$$g = \langle g\rangle = \Sigma\,(A_i/w^{o}_i{}^2)g_i/(A_i/w^{o}_i{}^2), \text{ and}$$
$$g^2 = \langle g^2\rangle = \Sigma(A_i/w^{o}_i{}^2)g_i{}^2/(A_i/w^{o}_i{}^2).$$

Here it is assumed that $g = \langle g\rangle^2 = \langle g^2\rangle$. The average temperature coefficients for the torsional modes are estimated from above equations by curve-fitting the experimental points and calculating the derivatives of v versus T' curves.

RESULTS

Potassium is a macro nutrient essential for growth of the plant. Monochloroacetic acid is an herbicide. To study the combine effect monochloroacetic acid and potassium on plant growth and to understand the biological implication, we have carried out extensive investigation on the temperature dependence of ^{35}Cl NQR frequency in potassium chloroacetate. Experimental data is shown in Fig.1. It has been found that the resonance frequency decreases with increase in temperature as expected and it is also clear from the Fig 1, that the sample do not exhibit phase transition in the temperature range studied. The difference between the resonance frequency at 77 K and that at room temperature is 826 kHz. The resonance frequency of the stationary molecule is obtained as 34.225 MHz by fitting the experimental data to a fourth order polynomial [5, 6, 7]. Table 1 gives the comparison of NQR frequency at room temperature in monochloro acetic acid and different chloroacetate complexes [8,9].

The moment of inertia for the potassium chloro acetate was calculated by using available crystal structure data [10]. The temperature variation of the torsional frequency obtained using numerical method is shown in Fig 2. The estimated values of torsional frequencies lie in the range 75 cm^{-1} to 39 $cm^{-1}$and 'g', the temperature co-efficient of torsional frequency is found to be 0.001568. To confirm the replacement of hydrogen from monochloro acetic acid by potassium, we obtained the X-ray diffraction spectra of monochloroacetic acid and potassium chloroacetate and details are shown in the Fig.3 and Fig 4 respectively. These are the preliminary studies done on temperature dependence of NQR frequency and internal motions in potassium chloroacetate, which is an essential plant nutrient. Because potassium plays vital role in plant physiological activities, vital regulatory functions in biochemical and physiological processes, that contribute to plant growth and development. Proper use of potassium with other nutrients helps to attain sustainable productivity and quality of crops and ensure nutritional food security for animals and human beings (11) and monochloroacetic acid is an herbicide. The combined effect of monochloroacetic

acid and potassium in the plant growth is very interesting research area to understand the biological implications of potassium chloroacetate. Further the effects of these salts need to be investigated on plants which require field studies in the agricultural areas.

CONCULSION

Temperature dependence of NQR frequency was measured in K-Salt of monochloroacetic acid. The sample investigated in the present case do not show any phase transition in the temperature range studied. We have evaluated the torsional frequency using Bayer's theory as a function of temperature. Generally the torsional frequencies of the molecules lie around 20 cm^{-1} to 100 cm^{-1} [5,6,7,8]. It has been found that the torsional frequencies obtained in the present case are in good agreement with the result obtained in the similar compounds [3]. Further the salts are to be experimented on plant system.

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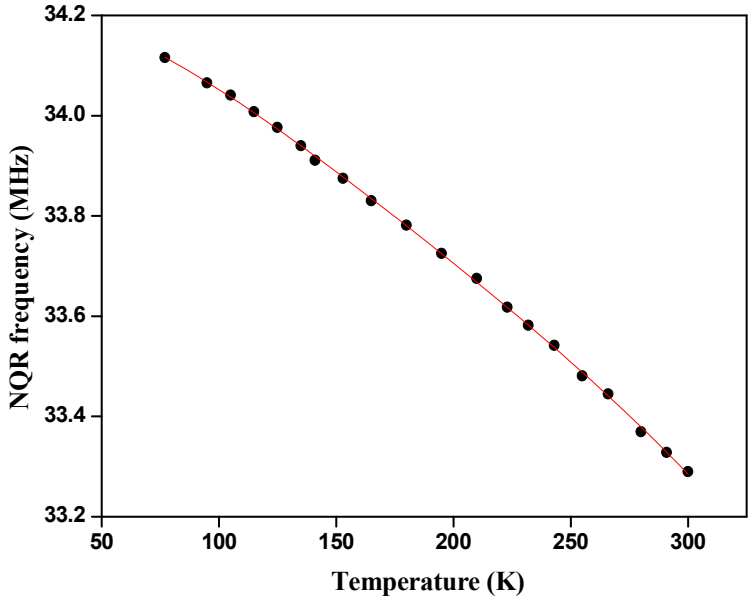

Figure 1.Temperature dependence of ^{35}Cl NQR frequency in Potassium Chloroacetate

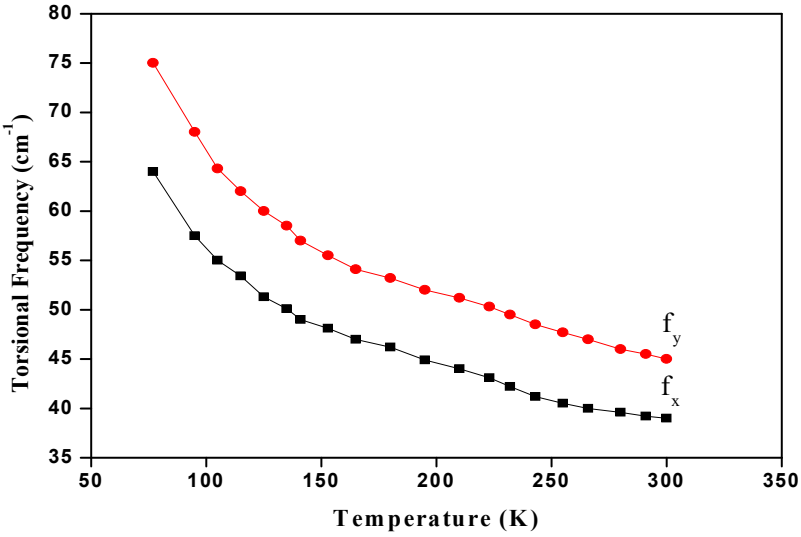

Figure 2.Temperature dependence of torsional frequency in Potassium Chloroacetate

Table 1.

Compound	M.P (⁰C)	Resonance Frequency (MHz)	Frequency Shift (MHz) at 300 K
1.Chloro acetic acid (α - phase)	62	34,904,35.406	-
2. Sodium chloroacetate	197	33.91	-1.25
3. Pottassium chloroacetate	156	33.29	-1.86
4. Rubidium chloroacetate	122	33.01	-2.15
5. Ammonium chloroacetate	105	33.21	-1.94

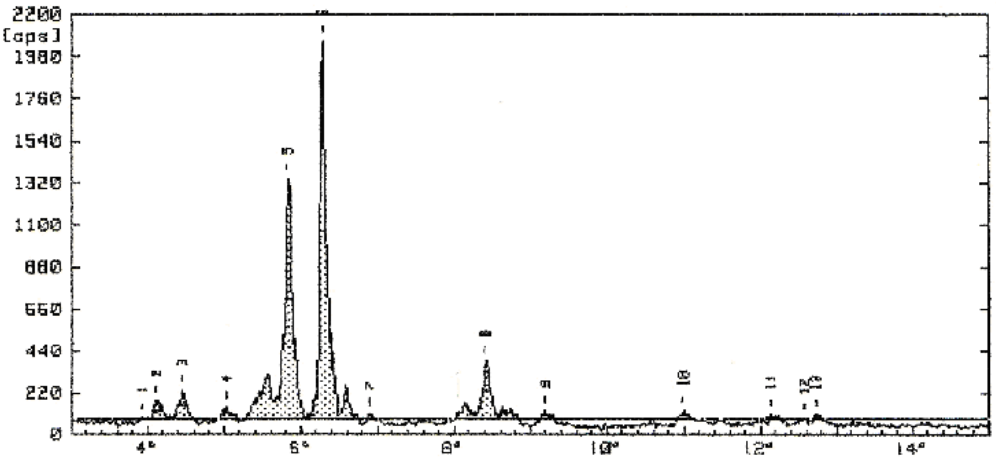

Figure 3. X-ray diffraction spectra of monochloroacetic acid

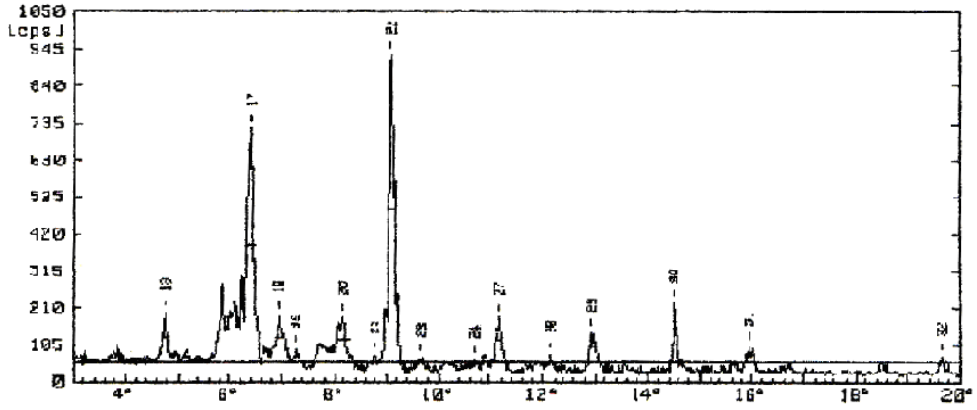

Figure 4.X-ray diffraction spectra of PotassiumChloroacetate

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RESEARCH ARTICLE

In-silico Analysis of Effects of *Stevia* Extract as Biopesticides on Leaf Blight

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ABSTRACT

Due to the ever-increasing worldwide plantation of sweet leaf *Stevia* rebaudiana (Bertoni), how to efficiently and effectively utilize the huge amounts of leaf residues that contain abundant nutrients after sweetener extraction becomes an eminent issue. One option is to return these residues into soil, as organic manure in the fresh or composted form, in order to both sustain soil fertility and avoid potential environmental pollution. In a field experiment, we studied if the *Stevia* leaf residue returning affected both plant and soil microbial growths as well as the possible change of soil microbial community composition. We have identified some molecules and plant diseases and have performed molecular docking and we got some good data to carry out our work further

Key words: Biopesticides, Leaf Blight, Molecular Docking, Pharmacophore, *Stevia*

INTRODUCTION

Approximately 80% of the world populations depend exclusively on plants for their health and healing. Whereas in the developed world, reliance on surgery and pharmaceutical medicine is more usual however in the recent years, more and more people are complementing their treatment with natural supplements (Dursum et al., 2004). Nowadays motivation of people towards herbs is increasing due to the concern about the side effects of synthetic chemical drugs. People want to concern their own health rather than submitting themselves to impersonal health

care system. Many herbal and some commonmedicinal plants are good sources of antioxidant compounds. Many of the biologically active substances found in plants, including phenolic compounds (flavonoid, phenolics) are known to possess potential antioxidant properties. The antioxidant activity of medicinal plants depends on the concentration of individual antioxidant entering into the composition (Larson, 1988). Antioxidants are micronutrients that have gained importance in recent years due to their ability to neutralize free radicals. Free radicals have been implicated in the etiology of several major human ailments including cancer, cardiovascular diseases, neural disorders, diabetes and arthritis (Devasagayam et al., 2004). Antiox- idants have been reported to prevent oxidative damage caused by free radical, they can interfere with the oxidation process by reacting with free radicals, chelating, catalytic metals and also by acting as oxygen scavengers (Buyukokuroglu et al., 2001). The potentially reactive derivatives of oxygen, attributed as reactive oxygen species (ROS), are continuously generated inside the human body which are detoxified by the antioxidants present in the body. However, overproduction of ROS and/or inadequate antioxidant defense can easily affect and persuade oxidative damage to various biomolecules including proteins, lipids lipoproteins and DNA (Farber, 1994). This oxidative damage is a critical etiological factor implicated in several chronic human diseases such as diabetes mellitus, cancer, atherosclerosis, arthritis and neurodegenerative diseases as well as ageing process. Recently there has been an upsurge of interest in the therapeutic potentials of plants, as antioxidants in reducing free radical induced tissue injury. Although several synthetic antioxidants, such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), are commercially available, but are quite unsafe and their toxicity is a problem of concern. Hence, strong restrictions have been placed on their application and there is a trend to substitute them with naturally occurring antioxidants. Natural plant-based antioxidants especially phenolics and flavonoids have been exploited commercially either as antioxidant additives or as nutritional supplements (Schuler, 1990). Also many other plant species have been investigated in the search for novel antioxidants (Chu et al., 2000). *Stevia* rebuadiana (Bert.), Bertoni is an herbaceous perennial plant of the Asteraceae family. It is native of Paraguay, where it grows wild in sandy soil (Goenadi, 1983). The main sweet component in the leaves of S. rebuadiana is stevioside (Geuns, 2000). *Stevia* sweetener extractives have been suggested to exert beneficial effects on human health, including antihypertensive (Chan et al., 2000), antihyperglycemic noncariogenic, anti human rota virus activities, glucose metabolism (Suanarunsawat and Chaiyabutr, 1997) and renal function (Jutabha and Chatsudthipong, 2000). Aqueous extract of S. rebuadiana dried leaves induce systemic and renal vasodilation, causing hypotension, diuresis and natriuresis in rats (Melis, 1995).

MATERIALS AND METHODS

Various pharmacophores of *Stevia* leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Asthama has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from *Stevia* were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from *Stevia* was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of *Stevia* with the selected targets of Leaf Blight. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from *Stevia* to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULTS AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structures are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 5 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-

methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the *Stevia* and can be commercialized as the natural drug for the Leaf Blight Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes

Sl.No.	*Stevia* Pharmacophores	Targeted Plant Gene Leaf Blight	PDB No of the Genes
1	Palmitic acid	IMMUNE SYSTEM	5H3C
2	Stevioside	OXIDOREDUCTASE	5ZF2
3	Steviol	CELL CYCLE	2QI2
4	Dulcoside A		

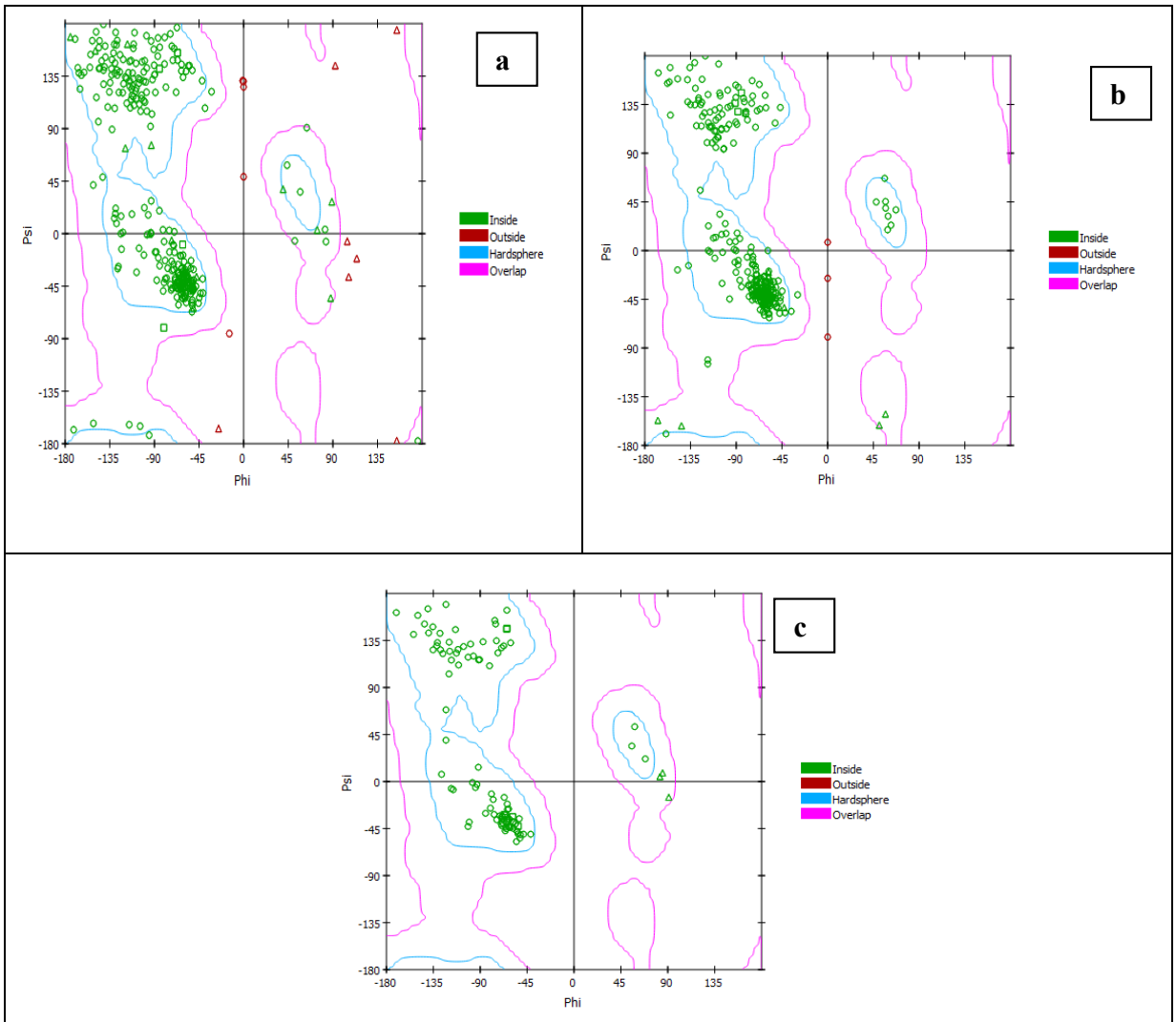


Fig 1. Ramachandran Plot of (a) 2QI2, (b) 5H3C, (c) 5ZF2

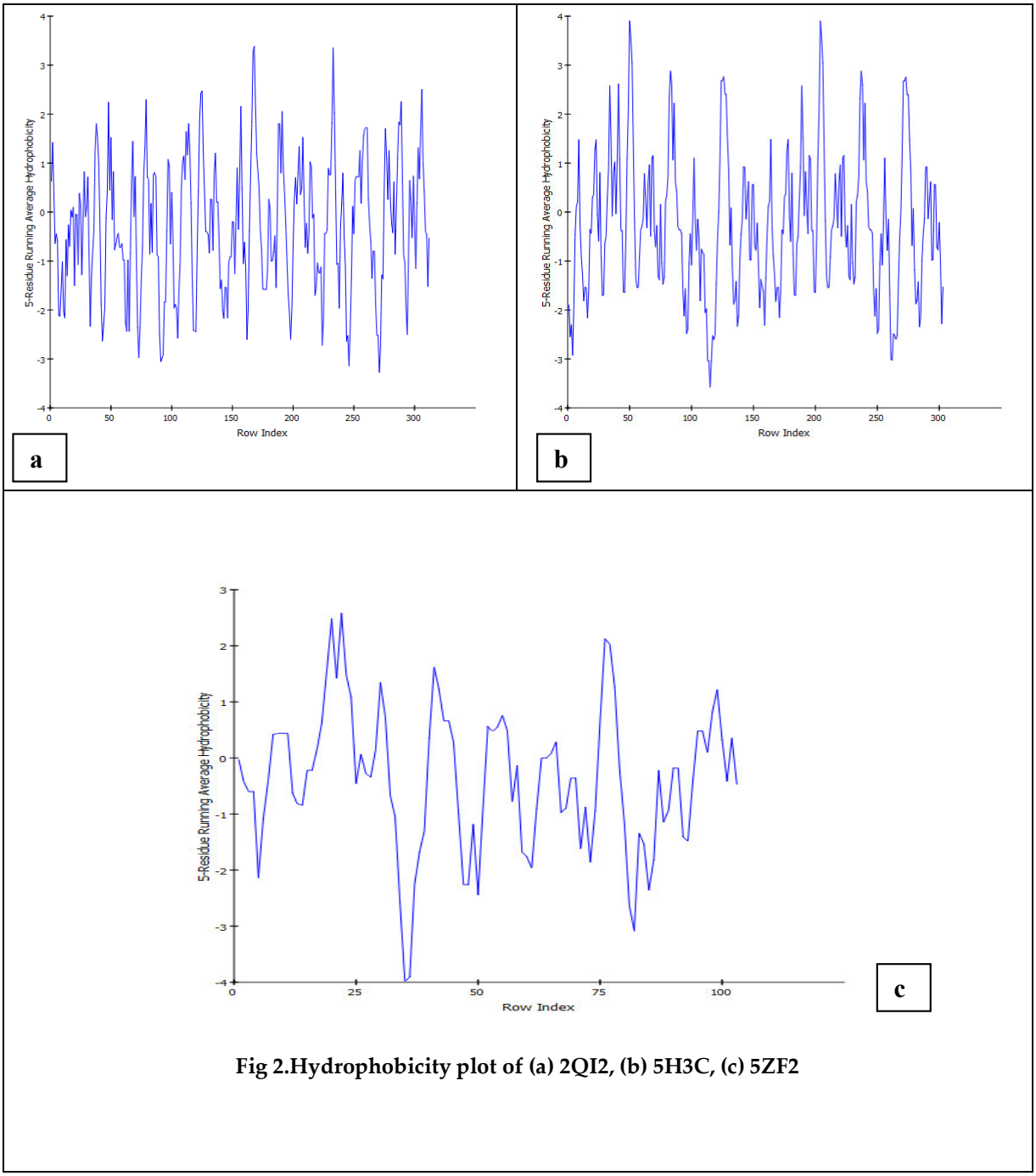


Fig 2.Hydrophobicity plot of (a) 2QI2, (b) 5H3C, (c) 5ZF2

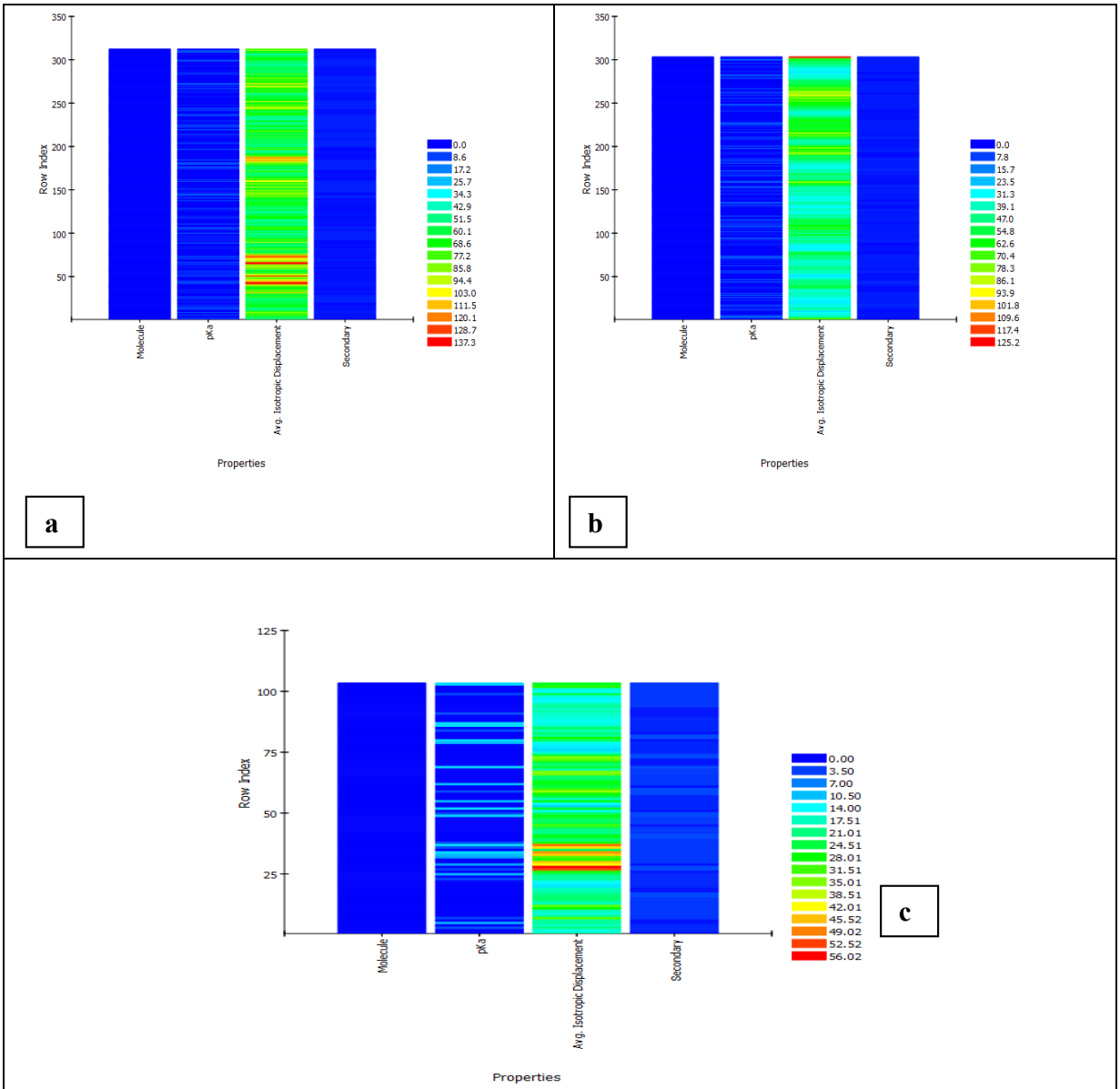


Fig 3.Heatmap of (a) 2QI2, (b) 5H3C, (c) 5ZF2

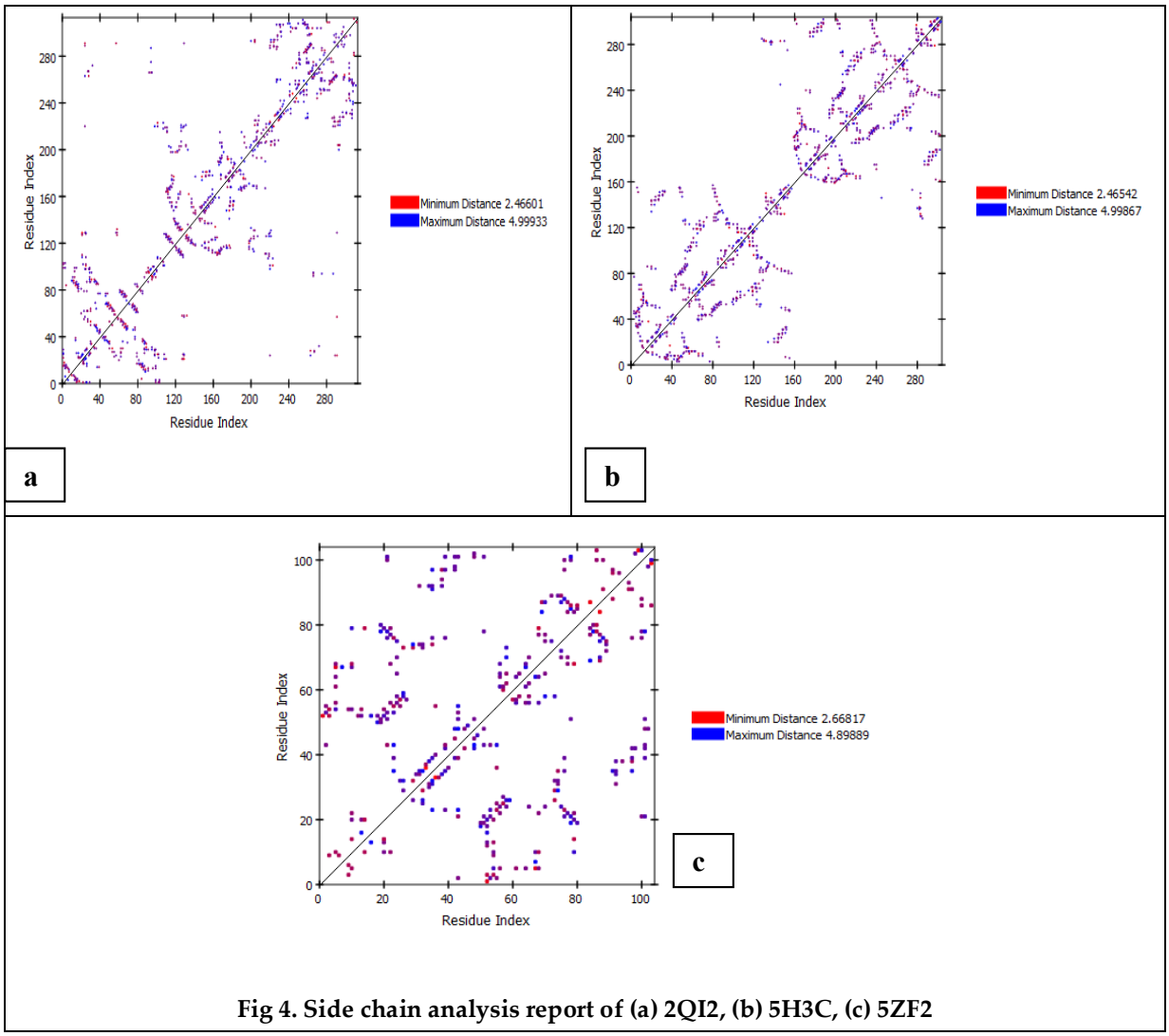


Fig 4. Side chain analysis report of (a) 2QI2, (b) 5H3C, (c) 5ZF2

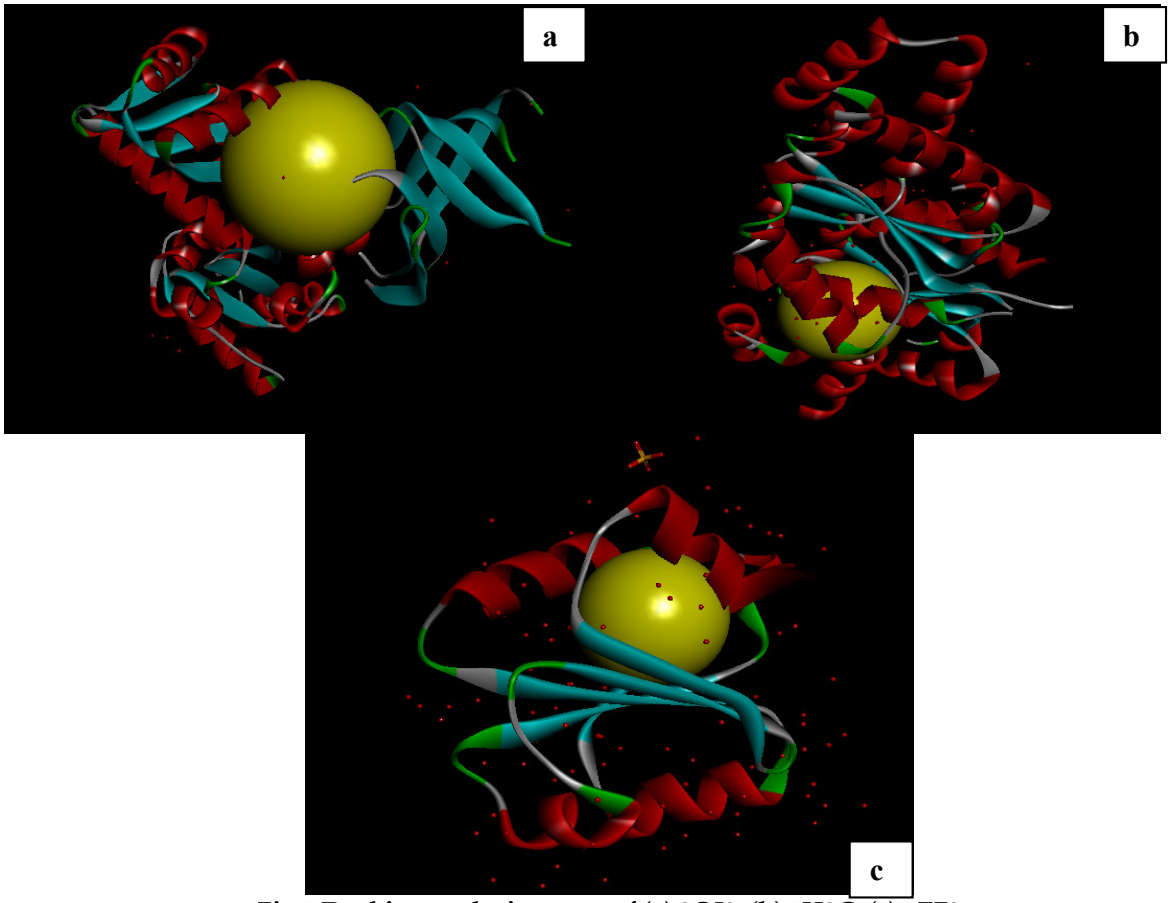
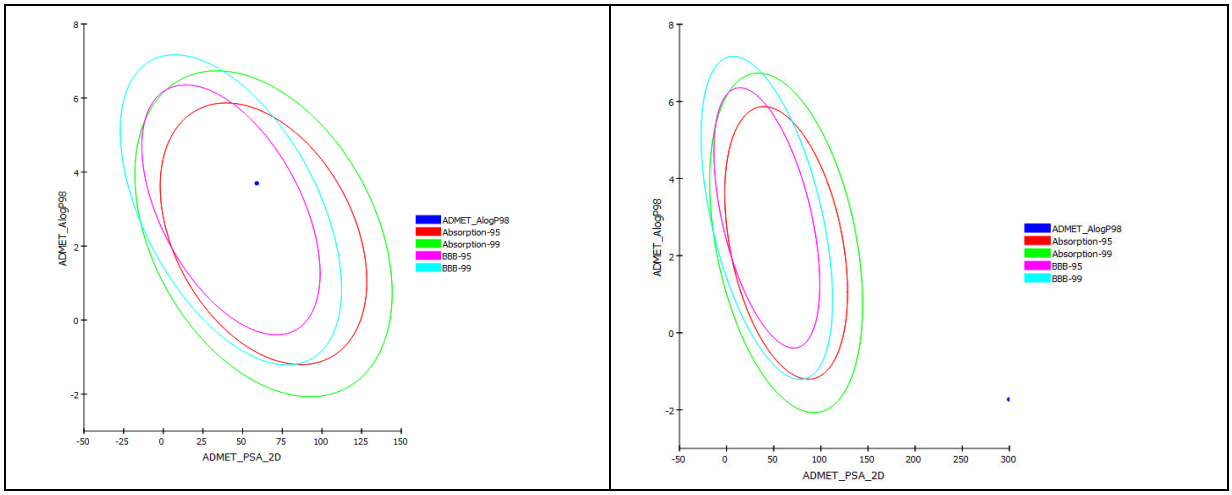


Fig 5.Docking analysis report of (a) 2QI2, (b) 5H3C, (c) 5ZF2



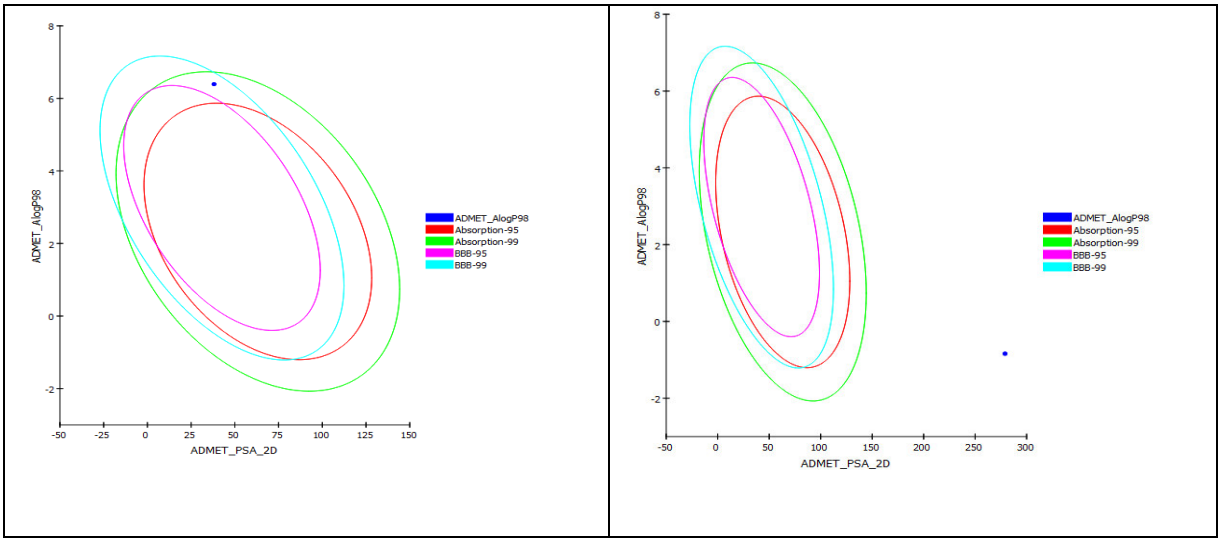


Fig.6. ADMET analysis report

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RESEARCH ARTICLE

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ABSTRACT

A clinical condition "Diabetes" is more often associated with the release of a massive amount of toxic free radicals, which significantly decrease the level of antioxidant enzymes, increase lipid peroxidation, and worsen the disease state by causing further hyperglycemia. Many plant extracts and plant-derived natural compounds have been reported to possess antioxidant activities, and useful in preventing the deleterious effects of oxidative stress. Here, we have demonstrated the free-radical scavenging effects of a natural sweetener or a dietary supplement *Stevia* rebaudiana bertoni standardized extract on diabetes-induced oxidative stress animal model. The present study was also aimed to investigate the effect of this extract on hyperglycemia and hepatic antioxidant enzymes of animal models of type 2, non-insulin dependent diabetes mellitus (NIDDM).

Key words: Diabetes, Molecular Docking, Pharmacophore, Stevia.

INTRODUCTION

Approximately 80% of the world populations depend exclusively on plants for their health and healing. Whereas in the developed world, reliance on surgery and pharmaceutical medicine is more usual however in the recent years, more and more people are complementing their treatment with natural supplements (Dursum et al., 2004). Nowadays motivation of people towards herbs is increasing due to the concern about the side effects of synthetic chemical drugs. People want to concern their own health rather than submitting themselves to impersonal health

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Diabetes mellitus is probably the fastest growing metabolic disease in the world. Because of its heterogenic nature, diabetes makes more challenging task and it needs more appropriate therapies. Traditional plant remedies have been used for very long time in the treatment of diabetes, but only a few of them have been significantly evaluated. Therefore, the present work aimed to evaluate the effect of purified standard *Stevia* rebaudiana extract on blood glucose profile and biomarkers of oxidative stress.

MATERIALS AND METHODS

Various pharmacophores of *Stevia* leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Asthama has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from *Stevia* were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from *Stevia* was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of *Stevia* with the selected targets of diabaties. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from *Stevia* to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule

can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULTS AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structures are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands.

Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 5 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

In conclusion, this study supports the contention that traditional medicines remain a valuable source in the potential discovery of natural product pharmaceuticals. The identified pharmacophores can be isolated from the *Stevia* and can be commercialized as the natural drug for the Diabetes Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products.

The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce. Significant antioxidant activity of aqueous leaf extract of S. rebaudiana provides a scientific validation for the traditional use of this plant as an accessible source of natural antioxidants with consequent health benefits. Further work on isolation and identification of active compounds and their efficacy needs to be done.

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Table 1. The list of pharmacophores and the targeted genes

Sl.No.	*Stevia* Pharmacophores	Targeted Animal Gene (diabaties)	PDB No of the Genes
1	Palmitic acid	Endocytosis/Exocytosis	1H6E
2	Stevioside	Growth Factor	1BU9
3	Steviol	Transcription	3SP9
4	Dulcoside A		

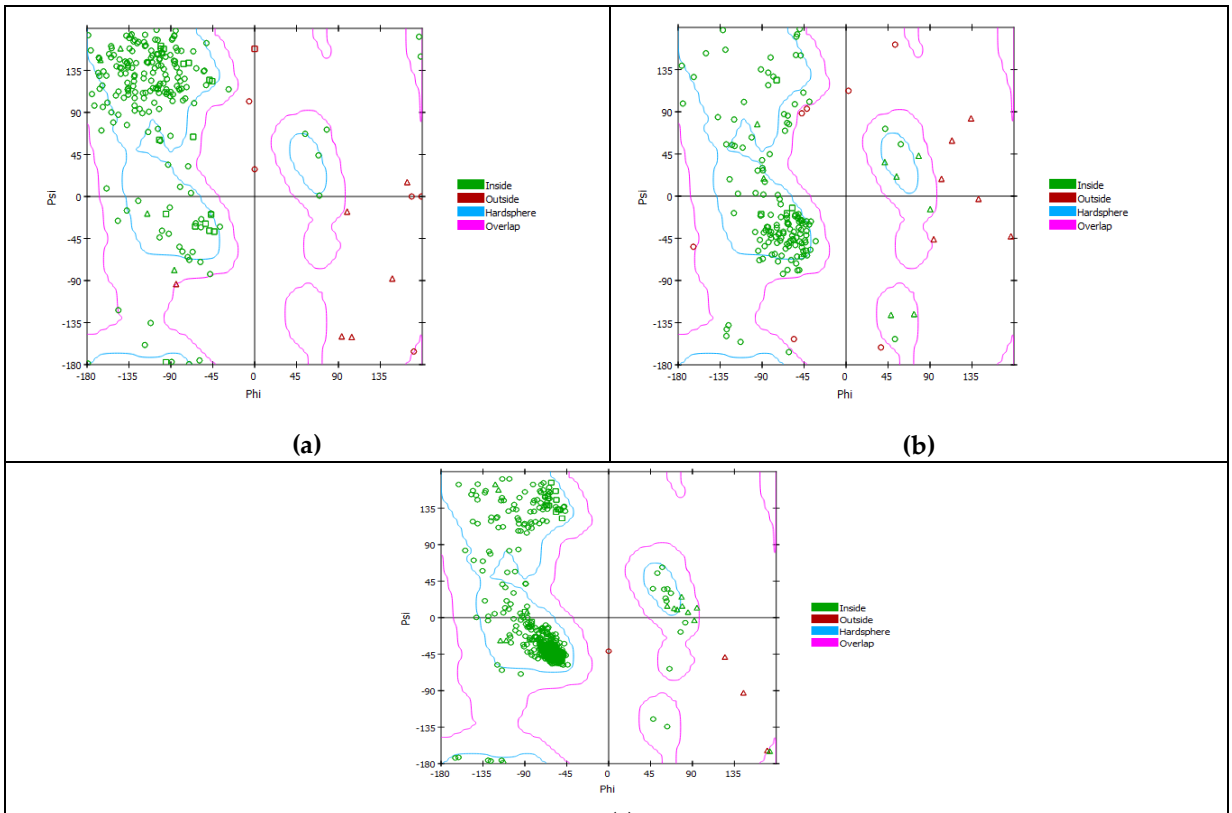


Fig 1: Ramachandran Plot of (a) 1H6E (b) 1BU9 (c) 3SP9

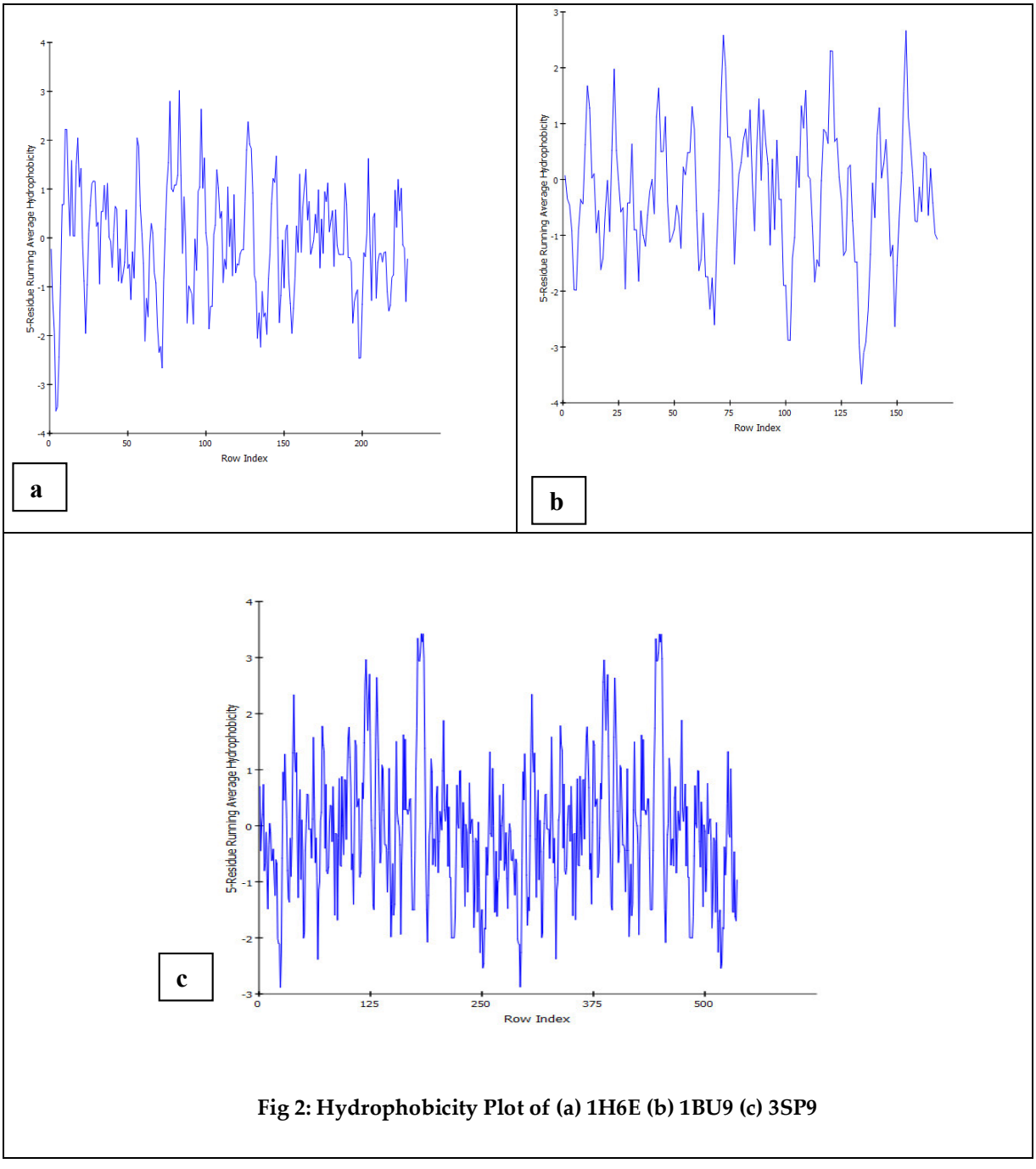


Fig 2: Hydrophobicity Plot of (a) 1H6E (b) 1BU9 (c) 3SP9

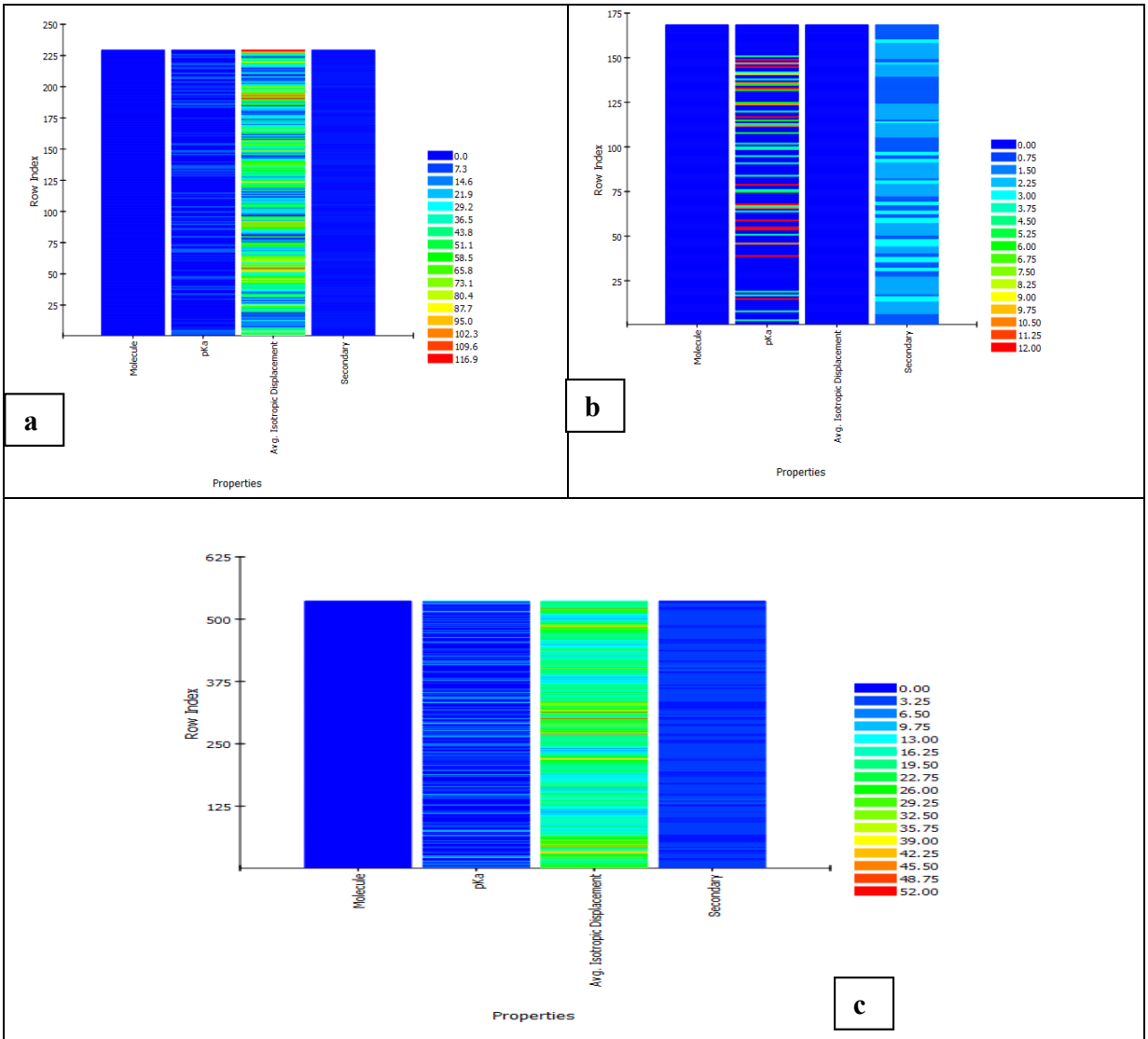


Fig 3.Heatmap of (a) 2QI2, (b) 5H3C, (c) 5ZF2

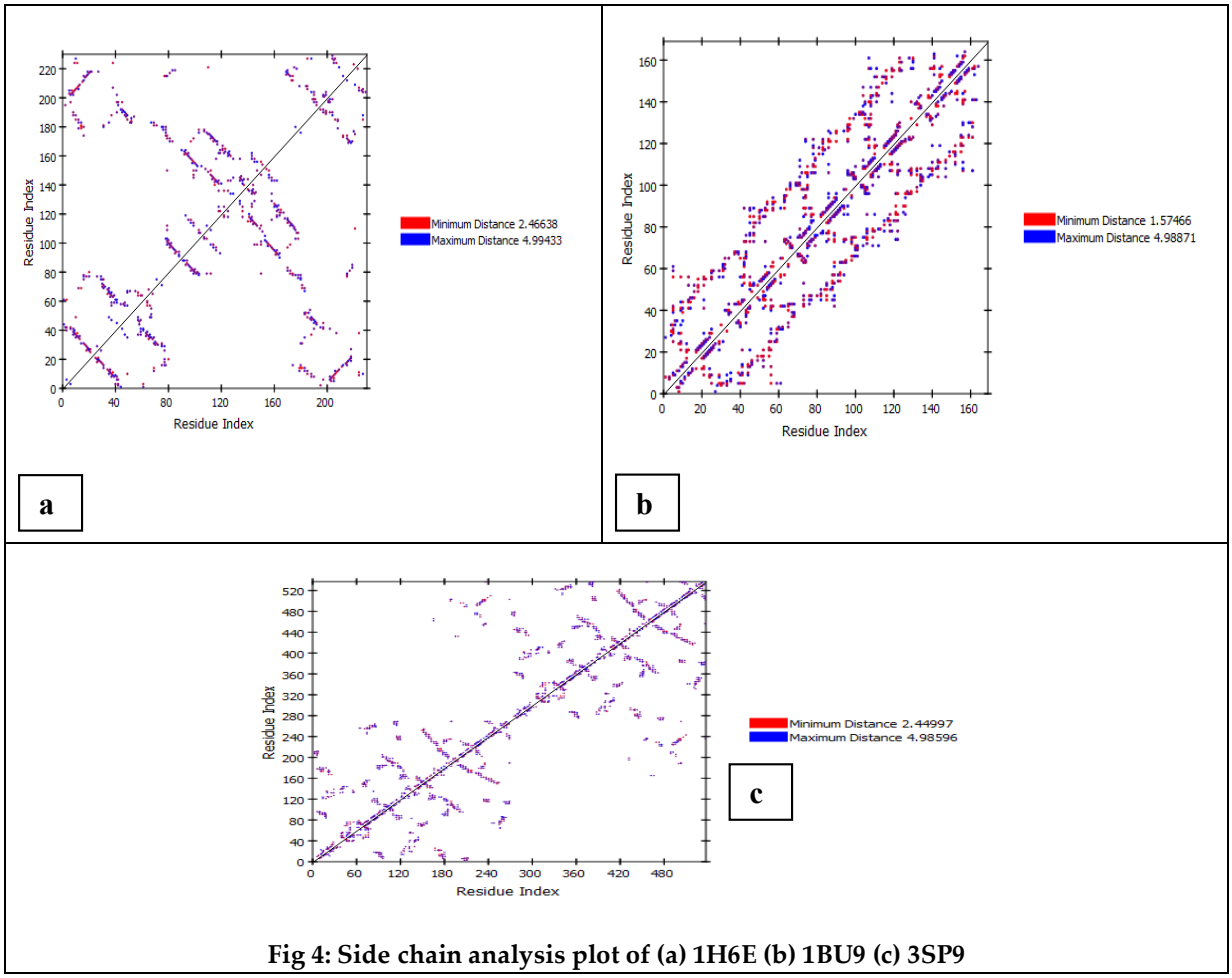
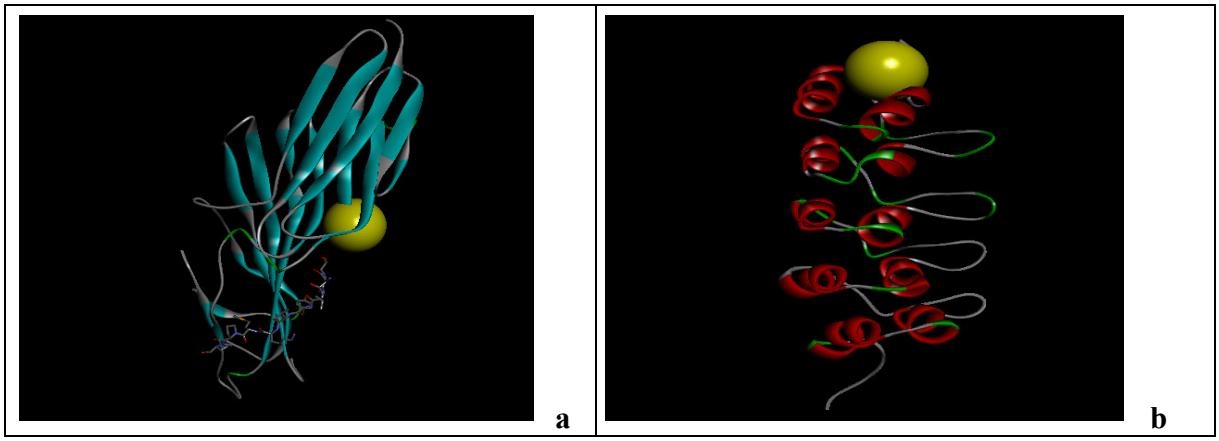
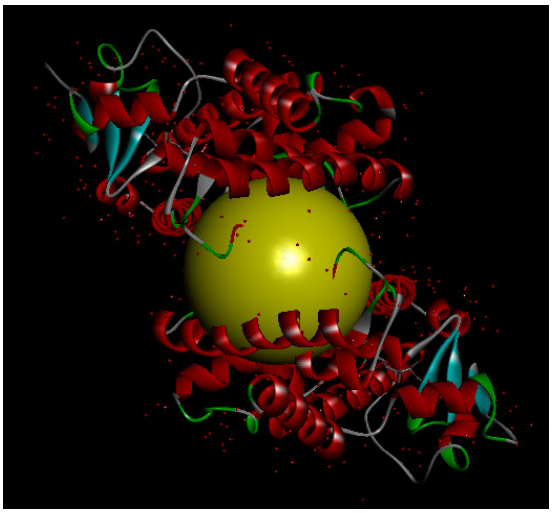


Fig 4: Side chain analysis plot of (a) 1H6E (b) 1BU9 (c) 3SP9





c

Fig 5: Docking results of (a) 1H6E (b) 1BU9 (c) 3SP9

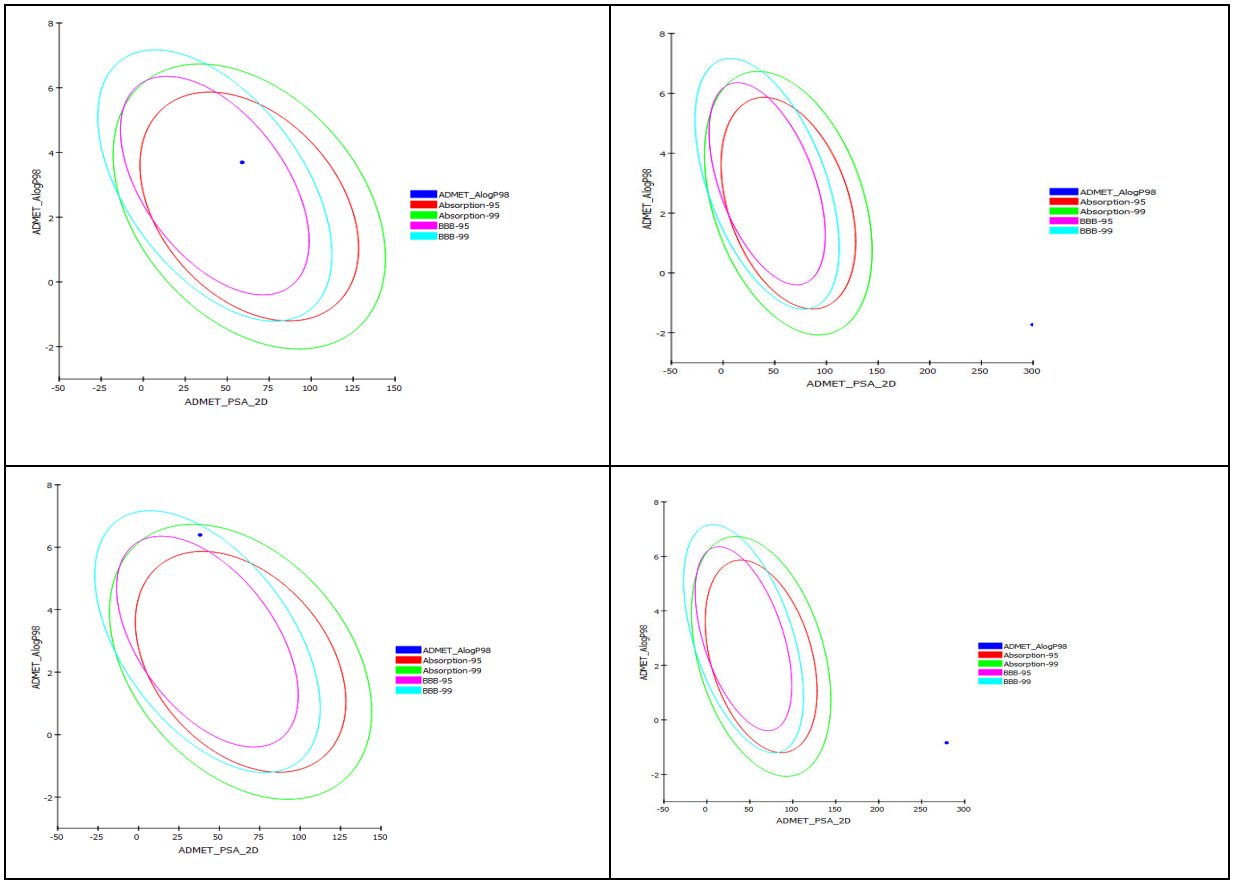


Fig.6. ADMET analysis report

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RESEARCH ARTICLE

Temperature Dependence of ^{35}Cl NQR Frequency and Internal Motions in the Complex of 1-Chloro - 2, 4 Dinitrobenzene and Parachloroaniline an Active Ingredient of Insecticides and a Biological Residue

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ABSTRACT

1-Chloro - 2, 4 Dinitrobenzene is used as insecticides and several other chemical preparation, parachloroaniline is also used widely in production of drugs, dyes and pesticides. It is an intermediate and precursor extensively used antibacterial chlorhexidine and it is used in manufacture of monolinuron, chlorphthalim, pyraclostrobin and anilofos, which are used as pesticides. These compounds enters into human body through food chain and food web and we have deduced bio-physical approach to investigate the effects initially, the temperature dependence of ^{35}Cl NQR frequencies was studied in the 1:1 ratio complex of 1-Chloro-2-4 dinitrobenzene and parachloroaniline has been investigated in the temperature range 77K to room temperature. Two resonance lines have been observed throughout the temperature range studied. The experimental results show a large shift in frequency (about 1.172 MHz) in comparison to the NQR frequency of parachloroaniline and there is no shift in the frequency in comparison to the NQR signal of 1-Chloro-2-4 dinitrobenzene. The present data are in good agreement with the earlier reported data. This data would be used for biological investigation.

Keywords: Nuclear quadrupole resonance (NQR), 1-Chloro-2-4 dinitrobenzene, parachloroaniline, donor-accepter complexes, electron density.

INTRODUCTION

Bio - Magnification is a serious problem harmful chemical enters food chain and reaches human. 1-Chloro - 2,4 Dinitrobenzene is used as insecticides and several others through sources of chemical preparation, parachloroaniline is widely used in production of drugs, dyes and pesticides. It is a intermediate and precursor extensively used antibacterial chlorhexidine and it is used in manufacture of monolinuron, chlorphthalim, pyraclostrobin and anilofos, which are used as pesticides. Residual parachloroaniline have significant impact on health, these chemicals have adverse effects on all living organisms. These chemicals are enters human body through food chain these chemical are mostly not digested in the living organism. Living organisms contain enzymes and biomolecules with antioxidant capabilities to protect them against the adverse effects of xenobiotics. Organism which inhabit soils and litter layers in most landscapes can offer an important tool to evaluate environmental toxicity and impacts of organic xenobiotics and agrochemicals [1, 2, 3]. Pesticides can exert both direct toxicity against biotic component of biosphere or produce latent effects on their growth, histology and fertility. In addition, pesticide-contaminated living organism can present a source of contamination of higher members of the food web, e.g. birds or mammals. Pesticides usually enter the soil as residues of sprays applied to crop web plants from the above ground and are less frequently applied directly on soils as in the case of pre-emergence herbicides, nematocides or root pest control agents [1]. Present integrated biophysical approach which would extensively pave way to tackle these chemicals in biological system.

^{35}Cl NQR frequency measurements are carried out in the complex 1-Chloro-2-4 dinitrobenzene and parachloroaniline as a function of temperature. Sample were procured from Aldrich Chemical Company (USA) and used directly to prepare the complex. The ^{35}Cl NQR frequency in the complex 1-Chloro-2-4 dinitrobenzene and parachloroaniline have been reported by Ramananda et al [4, 5] at room temperature. In the present work we have carried out temperature variation NQR frequency at different temperature from 77K to 300K.This study can be used to encounter the negative effects of these chemicals in biological system.

MATERIALS AND METHODS

In the present investigation a homemade frequency modulated, self-quenched super generative spectrometer working in the range 20 MHz to 40 MHz has been used for detecting the resonances. The resonance frequencies were measured with a signal generator with an accuracy of ± 1KHz and the temperatures were measured with a Pt-100 temperature sensor with an accuracy of ± 0.5K.The formation of donor –accepter complexes is due to partial transfer of charges or shift of electron density from the higher molecular orbital of the donor to the lower free molecular orbital of the acceptor [6]. This results in change in the electronic structure of the interacting molecules and hence a significant modification in the EFG on each atom of the complexes. In addition, during complex formation new spatial interaction may appear. Also, crystal field effect plays an important role. Therefore complex formation leads to major shifts in NQR frequency and change in multiplicity of the spectra.

The range of possible frequency shifts in the case of charge transfer complexes of donor and acceptor type is about 10-20%. Previous experimental results [6] shows that the frequency shift for the carbon – chlorine bond is about 9%, carbon – bromine bond is about 12% and carbon – iodine bond is about 18.5%.In case of charge transfer complexes one can observe considerable change in the melting point of the complexes, when compared to the melting point of the corresponding compounds. Hence it is interesting to study the shelf life and thermal stability of these complexes. The charge complex prepared for the present investigation has been kept for long time to check for changes in colour or chemical nature. However, the sample did not show any such changes indicating that the sample is stable.

RESULTS AND DISCUSSION

The 1-Chloro-2-4 dinitrobenzene + parachloroaniline (1:1 ratio) sample is prepared by adding slowly the 1 – Chloro – 2 - 4 dinitrobenzene (electron acceptor) to molten parachloroaniline (electron donor) in equi-molar ratio1:1. The resulting mixture is then allowed to cool slowly to about 15°C [4,5].The sample obtained is kept for drying in a desiccators bottle for about 24 hours. The 1-Chloro-2-4 dinitrobenzene / Parachloroaniline complex gives two signal (one in the neighbourhood of parachloroaniline and other coinciding with the position of 1-Chloro-2-4 dinitrobenzene). The colour of the complex is found to be different from those of the starting compounds. The complex is light red in colour and the melting point of the complex has been found to be 76 °C. It is slightly higher than any of its component values. This change in colour and increase in melting point of the complex provides an evidence of formation of charge transfer complex [4,5].

The NQR frequency has been measured at different temperatures from 77 K to 300 K. The temperature variation of NQR frequency for line I and line II are given in table 1 and are plotted in Fig.1 and Fig.2. Both lines shows decrease of NQR frequency with increase in temperature. The NQR frequency at room temperature for line I is 34.9504 MHz and at 77 K, it is 35.5764 MHz. While for line II it is 37.2658 MHz at 300 K and 37.7045 MHz at 77 K. A fourth order polynomial in temperature has been used to fit the measured data [7,8,9,10,11] and the best fit values are given below the Fig.1 and Fig.2. The theoretical fit is shown by the continuous line, while the dots show the experimental points.

A variety of chemicals often act simultaneously on biota in contaminated ecosystems [12,13,14,15]. Chemical contaminants are fairly common in nature and ecologists are challenged to understand and predict the impacts of these contaminants on natural communities and problems associated with food web and food chain [16]. There are several biological study on how to handle this chemical in the biological system, present study would increase the biological efficacy to handle these residual chemical in the human body.

CONCLUSION

The experimental results show a large shift in frequency (about 1.172 MHz) in comparison to the NQR frequency of parachloroaniline. In case of line II, there is no shift in frequency in comparison to the NQR signal of 1-chloro 2, 4-dinitrobenzene. The present study is good probe to understand the biological efficacy of residual chemicals in the human body. [5,6].

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Table.1.Temperature dependence of ^{35}Cl NQR frequency in 1-Chloro-2-4 dinitrobenzene + Chloroaniline

Temperature (K)	NQR Frequency (MHz)	
	Line-I	Line-II
77	35.5764	37.7045
84	35.5604	37.6897
101	35.5218	37.6687
118	35.4801	37.6431
135	35.4248	37.6145
152	35.3892	37.5902
169	35.3412	37.5562
186	35.2925	37.5294
203	35.2345	37.4959
221	35.2059	37.4656
238	35.1554	37.4256
255	35.0935	37.3798
278	35.0417	37.3390
289	34.9863	37.2969
297	34.9624	37.2756
300	34.9504	37.2658
307	34.9291	37.2429
316	34.8984	37.2258
324	34.8732	37.2070
332	34.8561	37.1852
341	34.8283	37.1594
348	34.8001	37.1270

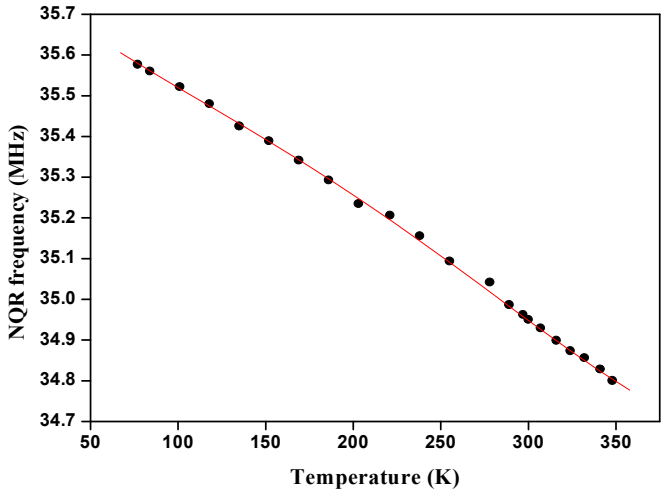

Fig.1. Temperature dependence of ^{35}Cl NQR frequency in 1-Chloro-2-4 dinitrobenzene + Chloroaniline (Line-I)
Best-fit values for Line – I

$$\nu_T = A + B_1{*}T + B_2{*}T^2 + B_3{*}T^3 + B_4{*}T^4$$

ν_o = A = 35.81881MHz B_1 = -0.00385 MHz K^{-1} B_2 = 1.34055 X 10^{-5}MHz K^{-2}

B_3 = -5.49649X 10^{-8} MHz K^{-3} B_4 = 6.93705 X 10^{-11} MHz K^{-4}

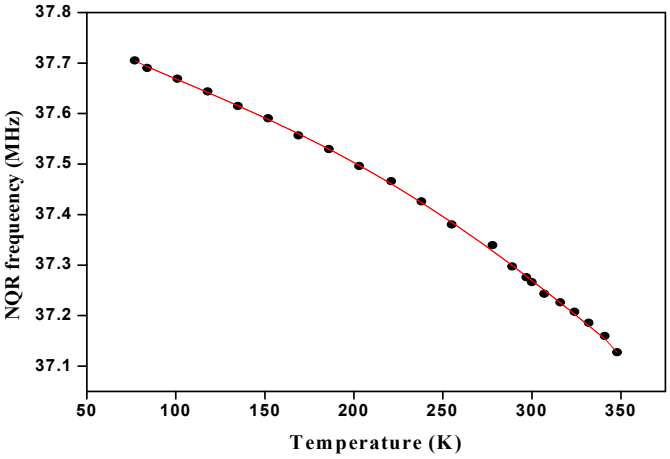

Fig.2. Temperature dependence of ^{35}Cl NQR frequency in 1-Chloro-2-4 dinitrobenzene + Chloroaniline (Line-II)
Best-fit values for Line – II

$$\nu_T = A + B_1{*}T + B_2{*}T^2 + B_3{*}T^3 + B_4{*}T^4$$

ν_o = A = 37. 84386 MHz B_1 = -0.00229 MHz K^{-1} B_2 = 8.57907 X 10^{-6}MHz K^{-2}

B_3 = -3.56921 X 10^{-8} MHz K^{-3} B_4 = 3.76744 X 10^{-11} MHz K^{-4}

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RESEARCH ARTICLE

In-silico Analysis of Effects of Methi Extract on Animal Disease Gestational Diabetes

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ABSTRACT

Antiquated India is one of the pioneers of investigations of plants as medication, for example Ayurveda. In our social and monetary life we barely deal with our food we are taking. One such novel herb is Methi which has frequently been viewed as a mind supporter. The entire plant including the blossoms can be utilized for restorative purposes. It has a harsh and sweet taste and is known to give a cooling vitality. Methi is loaded with cancer prevention agents that are basic for carrying on with a sound life. We are utilizing this property of Methi to get some new medications for gestational diabetes. The employments of different pesticides, additives, and so on transform the nourishments into poison. Also the reactions of these pesticides and additives, and so on are perilous as on the grounds that it prompts commencement of various malignant growth. In this entire world, the quantity of patients kicking the bucket from malignant growth is expanding in a compromising manner. In-silico investigation has done utilizing programming and we further focused on a portion of the qualities answerable for gestational diabetes and pharmacophores from Methi and destroyed some silico examination. In this we have discovered that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Methi, Docking, *In silico* Analysis, Gestational Diabetes, Pharmacophore

INTRODUCTION

Plants made due for many years on planet earth by constantly developing and adjusting. Prescriptions acquired from Mother Nature, particularly got from plants, have been all around archived for quite a long while. Indeed, even

today, as indicated by World Health Organization, about 80% of total populace from the creating and immature nations despite everything rely upon plant-inferred prescriptions for their human services prerequisites. Fenugreek (*Trigonella foenum-graecum* Linn.), is a shortliving yearly plant, has a place with the *Fabaceae* family. It is developed in numerous pieces of Asia, Africa, and Europe as food, condiment, zest, and as local medication. The variety *Trigonella* is named concerning its triangular formed blossoms, and in Latin little triangle is alluded to as *Trigonella*. The species *foenum-graecum* gets its name from verifiable point of view of Romans, since it is utilized as regular yield grub for creatures in Greece . Fenugreek plant achieves the stature of 1–2 feet and bears green trifoliate leaves. The blossoms are white to yellow in shading and the plant conveys slight cases. The units are around 15 cm long and they contain on a normal 10–20 seeds. Fenugreek seeds are brilliant yellow in shading and their normal stature, width, and thickness are 4.01–4.19, 2.35–2.60, and 2.40–2.66 mm, separately.

Fenugreek seeds are the most significant and all around concentrated piece of fenugreek plant. The dried fenugreek seeds are grounded to acquire fenugreek seed powder which is utilized as fixing. Fenugreek gum is acquired from the endosperm of the seeds. Fenugreek is utilized as a zest and herb in numerous culinary dishes and its green leaves used to enhance dishes or eaten as greens and seeds are utilized for seasonings or squashed to get ready curry powders and glues' utilized for seasonings or squashed to plan curry powders and glue. Notwithstanding being utilized in different food arrangements, fenugreek likewise has recuperating benefits. Fenugreek is one of the most seasoned restorative plant and the therapeutic properties are very much reported in the old clinical writing. In Ayurveda, the customary Indian clinical framework, fenugreek was utilized as a stomach related guide and old Egyptians utilized it as lactation help . In customary Chinese medication, fenugreek was utilized to treat edema in the legs. There are number of employments of fenugreek, including the treatment of lung blockage and sinus, heartburn, sparseness in men, hair tonic and conditioner and as galactogogue. As of now, an enormous number of studies have revealed positive insight into fenugreek's therapeutic properties, for example, antioxidant , anti-inflammatory, antidiabetic, antiobesity, anticancer , hepatoprotective , anti-hyperlipidemic ladies' wellbeing and sexual health modulating activities. All These disease avoidance properties of fenugreek are because of essence of various exhibits of phytochemicals and their distinctive diverse pharmacological and organic exercises. In light of all these assortment of restorative properties, Fenugreek is picked as a therapeutic plant for this work with the goal that it might be useful to fix some disease.

During pregnancy, the body produces a larger amount of certain hormones that impact the placenta, and help to maintain a healthy pregnancy. This increase in hormones leads to insulin resistance, which increases the amount of glucose in the blood stream. This is normal in pregnancy, as this extra glucose is needed to support the baby. However, when insulin resistance becomes too great, and the amount of glucose in the bloodstream is very high, gestational diabetes can result .It is a form of high blood sugar affecting pregnant women. Those who develop gestational diabetes are at higher risk of developing type 2 diabetes later in life.More than 1 million cases of gestatinal diabetes found in India per year. During pregnancy, certain hormones such as chorionic gonadotropin (hCG), estrogen, and progesterone are released that can lead to a mass amount of glucose in the blood. In addition, pregnancy hormones like placental lactogen can interfere with susceptible insulin receptors, which further increases blood glucose levels. When the amount of insulin produced is less than the amount needed to handle blood glucose levels, gestational diabetes can arise .Gestational diabetis can cause birth injury.

MATERIALS AND METHODS

Various pharmacophores of Methi leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of gestational diabetes has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in

Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

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Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism,

excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

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Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties

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4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism,

Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the Fenugreek and can be commercialized as the natural drug for the gestatinal diabetes Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from gestational diabetes

Sl.No	Pharmacophores from Methi	Targeted Animal Gene (Gestational Diabetes)	PDB No of the Genes
1	Trigonelline	Adiponectin, C1q And Collagen Domain Containing	6U6N
2	Methyl Coumarin	Peroxisome Proliferator Activated Receptor Gamma	6ONI
3	Carpaine	C-Reactive Protein	6NMT
4	Choline	Leptin	6E2P

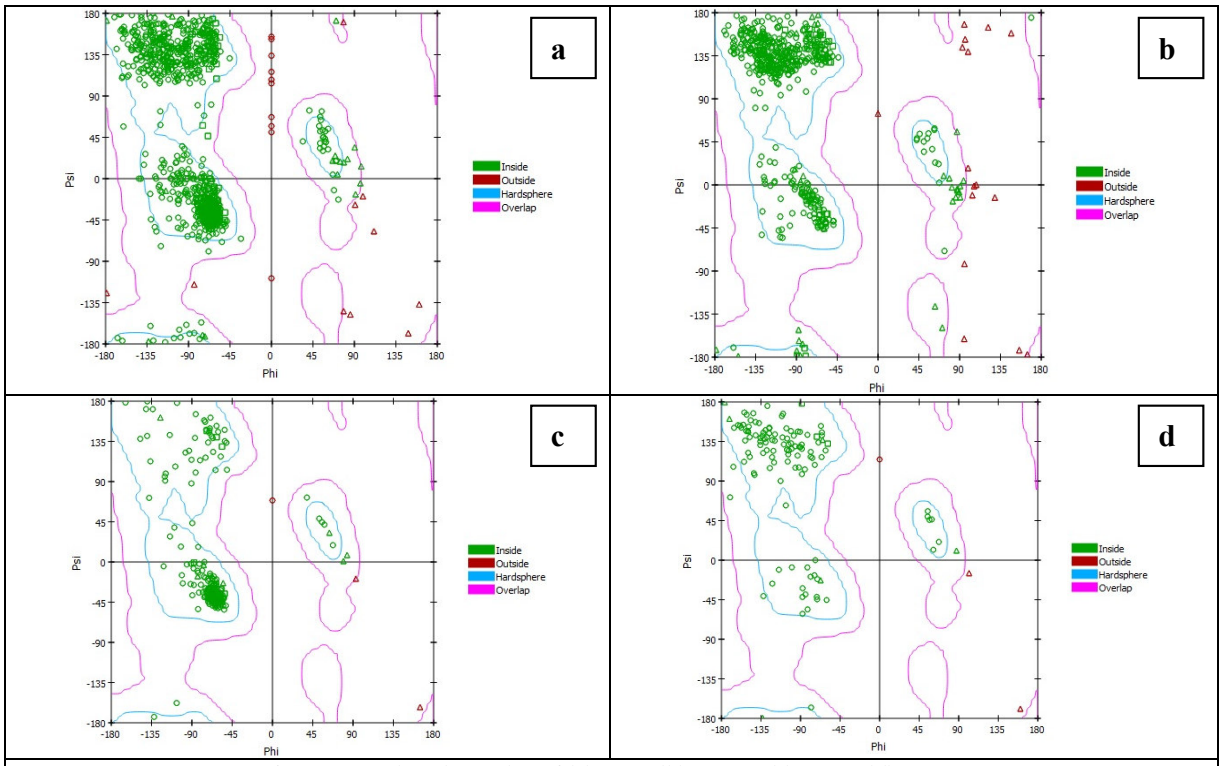


Fig 1: Ramachandran plot of (a) 6E2P (b) 6NMT (c) 6ONI (d) 6U6N

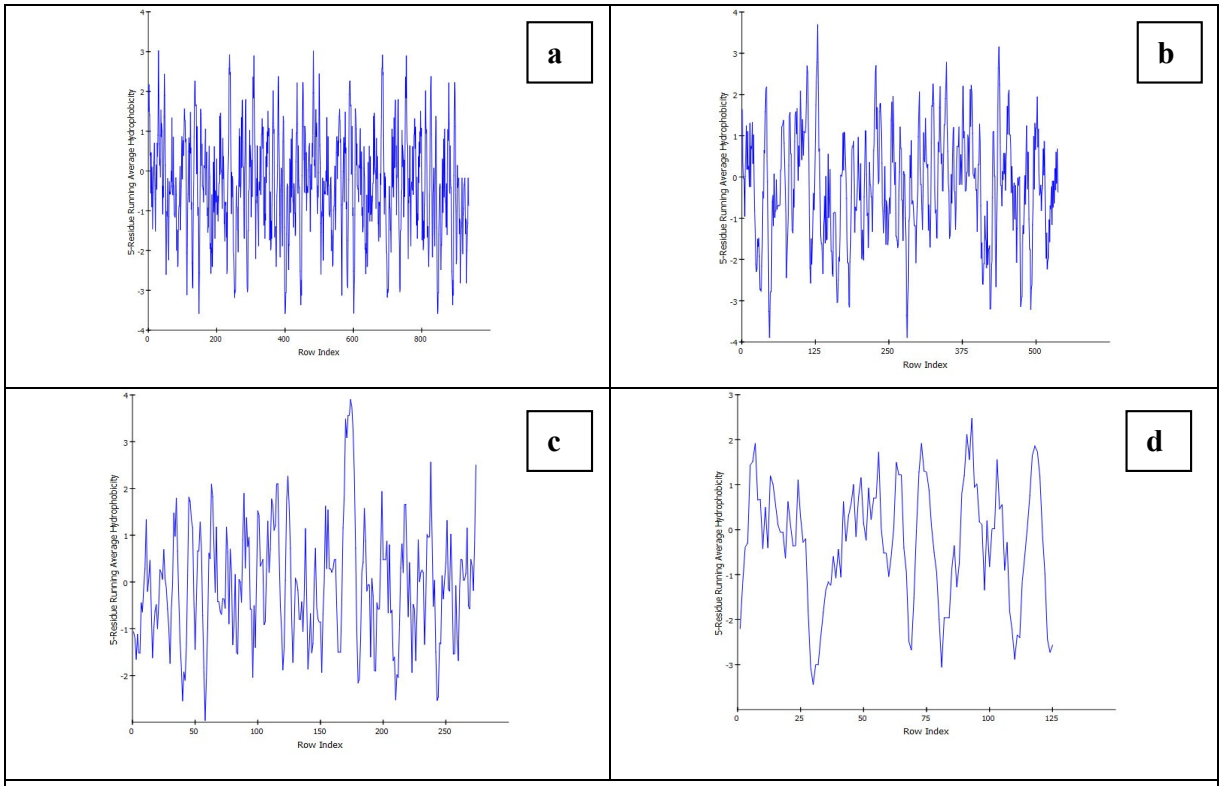
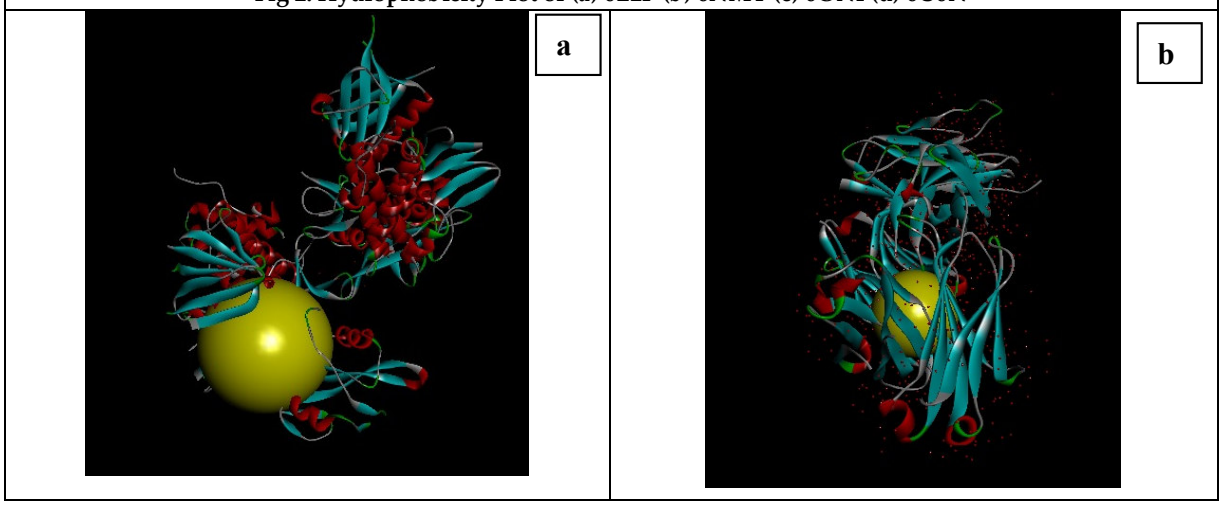


Fig 2: Hydrophobicity Plot of (a) 6E2P (b) 6NMT (c) 6ONI (d) 6U6N



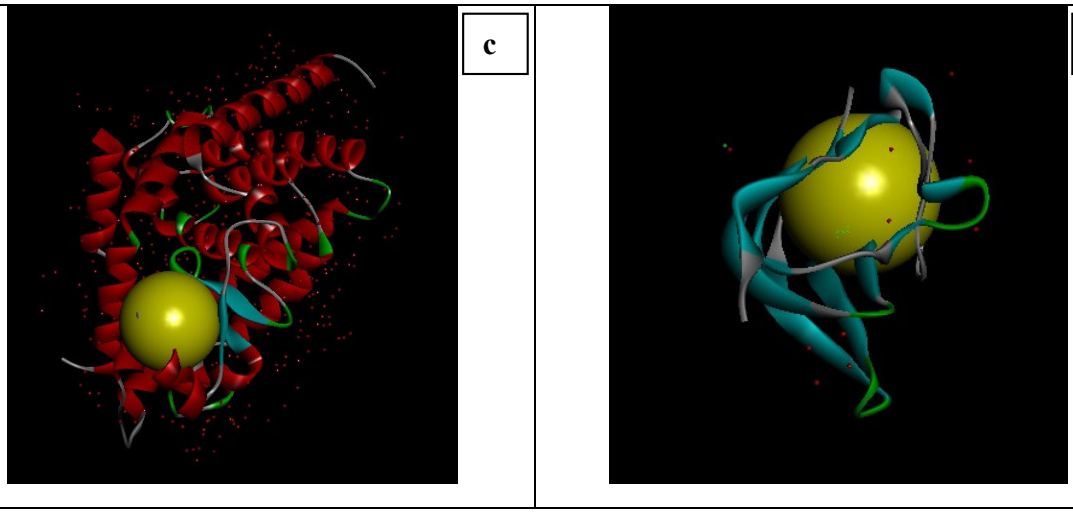


Fig 3: Docking Result of (a) 6E2P (b) 6NMT (c) 6ONI (d) 6U6N

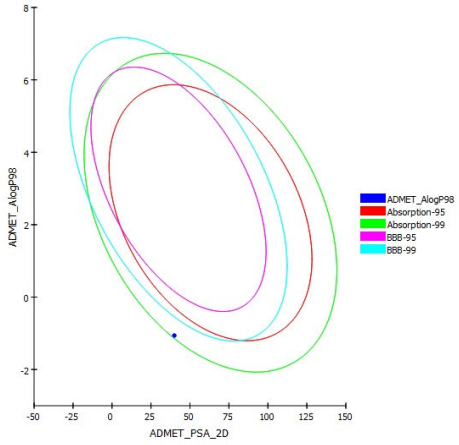


Fig 4: ADMET test analysis report

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RESEARCH ARTICLE

In-silico Analysis of Effects of Black Pepper Extract on Pulm Pox Virus as Biopesticides

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ABSTRACT

Black pepper (*Piper nigrum* L.) is the most important spice traded internationally and is cultivated in many tropical regions of the world like India, Brazil, Vietnam, Indonesia, Malaysia and Sri Lanka. A variety of trees species are used as live stakes for supporting black pepper. However, not all are considered ideal. In ancient India spices were mixed along with different solvent and used as medicine to treat different diseases. This spice plants are having extraordinary chemical which we will find as fragrance, taste . We have used these properties of these spice plants and spices to get some targeted medicine for different diseases. We have taken Black Pepper for the targeted therapy for the Pulm Pox Virus, which is a common disease in the topical region of the country.

Key Words: Black Pepper, Molecular Docking, Pharmacophore, Pulm Pox Virus

INTRODUCTION

Black Pepper is basically produced in southeast and south Asia and has been known to India cooking since at least 2000 BCE. *Piper nigrum L.* (*P. nigrum;* black pepper) belonging to the family Piperaceae is considered the king of spices due to its spicy savor (Abbasi et al., 2010; Ahmad et al., 2012a, 2013). *P. nigrum* is cultivated throughout the world and is native to tropical and subtropical regions of India (Ahmad et al., 2010, 2012a). High pungency in black pepper fruits indicated the presence of piperine. Piperine, the most active component in the fruits of *P. nigrum* L., denotes the quality and value of spiciness (Ahmad et al., 2011a; Bhat et al., 1995; Philip et al., 1992). Peppercorn from *P. nigrum* can be used in food processing, as crude drugs, and can also be used as food additives (Srinivasan, 2007). Regarding medicinal applications, *P. nigrum* has pronounced antibacterial, antifungal, antiviral, antimutagenic, and

antioxidant activities (Abbasi et al., 2010; Ahmad et al., 2010, 2012a; Dorman and Deans, 2000; Saxena et al., 2007). Nerolidol and b-caryophyllene isolated from *P. nigrum* have anesthetic activity (Santra-Mantra et al., 2005). The fruits of this species are also used to treat respiratory tract diseases and infections such as Pulm Pox Virus, cold extremities and sore throat, digestive problems including chronic indigestion, colon toxins, colic, and diarrhea, and fevers including congestion fever and intermittent fever and also control obesity (Ahmad et al., 2011a; Ravindran, 2000). *P. nigrum* also claimed to possess antiapoptotic activity, antidepressant, analgesic, antiinflammatory, antimetastatic, antispasmodic, antispermatogenesis, antithyroid, hepatoprotective, insecticidal, larvicidal, and pesticidal activities (Balkrishna, 1995; Kumar et al., 2007; Li et al., 2007; Mishra and Singh, 2009; Pathak and Khandlewal, 2006; Scott et al., 2008). Plants produced a variety of active metabolites that act as a defense system against various pathogenic agents (Ahmad et al., 2011b, 2012b, 2012c). Black pepper photochemical name is piperine. basically useful for health problems in home. Black pepper properties include for the bioactive and preservative. It uses for spices Worldwide. It is good for improve metabolic rate and inhibits adipose cell growth. It helps for also digestion due to the piperine which stimulate the gastric fluids. The piperine present in black pepper helps body to absorb some of the nutrients found in certain foods. Piperine treatment has also been evidenced to lower lipid peroxidation in vivo and beneficially influence cellular thiol status, antioxidant molecules and antioxidant enzymes in a number of experimental situations of oxidative stress. The chemicals of piperine is C17H19NO3 .

MATERIALS AND METHODS

Various pharmacophores of Black Pepper leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Asthama has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

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Table 1: The list of pharmacophores and the targeted genes

Sl.No	Black Pepper Pharmacophores	Targeted Plant Disease Causing Microbial (Pulm pox virus) Gene	PDB No of the Genes
1	Beta-pinene	polyprotein	6QZU
2	Limonene	PiPO	6KZW
3	P- cymene	PIPO	5UVR
4	Piperazine		

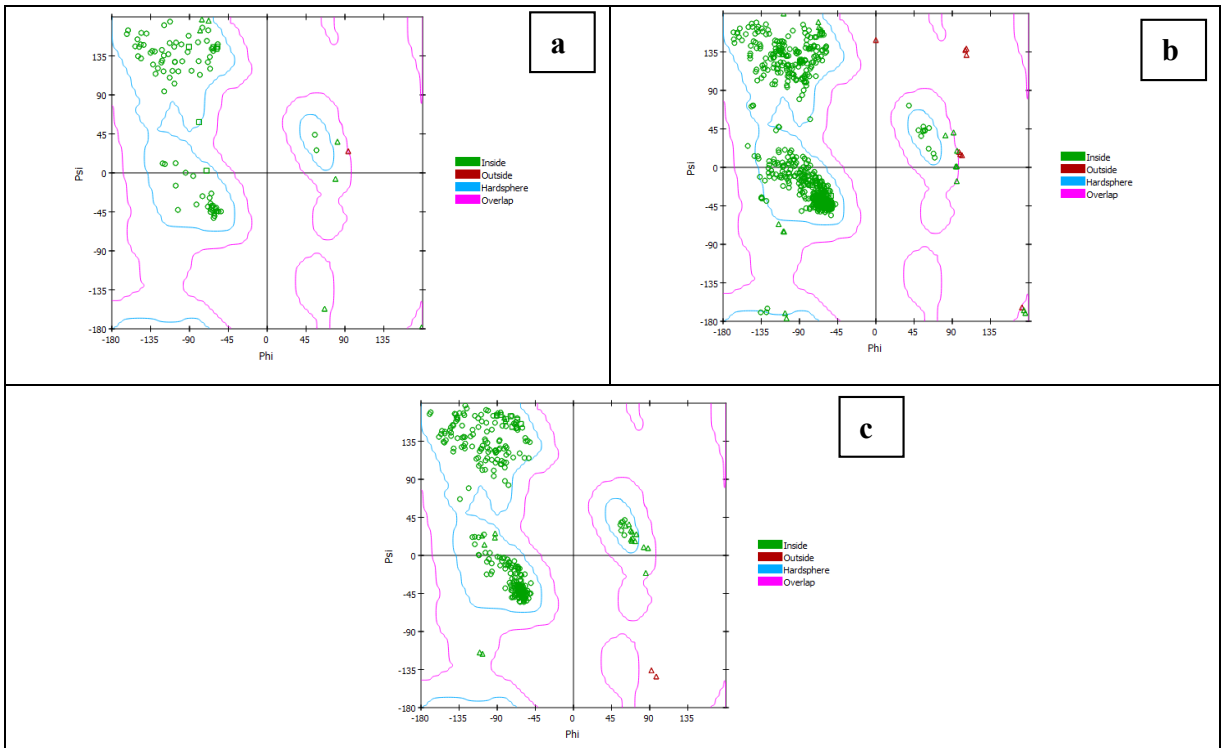
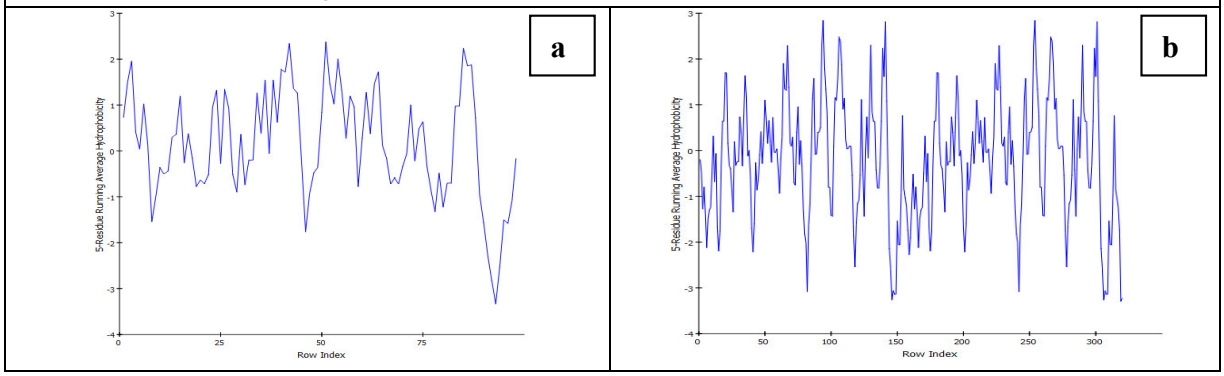


Fig 1: Ramachandran Plot of (a) 5UVR, (b) 6KZW, (c) 6KZU



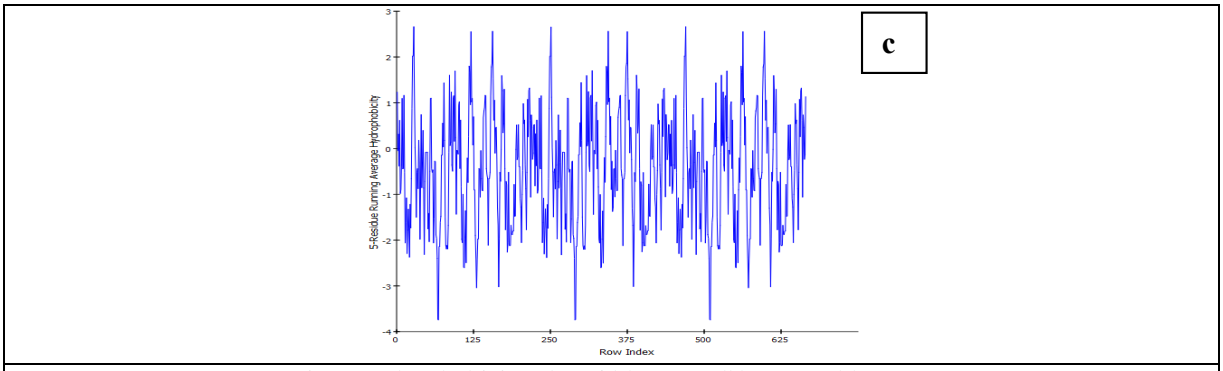
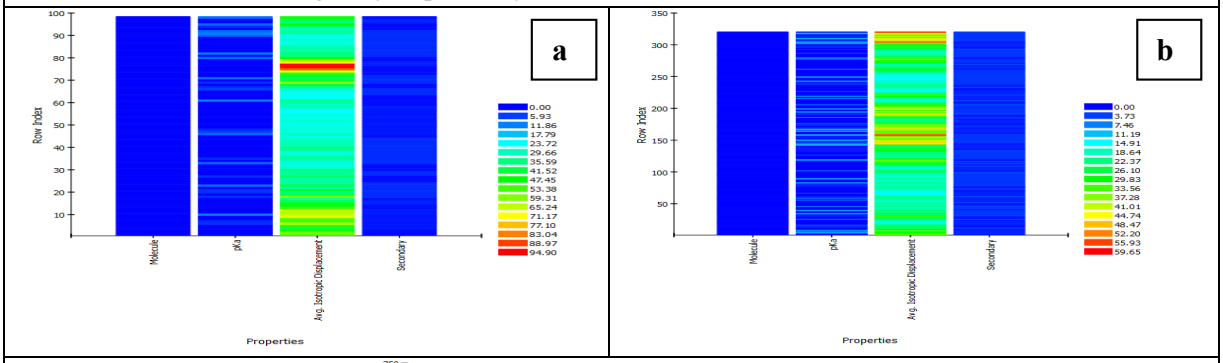


Fig 2: Hydrophobicity Plot of (a) 5UVR, (b) 6KZW, (c) 6KZU



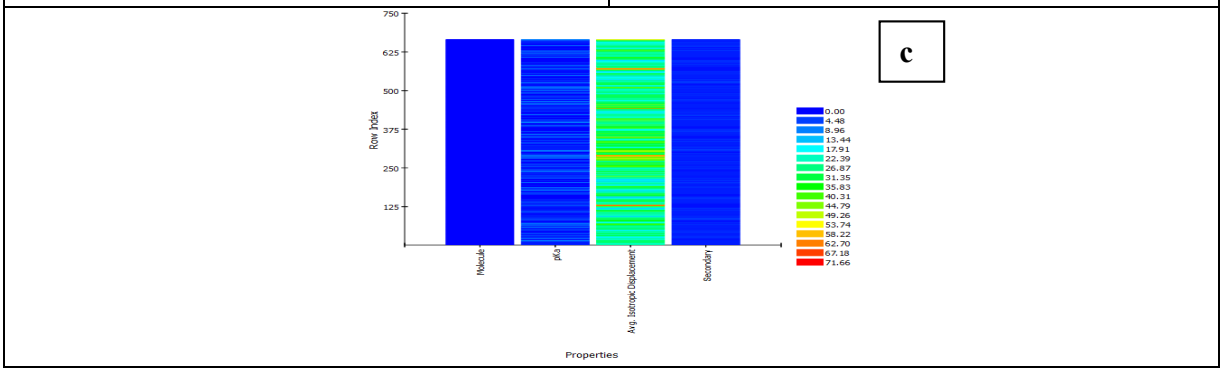
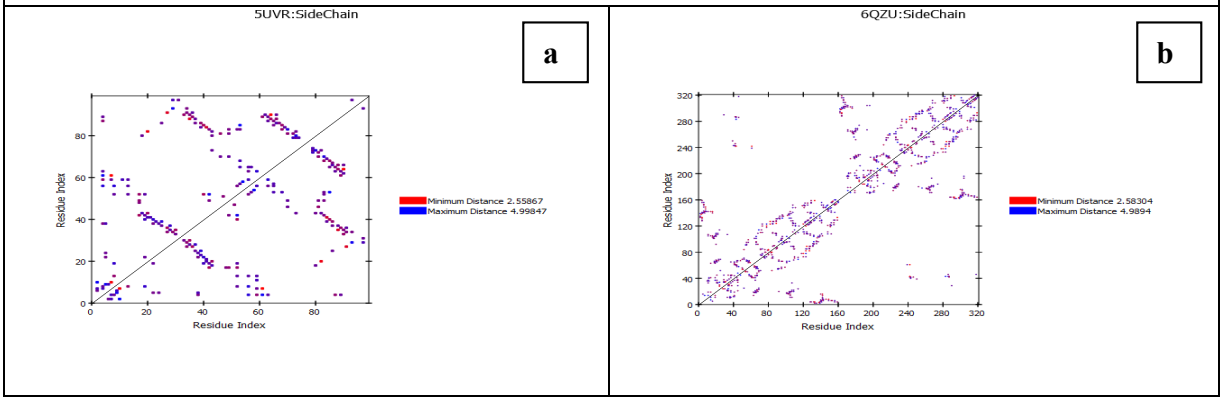


Fig 3: Heatmap of (a) 5UVR, (b) 6KZW, (c) 6KZU



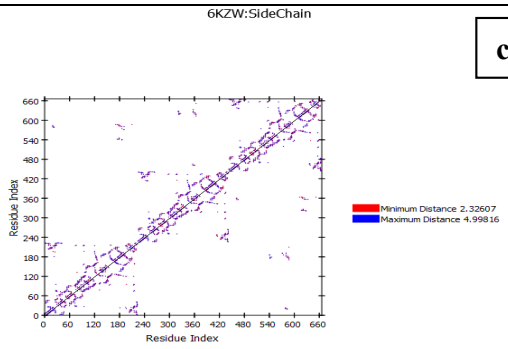


Fig 4: Side chain Analysis Plot of (a) 5UVR, (b) 6KZW, (c) 6KZU

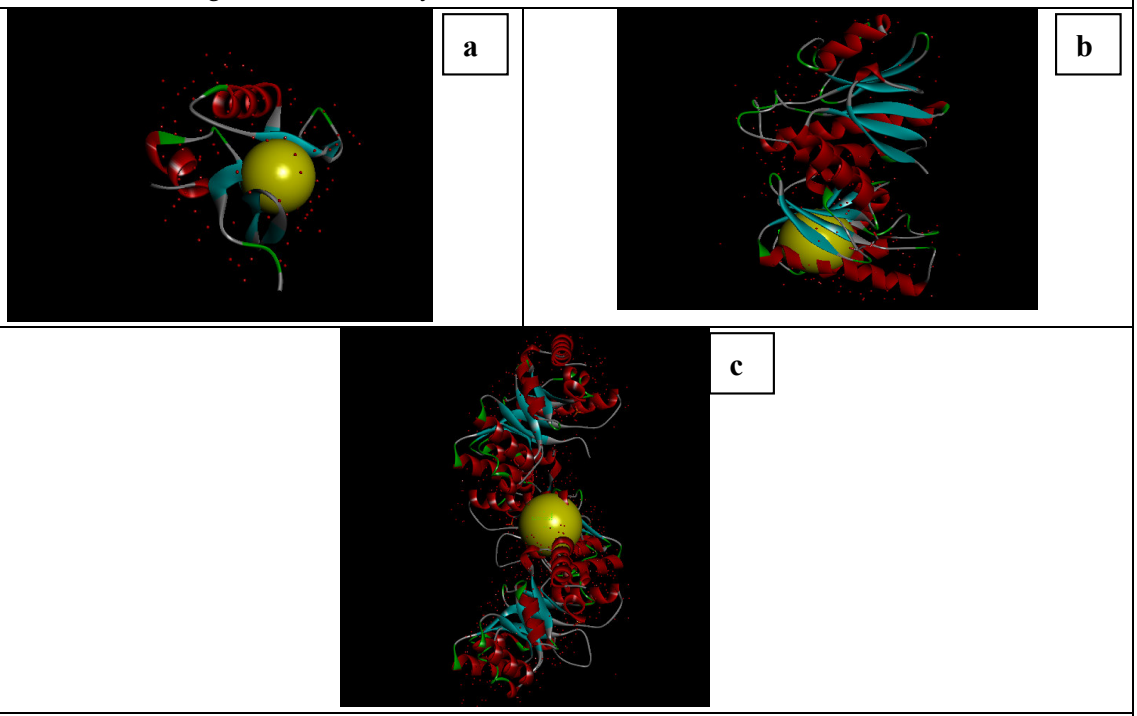


Fig 5: Docking Aaalysis of (a) 5UVR, (b) 6KZW, (c) 6KZU

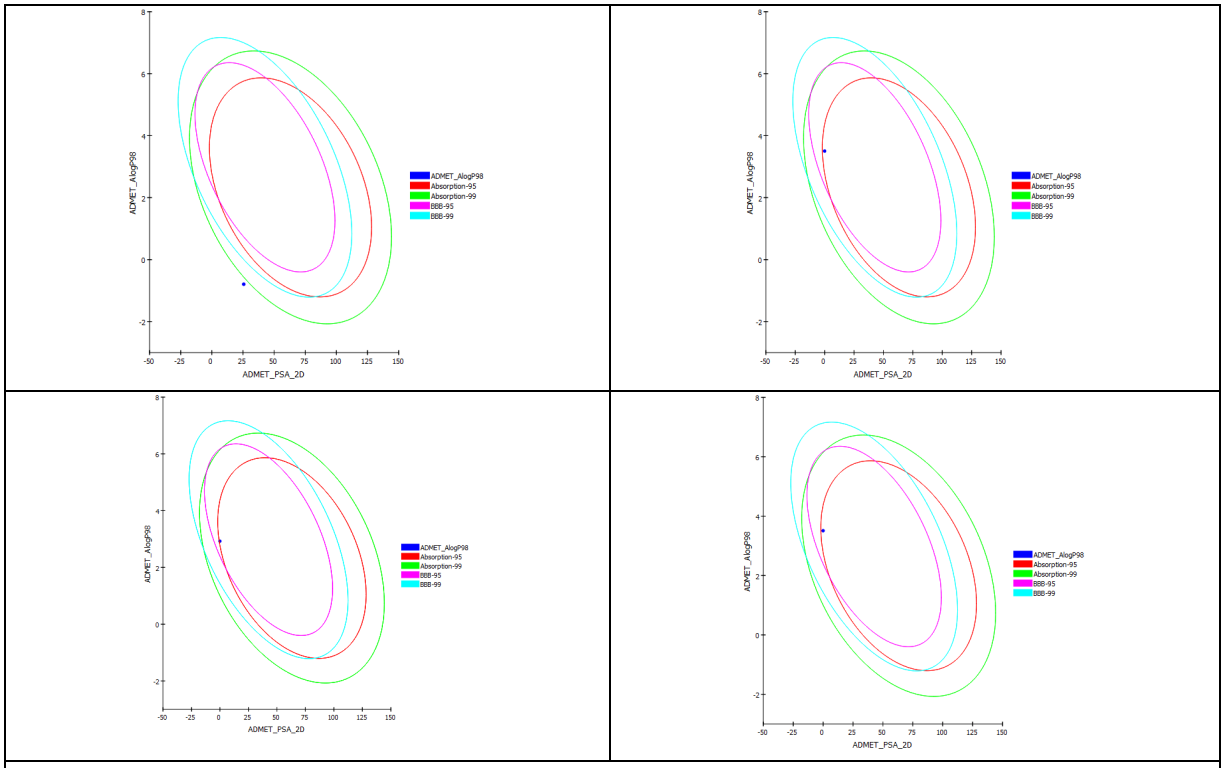


Fig 6: ADMET analysis Report of the Pharmacophores of the Pepper

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RESEARCH ARTICLE

In-silico Analysis of Effects of Methi Extract on Plant Disease

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ABSTRACT

Antiquated India is one of the pioneers of investigations of plants as medication, for example Ayurveda. In our social and monetary life we barely deal with our food we are taking. One such novel herb is Methi which has frequently been viewed as a mind supporter. The entire plant including the blossoms can be utilized for restorative purposes. It has a harsh and sweet taste and is known to give a cooling vitality. Methi is loaded with cancer prevention agents that are basic for carrying on with a sound life. We are utilizing this property of Methi to get some new medications for Wilt disease. The employments of different pesticides, additives, and so on transform the nourishments into poison. Also the reactions of these pesticides and additives, and so on are perilous as on the grounds that it prompts commencement of various malignant growth. In this entire world, the quantity of patients kicking the bucket from malignant growth is expanding in a compromising manner. In-silico investigation has done utilizing programming and we further focused on a portion of the qualities answerable for Wilt disease and pharmacophores from Methi and destroyed some silico examination. In this we have discovered that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Methi, Docking, *In silico* Analysis, Wilt, Pharmacophore

INTRODUCTION

Plants made due for many years on planet earth by constantly developing and adjusting. Prescriptions acquired from Mother Nature, particularly got from plants, have been all around archived for quite a long while . Indeed, even

today, as indicated by World Health Organization, about 80% of total populace from the creating and immature nations despite everything rely upon plant-inferred prescriptions for their human services prerequisites. Fenugreek (*Trigonella foenum-graecum Linn*.), is a shortliving yearly plant, has a place with the *Fabaceae* family. It is developed in numerous pieces of Asia, Africa, and Europe as food, condiment, zest, and as local medication. The variety *Trigonella* is named concerning its triangular formed blossoms, and in Latin little triangle is alluded to as *Trigonella*. The species *foenum-graecum* gets its name from verifiable point of view of Romans, since it is utilized as regular yield grub for creatures in Greece . Fenugreek plant achieves the stature of 1–2 feet and bears green trifoliate leaves. The blossoms are white to yellow in shading and the plant conveys slight cases. The units are around 15 cm long and they contain on a normal 10–20 seeds. Fenugreek seeds are brilliant yellow in shading and their normal stature, width, and thickness are 4.01–4.19, 2.35–2.60, and 2.40–2.66 mm, separately. Fenugreek seeds are the most significant and all around concentrated piece of fenugreek plant. The dried fenugreek seeds are grounded to acquire fenugreek seed powder which is utilized as fixing. Fenugreek gum is acquired from the endosperm of the seeds.

Fenugreek is utilized as a zest and herb in numerous culinary dishes and its green leaves used to enhance dishes or eaten as greens and seeds are utilized for seasonings or squashed to get ready curry powders and glues' utilized for seasonings or squashed to plan curry powders and glue. Notwithstanding being utilized in different food arrangements, fenugreek likewise has recuperating benefits. Fenugreek is one of the most seasoned restorative plant and the therapeutic properties are very much reported in the old clinical writing. In Ayurveda, the customary Indian clinical framework, fenugreek was utilized as a stomach related guide and old Egyptians utilized it as lactation help . In customary Chinese medication, fenugreek was utilized to treat edema in the legs. There are number of employments of fenugreek, including the treatment of lung blockage and sinus, heartburn, sparseness in men, hair tonic and conditioner and as galactogogue. As of now, an enormous number of studies have revealed positive insight into fenugreek's therapeutic properties, for example, antioxidant , anti-inflammatory, antidiabetic, antiobesity, anticancer , hepatoprotective , anti-hyperlipidemic ladies' wellbeing and sexual health modulating activities. All These disease avoidance properties of fenugreek are because of essence of various exhibits of phytochemicals and their distinctive diverse pharmacological and organic exercises. In light of all these assortment of restorative properties, Fenugreek is picked as a therapeutic plant for this work with the goal that it might be useful to fix some disease.

Wilt is a disease that influence the vascular arrangement of plants. Assaults by organisms can cause quick murdering of plants, huge tree limbs or even whole trees. Shrink ailments in woody plants will in general fall into two significant classes, those that start with the branches and those that start with the roots. Those that start with the branches regularly start with pathogens that feed on the leaves or bark, those that start with the roots start with injuring or direct passage by the pathogen into the roots, some are spread starting with one plant then onto the next by method of root grafts.The normal indication of this disease coming about because of water misfortune in leaves and stems. Influenced parts lose their bloat and hang. Explicit shrink sicknesses brought about by an assortment of growths, microbes, and infections are effortlessly mistaken for root and crown spoils, stem blisters, bug wounds, dry spell or overabundance water, soil compaction, and different noninfectious issues.

MATERIALS AND METHODS

Various pharmacophores of Methi leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Aster Yellow has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for Wilt disease Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 4 phytocompound from Fenugreek were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from Fenugreek was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Fenugreek with the selected targets of Wilt. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Fenugreek to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new

drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the

compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the Fenugreek and can be commercialized as the natural drug for the Wilt Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Wilt disease

Sl.No	Pharmacophores from Methi	Targeted Plant Disease Causing Microbial (Wilt, *Solanum Lycopersicum*) Gene	PDB No of the Genes
1	Trigonelline	Verticillium Wilt Disease Resistance Protein	1QTO
2	Methyl Coumarin	Protein Spotted Wilt Resistance-5	5Y6J
3	Carpaine	Xylem Sap Protein 10 Kda	6FC3
4	Choline	Transcription Factor Related To Abi3/Vp1 2	5URN

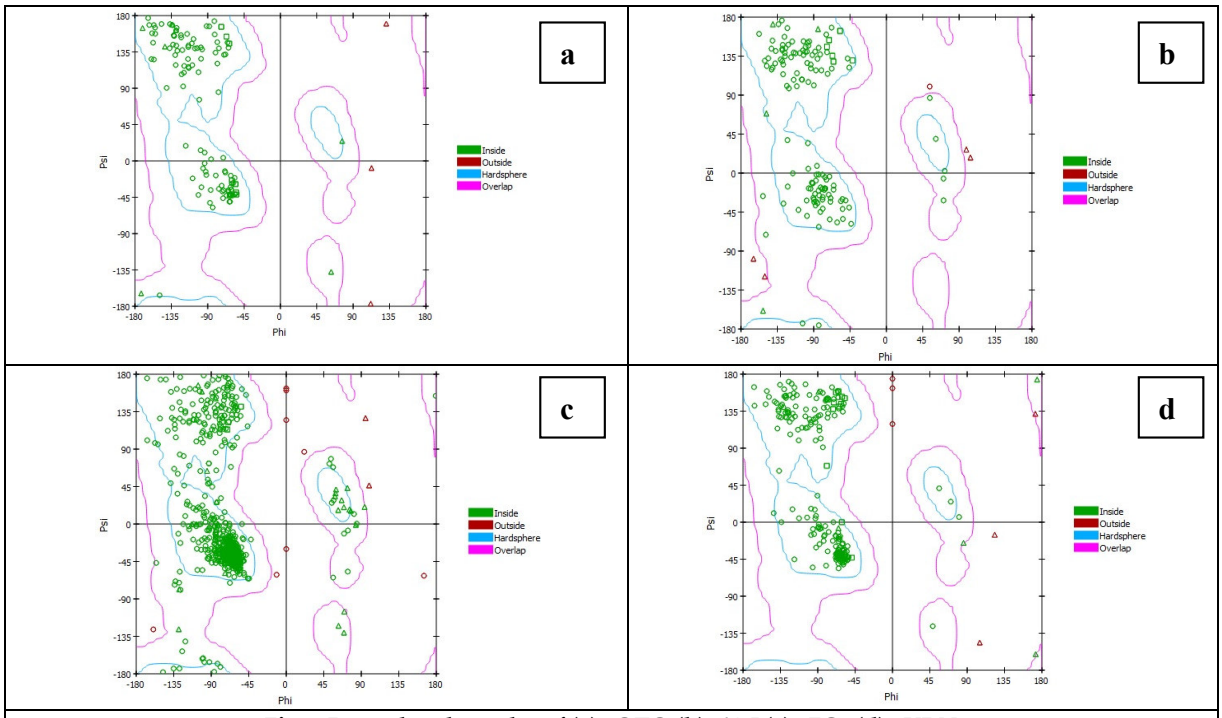
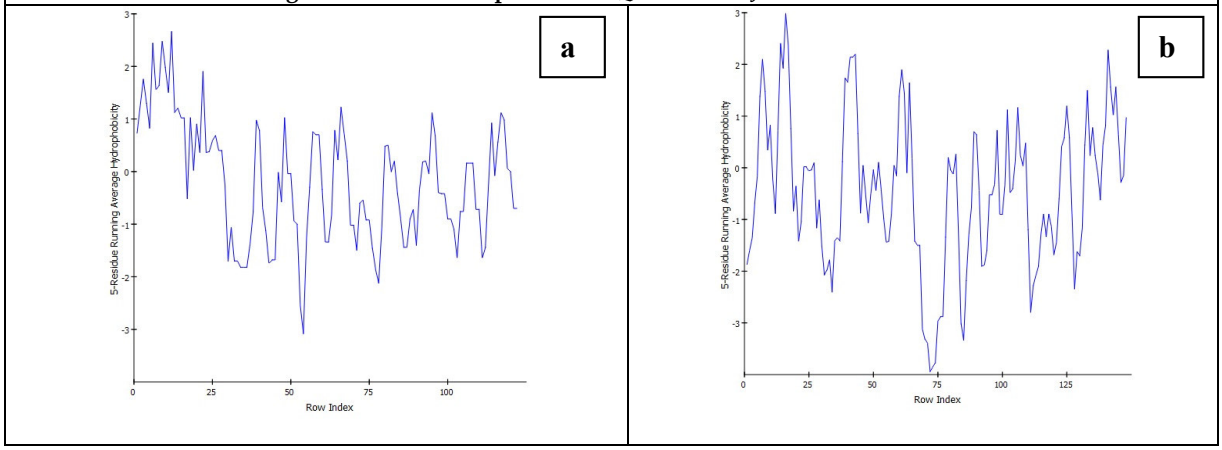


Fig 1: Ramachandran plot of (a) 1QTO (b) 5Y6J (c) 6FC3 (d) 5URN



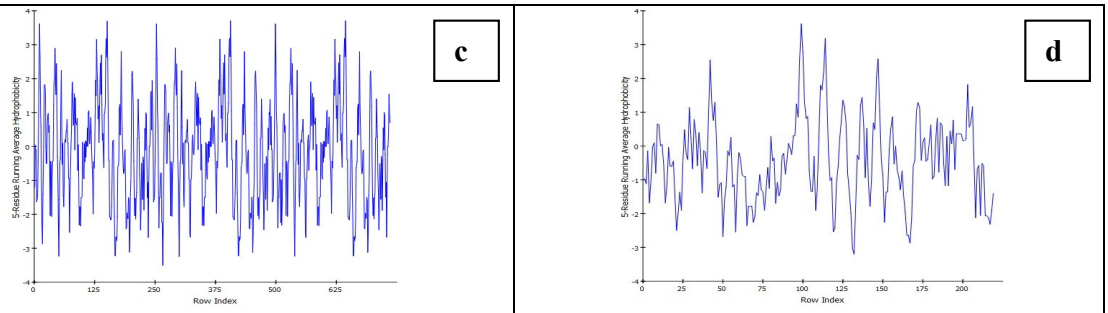


Fig 2: Hydrophobicity Plot of (a) 1QTO (b) 5Y6J (c) 6FC3 (d) 5URN

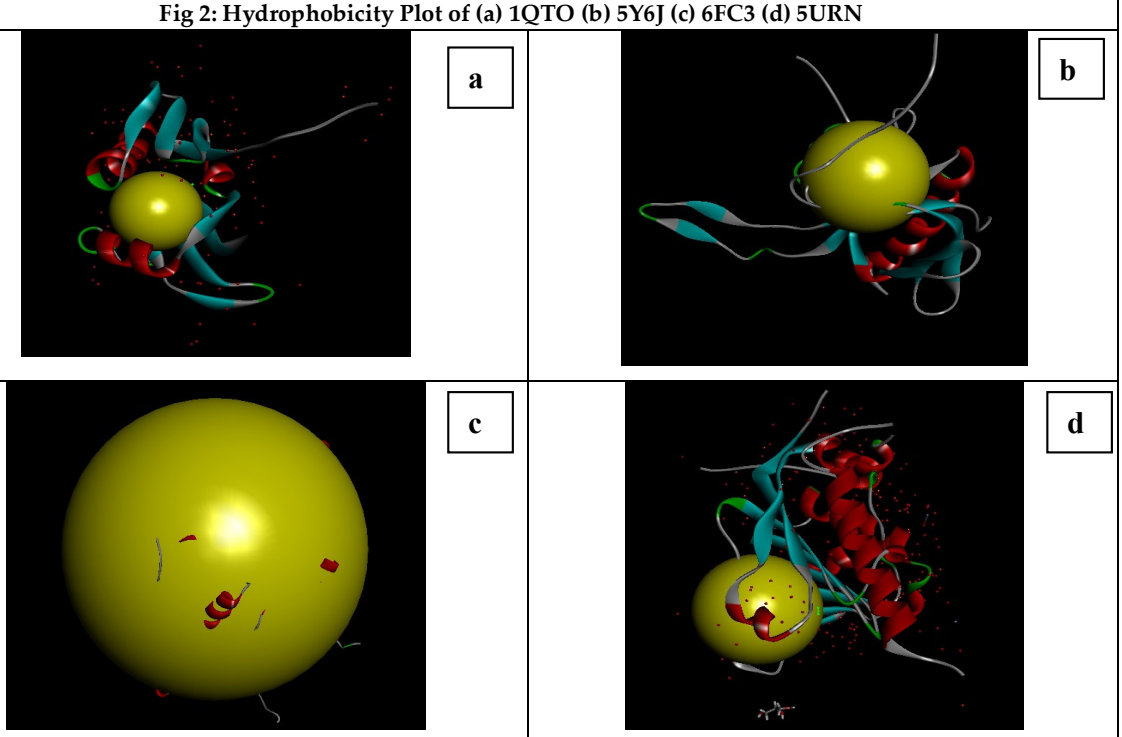


Fig 3: Docking Result of (a) 1QTO (b) 5Y6J (c) 6FC3 (d) 5URN

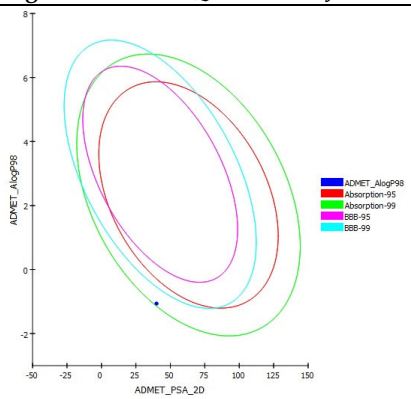


Fig 4: ADMET test analysis report

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RESEARCH ARTICLE

In-silico Analysis of *Gymnema sylvestre* in Diabetes

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ABSTRACT

Diabetes is a metabolic disorder characterized by higher than normal glucose in blood. Most of the oral hypoglycemic drugs available in the market produce adverse side effects which lead to continuous search in the alternative therapeutic drugs with little side effects. Herbal drugs are considered relatively safer alternatives and Gymnema Sylvestre is one of the most well known natural remedy for diabetes and it is traded under several brands world wide.

Keywords: glucose, blood, drugs, remedy, diseases

INTRODUCTION

The naturopathic treatment for diseases has been explored extensively since ancient times and gaining momentum in the present scenario. Indian flora accounts for about 45,000 plant species out of which several thousands have pharmacological significance Diabetes mellitus is a major endocrine disorder affecting nearly 10% of the population worldwide and a key issue of concern. The disease in its severe state affects major systems of the body, leading to multiorgan complications. Oral hypoglycemic agents like sulphonylureas and biguanides are the conventional drugs used for the treatment, but the adverse side effect associated with these drugs is a major limitation. The herbal medicines are becoming popular due to better results and safe use as compared to marketed drugs and more effective treatment of health problems. Plants possessing antidiabetic activities are of significant interest for ethnobotanical community as they are recognized to contain valuable medicinal properties in different parts and a number of them have shown varying degree of hypoglycemic and antihyperglycemic activity. The bioactive constituents found in many plant species are isolated for direct use as drugs, lead compounds, or pharmacological agents. These traditional approaches might offer a natural key to unlock diabetic complications. The chemical

structures of a phytomolecule play a critical role in its antidiabetic activity. Several plant species being a major source of terpenoids, flavonoids, phenolics, coumarins, and other bioactive constituents have shown reduction in blood glucose levels .Various antidiabetic plant extracts like aloe (*Aloe vera L*), bitter Melon (*Momordica charantia*), fenugreek (*Trigonella foenum-graecum*), Asian ginseng (*Panax ginseng C.A.Meyer*) and American ginseng (*Panax quinquefolius L*), gymnema (*Gymnema sylvestre*), milk thistle (*Silybum marianum*), nopal (*Opuntia streptacantha*), salacia (*Salacia oblonga; Salacia Reticulate*), and formulations like those of chromium have been used and clinically tested for their activity as well as potential side effect .

The present review is a research update on *Gymnema sylvestre*, a rare herb with significant medicinal attributes with an overview of its ethnobotanical uses, phytochemistry dealing with an in-depth study of its phytochemicals, and their bioactivities. It also explores the facts and prospects of its development into a modern and efficient therapeutic, contemporary with the present trends of pharmacology and drug development. Furthermore, it holds significant prospects in major health problems like cardiovascular disorders, obesity, osteoporosis, and asthma besides being a popular medication for number of other health ailments. The herb finds significant application in various food preparations for control of obesity and blood cholesterol levels besides regulation of sugar homeostasis. The herbal preparations of *G. sylvestre* are presently used in tea bags, health tablets and supplements, beverages, and confectioneries.

Analysis of Gymnemagenin from Gymnema Sylvestre R.Br. with targets related to diabetes.

In the present study an attempt has been made to use in-silico techniques to understand and predict the drug likeliness of Gymnemagenin, one of the key constituents of G.sylvestre against 15 proteins having key role in carbohydrate metabolism. 'Gymnemagenin was found to dock well with crystallographic structures of 7 of the 15 selected targets and was found even better than the two known clinically used anti-diabetic compounds , repaglinide &sitaglipin taken in study for comparison. Gymnemagenin therefore can be considered further for development into a potent anti-diabetic drug'.

Phytochemical profiling

The leaves of *G. sylvestre* contain triterpene saponins belonging to oleanane and dammarane classes. The major constituents like gymnemic acids and gymnemasaponins are members of oleanane type of saponins while gymnemasides are dammarane ssaponin. Other phytoconstituents include anthraquinones, flavones, hentriacontane, pentatriacontane, phytin, resins, tartaric acid, formic acid, butyric acid, lupeol, β-amyrin related glycosides, stigmasterol, and calcium oxalate. The presence of alkaloids had been detected in plant extracts. Leaves of *G. sylvestre* have acidic glycosides and anthraquinones and their derivatives.The major secondary metabolites in *Gymnema* includes a group of nine closely related acidic glycosides, the main are gymnemic acid A–D and found in all parts of the plant. The maximum content of gymnemic acid is found in shoot tips (54.29 mg-g^{-1} DW) and least in seeds (1.31 mg-g^{-1} DW). Antisaccharin property of gymnemic acid A_1 was greatly reduced on conversion into A_2, while no activity was observed in case of A_3 suggesting that the ester group in the genin portion of gymnemic acid imparts the antisweet property to the triterpene saponins, the gymnemic acids. Gymnemic acids A_2 and A_3 possessed both glucuronic acid and galactose in their molecular structures while glucuronic acid was found to be the only moiety in gymnemic acid A_1 . Further, a series of gymnemic acids (gymnemic acid I, II, III, IV, V, VI, and VII) were isolated and characterized from the hot water extract of dry leaves of *G. sylvestre*. The Gymnemic acids comprise of several members designated as gymnemic acids I–VII, gymnemosides A–F, and gymnemasaponins. The derivatives of gymnemic acids are several acylated tigloyl, methylbutyryl group substituted members, derived from deacylgymnemic acid (DAGA) which is a 3-O-β-glucuronide of gymnemagenin (3β, 16β, 21β, 22α, 23, 28-hexahydroxy-olean-12-ene). Gymnemic acid A comprises of gymnemic acids A_1, A_2, A_3, and A_4 and named gymnemagenin. This constituent is a D-glucuronide of hexahydroxy-triterpene that esterifies with acids . Other five gymnemic acids, namely, VIII, IX, X, XI, and XII, were isolated and characterized later. Gymnemasaponins III, another antisweet compound, isolated from *G. sylvestre* was found to consist of 23 hydroxylongispinogenin as the aglycone moiety glycosylated with either one or two glucose molecules at both the 23 or 28 hydroxyl groups. These

compounds exhibited lesser antisweet effect than those of gymnemic acids. Diabetes mellitus can be defined as a group of syndromes characterized by hyperglycemia, altered metabolism of lipids, carbohydrates and proteins along with an increased risk of complications from vascular disease. It is characterized by polydipsia (chronic excessive thirst and fluid intake), polyphagia excessive eating), glycosuria (excessive glucose in the blood) and "acetone breath" i.e. the breath of the patient smells of acetone due to an abnormal increase of ketone bodies in the blood. The classification of diabetes can be done in two types as: Type-1 (insulin-dependent diabetes mellitus, IDDM) and Type-2 (non-insulin-dependent diabetes mellitus, NIDDM).

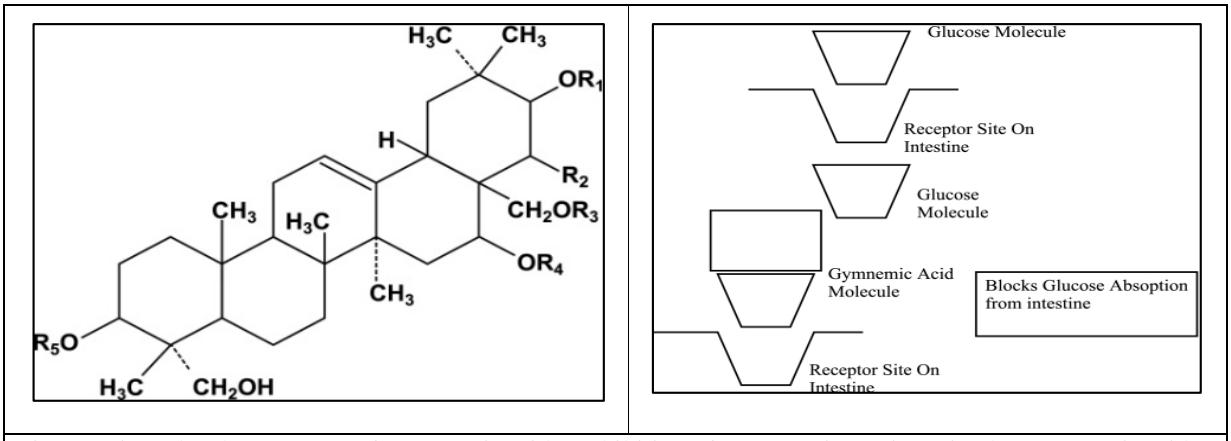

Fig.1. Basic molecular structure of Gymnemic acid& Inhibition of receptor site on intestine by Gymnemic acid.

Docking:

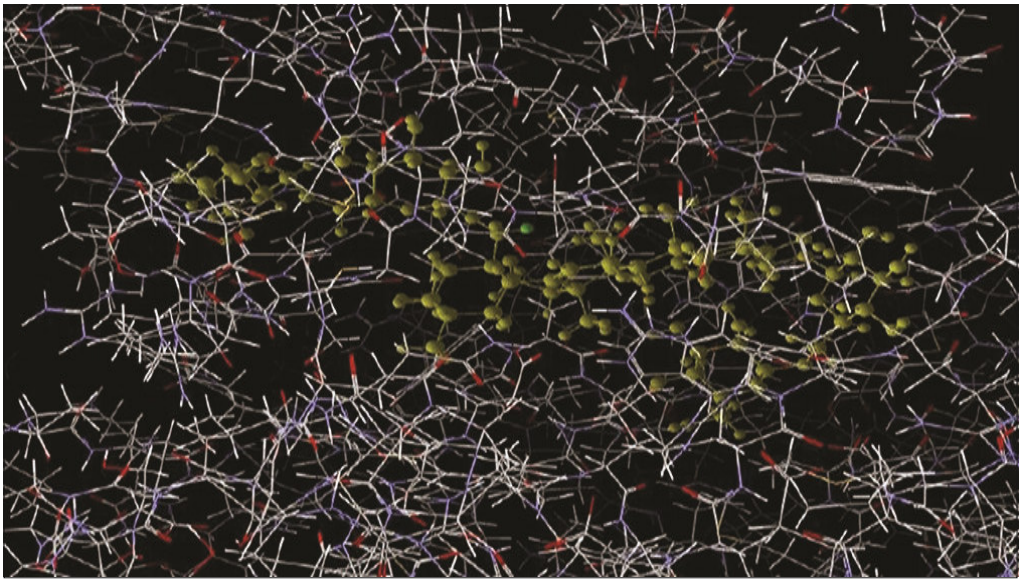

Fig.2. Target and energy values after docking with Gymnemagenin with endothelial nitric oxic synthase.

CONCLUSION

Although there are many phytoconstituents that could combat diabetes and obesity, a single phytoconstituent that could be used in the treatment of both the diseases simultaneously would be a welcome addition. Gymnemic acid fulfills this criterion. The common masses do not avail of the fact that obesity can also be caused due to over-accumulation of sugar molecules specially sucrose, along with fat molecules. The common man layman needs to be made aware of these facts, since they are posing a big threat after cardiac problems and cancer. This review paper aimed at putting forth a molecular perspective of the medicinal aspect of gymnemic acids, and also a possible linkage between obesity and diabetes via a potential common medicine.

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RESEARCH ARTICLE

In silico Analysis of Hepatoprotective Properties of Bael Leaves

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is Bael which has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. Bael is full of antioxidants that are essential for living a healthy life. We are using this property of Bael to get some new drugs for Tobacco mosaic virus. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Tobacco mosaic virus and pharmacophores from Bael and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others.

Key Words : Admet Analysis, Bael, Docking, Hepatities.

INTRODUCTION

Plants have been used for medicinal purposes long before prehistoric period. Indian vedas and European cultures were using medicinal herbs for over 4000 years as medicine. The uses of medicinal herbs has increased during the past three decades and the screening of plant extracts have been done frequently for discovering new drugs(Rajamanickam et al., 2007). *Aegle marmelos* (Bael) is a deciduous shrub or small to medium-sized tree belonging to the family of Rutaceae. It is found in India, Pakistan, Bangladesh and Myaanmar. The medicinal properties of this plant has been described in Ayurveda. The roots, leaves, bark, seeds and fruits consists medicinal values. The bael leaves are used to treat diarrhea , weakness of heart, blood sugar, backache,ulcers(Dutta et al., 2014).

Various compounds such as Skimmianine, Aegelin, Lupeol, Cineol, Citral, Citronellal, Cuminaldehyde, Eugenol, Marmesenin have been refined from leaves of bael which shows anticancer, antiulcer, hepatoprotective, antibacterial, cardioactive , anti-inflammatory, antiseptic, antimalarial, antiallergic, antihyperglycemic, and antioxidant properties (Maity et al., 2009). Hepatitis A (HAV),also called hep A, is an epidemic liver infection caused by hepatitis A virus. It is apicornavirus and can commonly spread through consumption after fecal contamination of mucous membranes , skin, food and water(Jennifer A. Cuthbert 2001). Some commonly observed symptoms of HAV are Jaundice (yellow eyes and skin),belly pain, dark urine, loss of appetite , vomiting, pale-colored poop.

Hepatitis B (HBV) is a viral infection that can cause both acute and chronic diseases of liver such as liver cancer. It is an epidemic liver infection caused by hepatitis B virus. There are approximately 350 million people worldwide remain chronically infected carriers of this disease among whom 500,000 people die due to liver cancer and cirrhosis (Chien-Jen Chen et al., 2009). Hepatitis B virus belongs to *Hepadnaviridae* family and commonly transmitted through contact with blood and other body fluids, as well as from mother to child during birth and delivery (world health organization, www.who.int/news-room/fact-sheets/detail/hepatitis-b). The most common symptoms of this disease are Jaundice(skin or the whites of the eyes turn yellow, and your pee turns brown or orange), loss of appetite, nausea, persistent fatigue for months.

Hepatitis C (HCV) is a liver infection caused by hepatitis C virus. It is generally symptomless but can cause appreciable liver damage. About 170 million people worldwide have the disease and is a major health burden as 60-80% of infected people progress to chronic liver infection (AA Modi and TJ Liang , 2008). Some commonly observed symptoms of HCV are dark urine, fatigue, yellow tint in skin or eyes, nausea, fever and it is transmitted through the infected person's body fluid and blood. The leaf extract of bael contains the chemical compound Eugenol and marmesinin which exhibits pharmalogical effects such as antioxidant, antibacterial, hepatoprotective and antiulcer(Maity et al., 2009). Considering the various medicinal properties of bael leaves, the present study was taken on to evaluate the hepatoprotective properties of bael leaves in liver infection such as HAV, HBV and HCV.

MATERIALS AND METHODS

Various pharmacophores of bael leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of HAV, HBV and HCV have been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for HepatitiesGene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Bael were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from Cumin was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Bael with the selected targets of Hepatities. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Bael to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structures are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 5 is showing the result.

ADMET analysis report

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the Bael and can be commercialized as the natural drug for the Hepatitis Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a

particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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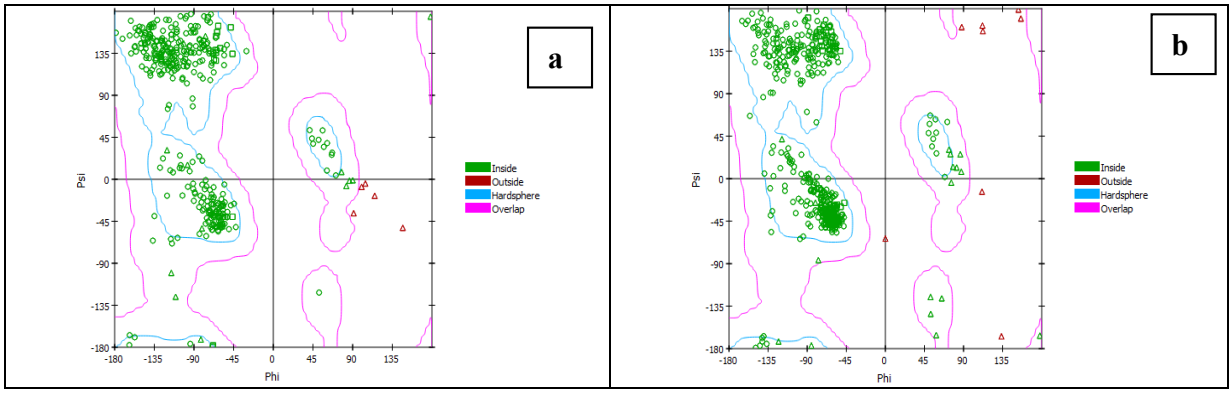
Table 1: The list of pharmacophores and the targeted genes from Hepatities Gene

Sl.No	Pharmacophores from Bael	Targeted Genes from Hepatities Gene	PDB No of the Genes
1	aegeline	Core Protein	5T2P
2	skimmianine(1)	BETA 2-MICROGLOBULIN	1HHH
3	d-limonene	NS3 protease,NS4A protein	3SU4
4	marmelosin	19-mer peptide from Genome polyprotein	3KF2
5	allocryptopine	RNA-dependent RNA polymerase	2XWH



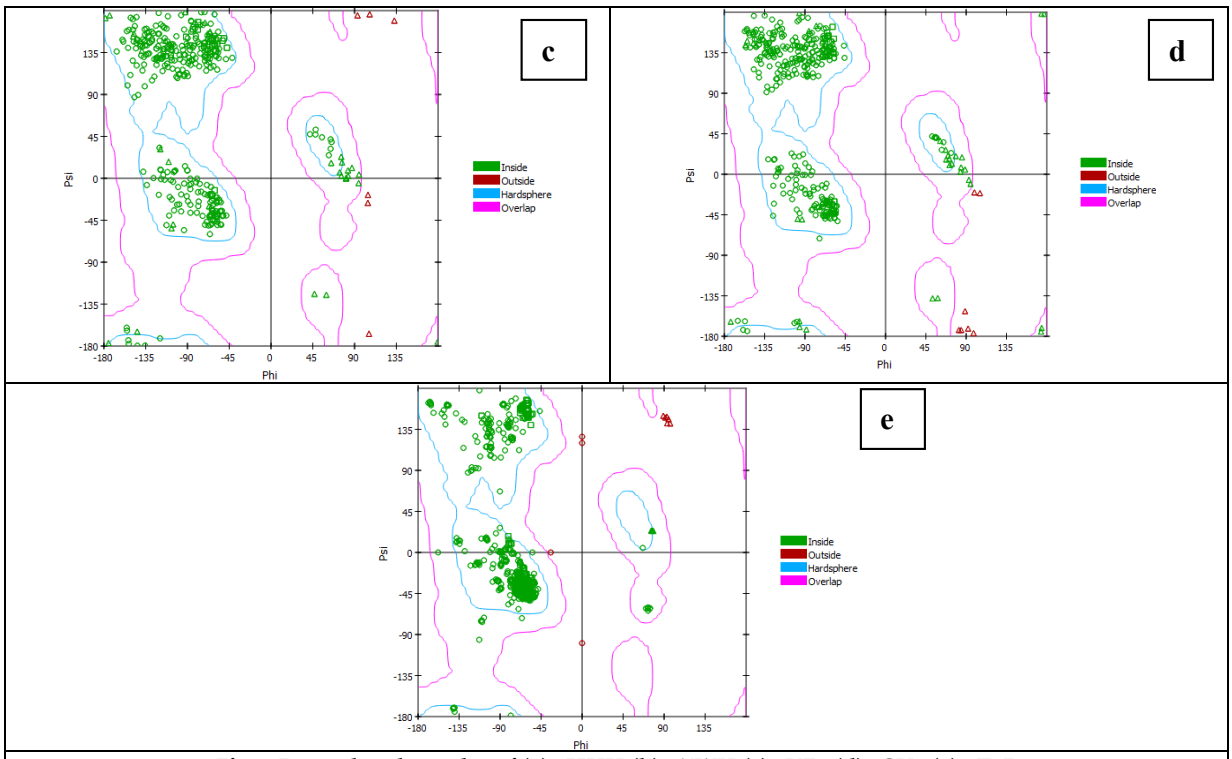
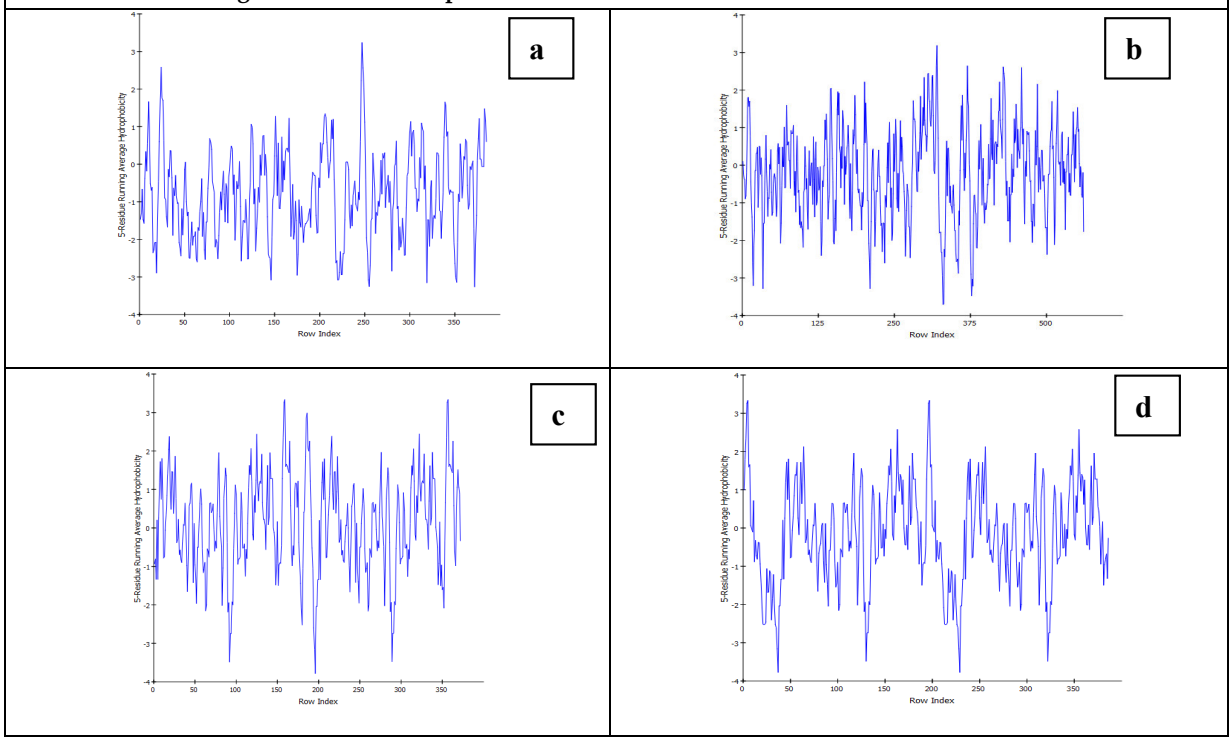


Fig 1: Ramachandran plot of (a) 1HHH (b) 2XWH (c) 3KF2 (d) 3SU4 (e) 5T2P



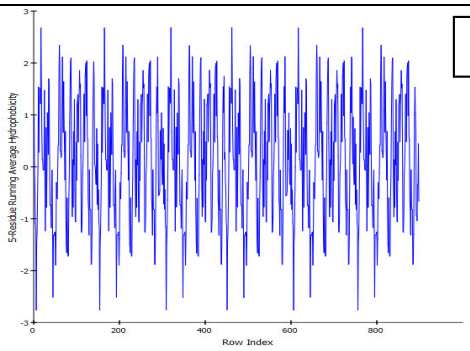


Fig 2: Hydrophobicity Plot of (a) 1HHH (b) 2XWH (c) 3KF2 (d) 3SU4 (e) 5T2P

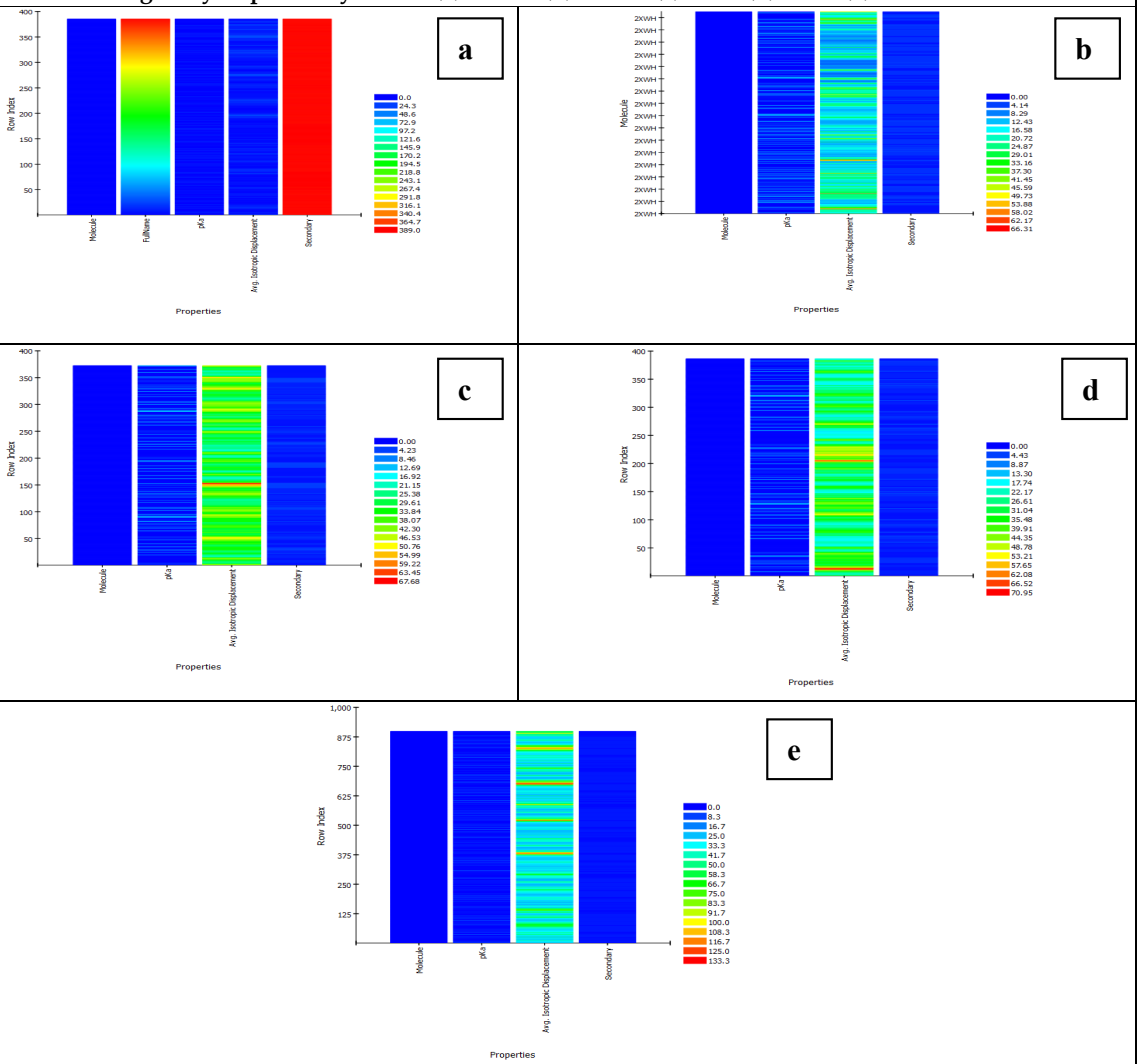


Fig 3: Heat Map Plot of (a) 1HHH (b) 2XWH (c) 3KF2 (d) 3SU4 (e) 5T2P

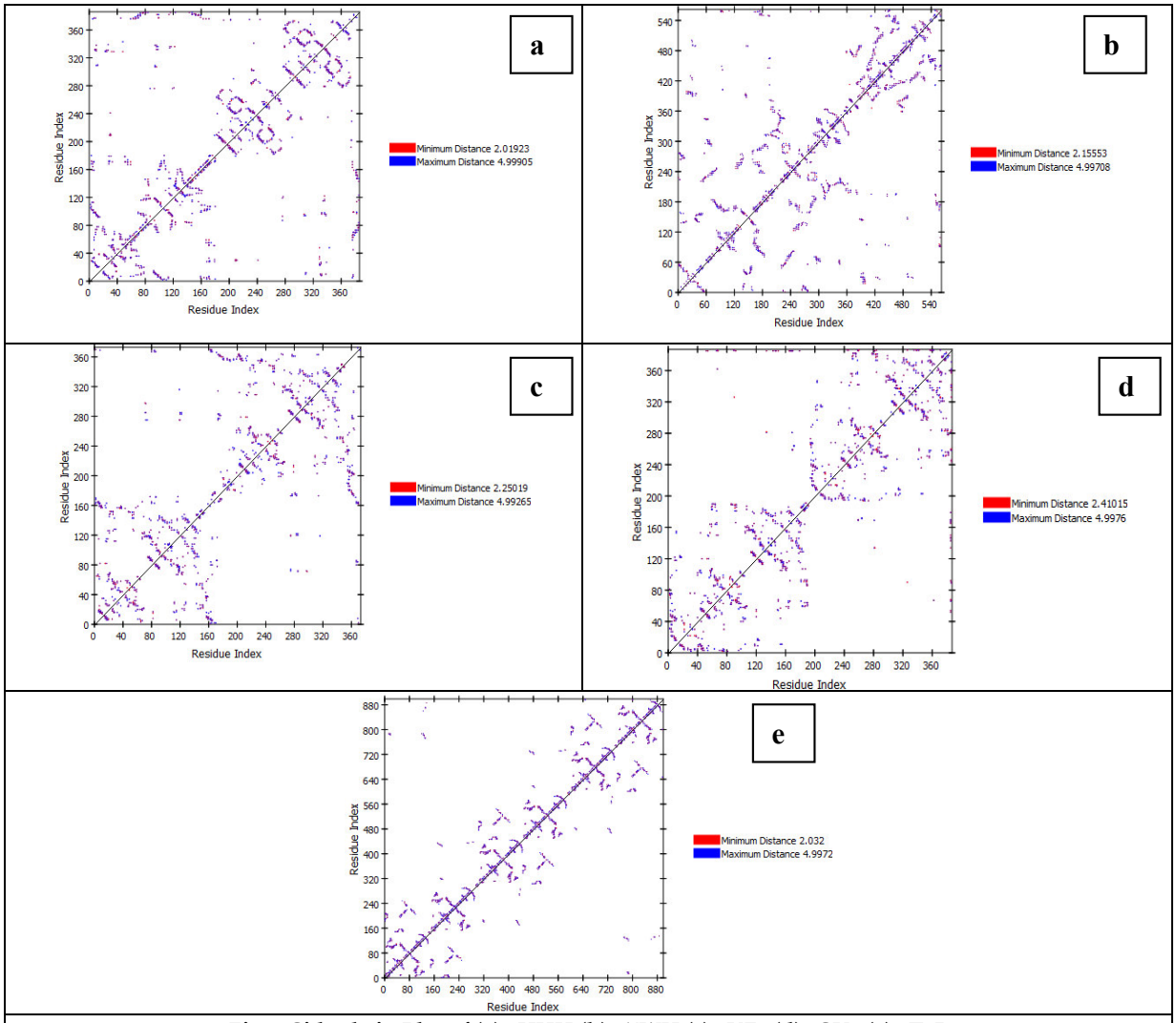
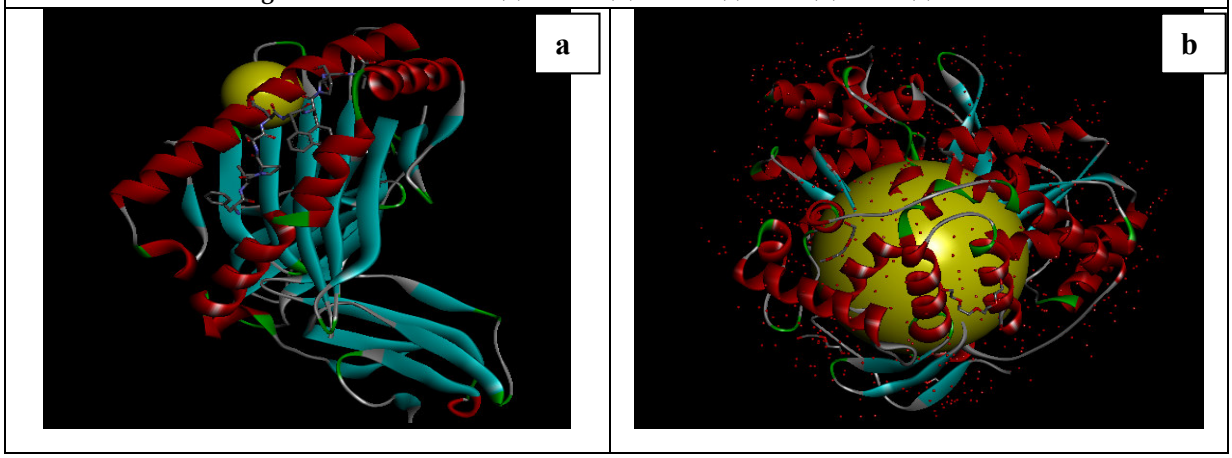
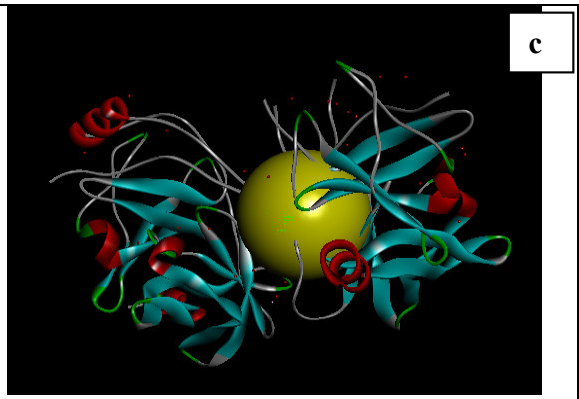
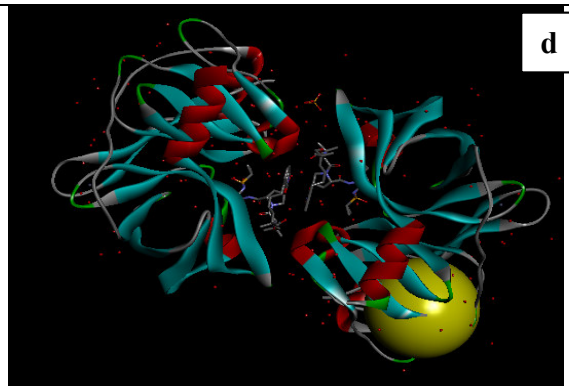


Fig 4: Side chain Plot of (a) 1HHH (b) 2XWH (c) 3KF2 (d) 3SU4 (e) 5T2P







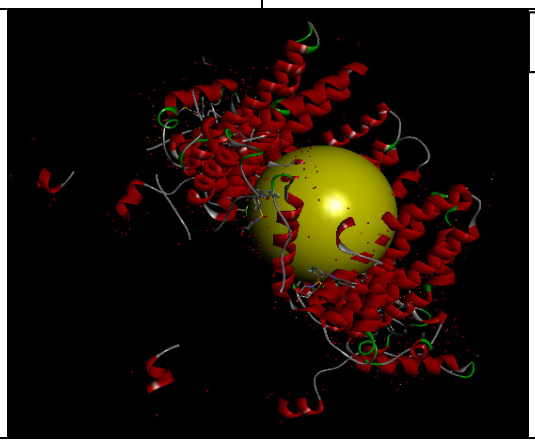
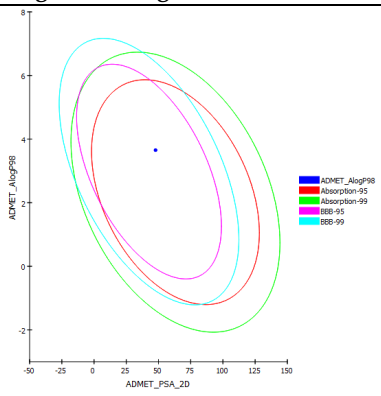
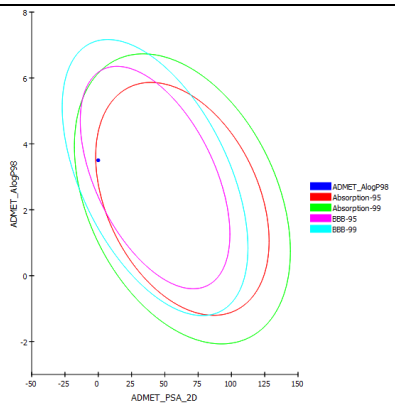
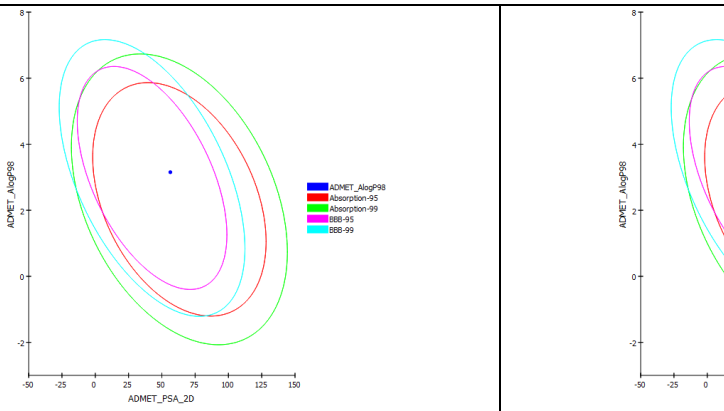
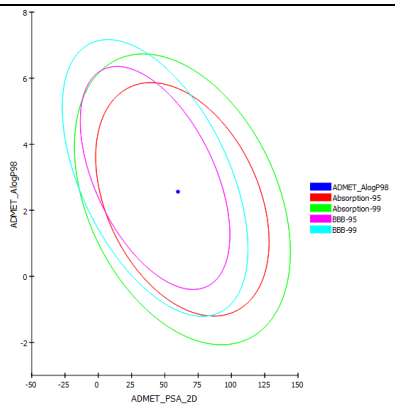


Fig 5: Docking Result of (a) 1HHH (b) 2XWH (c) 3KF2 (d) 3SU4 (e) 5T2P ADMET Evaluation









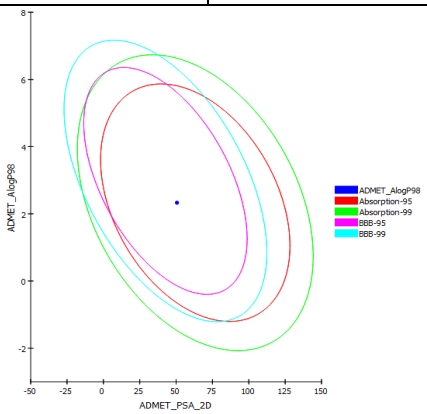


Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

In- silico Analysis of Roselle (*Hibiscus sabdariffa* L.) for Antidiabetic

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ABSTRACT

The research was conducted by in silico docking of protein enzyme Phosphoenolpyruvatee Carboxykinase (PEPCK) with Roselle Calyces (*Hibiscus sabdariffa* L.) chemical compounds. The objective research was to determine the activity of the active compounds from Roselle Calyces (*Hibiscus sabdariffa* L.) as a potential inhibitor for protein enzyme Phosphoenolpyruvatee Carboxykinase (PEPCK) by using in silico docking method. The research was conducted using chemical compounds Roselle Calyces (*Hibiscus sabdariffa* L.) and models of protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) downloaded via Protein Data Bank (PDB) with code 1KHB, then performed docking process using the PLANTS program, and then evaluated of the docking score as docking process results. Docking score as the docking results for Quercetin, Hibiscetin, Gossypetin, Protocatechuic Acid, and Metformin respectively are – 89.2883; – 85.6101; – 83.7724; – 70.9521; and – 64.9661. Result show that 4 of the Roselle Calyces (*Hibiscus sabdariffa* L.) chemical compounds (Quercetin, Hibiscetin, Gossypetin, Protocatechuic Acid) have the lower docking score and better potential as inhibitors of protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) than Metformin.

Key Words : Docking, In Silico, *Hibiscus Sabdariffa*, Antidiabetic, Phosphoenolpyruvate Carboxykinase, PLANTS Program

INTRODUCTION

Diabetes Mellitus is affecting disorder to people of all age groups worldwide. Many synthetic medicines available for type 2 diabetes mellitus in the market. However, there is a strong requirement for the development of better antidiabetes compounds sourced especially from natural sources like medicinal plants [1]. Literature showed that flavonoids are good antidiabetic metabolites; alkaloids, have similarly been implicated in the antidiabetic activities of plant [2]. Roselle Calyces (*Hibiscus sabdariffa* L.) can treat many diseases and conditions (for example, diabetes and aging) are involve lipid peroxidation and the generation of free radicals [3]. Roselle Calyces (*Hibiscus sabdariffa* L.) contains flavonoids, such as: gossypetin, hibiscetin, and sabdaretin. Roselle Calyces (*Hibiscus sabdariffa* L.) also contains alkaloids, such as: protocatechuic acid, quercetin, anthocyanin, β-sitosterol, pectin, and wax [4]. The diet high in fructose and fat can cause insulin resistance, impaired glucose tolerance and hyperinsulinemia. These metabolic changes have been implicated as contributing factors to the development of type 2 diabetes mellitus. Investigation of antidiabetic efficacy of Roselle Calyces (*Hibiscus sabdariffa* L.) extract for type 2 diabetes mellitus examined by given extract of Roselle Calyces (*Hibiscus sabdariffa* L.) on high fructose and fat diet induced rats [5].

Protein Enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) is expressed at high levels in liver, kidney, and adipose tissue. This enzyme catalyzes the rate limiting step in hepatic gluconeogenesis, renal gluconeogenesis, and adipose tissue glyceroneogenesis [6]. Therefore plays a central role in glucose homeostasis [7]. Binding site and coding regions of protein enzyme PhosphoenolpyruvateeCarboxykinase (PEPCK) have been sequenced from cytosolic genomic Deoxy Nucleic Acid (DNA) of subjects with type 2 diabetes mellitus [8]. Protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) contributes to the regulation of the triglyceridecycle in adipose tissue and liver. Investigation of protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) expression and its regulation in the triglyceride/ fatty acid cycle is necessary for our understanding of maintenance of glucose homeostasis, lipid homeostasis, and disease prevention [9]. Metformin inhibits protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) gene expression either through the insulin independent pathway or an interacting with insulin manner [10]. Table 1 shows the chemical structure of Metformin and several Roselle Calyces (*Hibiscus sabdariffa* L.) chemical compounds.

Lead discovery was the main components of today's early pharmaceutical research. The aim of target discovery is the identification and validation of suitable drug targets for therapeutic intervention. Computational methods are being developed to predict the drug likeness of compounds. Thus, drug discovery is already on the road towards electronic Research & Development. In silico approaches contribute significantly to early pharmaceutical research and are especially important in target discovery and lead discovery. The need for timely adaptation and application of in silico approaches in pharmaceutical research has clearly been recognized and is expected to improve further the overall efficiency of drug discovery [11]. Therefore, there is an increased interest to identify potential activity of Roselle Calyces (*Hibiscus sabdariffa* L.) chemical compounds to protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) as the type 2 diabetes mellitus protein enzyme target compared with Metformin as the standard compound by in silico docking.

RESULT AND DISCUSSION

GCP704 which was cocrystallized in the structure of 1KHB protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) was extracted and redocked into its original binding pockets. The Root Mean Square Deviation (RMSD) values resulted from these ligands redocking was 0.7757 Å, which was less than 2.0000 Å, a value typically used in evaluating the success of docking algorithms, indicating the docking methods was valid12. Figure 1 shows the redocking of GCP704 into the binding pocket 1KHB protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK).

In silico docking by PLANTS Program between protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) with Metformin as the standard compound and with Roselle Calyces (*Hibiscus sabdariffa*L.) chemical compounds (Quercetin, Hibiscetin, Gossypetin, Protocatechuic Acid) as the test compound resulting docking score. Table 2 shows docking result between ligand with the receptor protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK).

Metformin as the standard compound which could inhibits protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) resulting higher docking score than Roselle Calyces (Hibiscus sabdariffa L.) chemical compounds (Quercetin, Hibiscetin, Gossypetin, Protocatechuic Acid) as the test compound. The docking score of the test compound with protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) is smaller than docking score of the standard compound. Docking score represents binding affinity of the ligand to the enzyme, smaller docking score value shows stronger interaction13. Quercetin has the smallest docking score and shows the strongest interaction to protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK). Figure 2 shows visualisation of interaction between Quercetin and protein enzimPhosphoenolpyruvate Carboxykinase (PEPCK).

CONCLUSION

Result show that 4 of the Roselle Calyces (*Hibiscus sabdariffa* L.) chemical compounds (Quercetin, Hibiscetin, Gossypetin, Protocatechuic Acid) have the lower docking score and better potential as inhibitors of protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK) than Metformin. Roselle Calyces (*Hibiscus sabdariffa* L.) chemical compounds with the lower docking score of bond means more stable and better for drug design because have the higher affinity.

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Table 1. Chemical structure of Metformin and several Roselle Calyces (*Hibiscus sabdariffa* L.) chemical compounds.

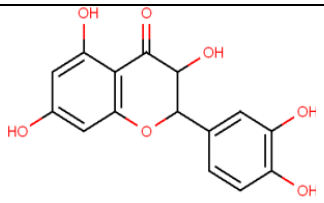
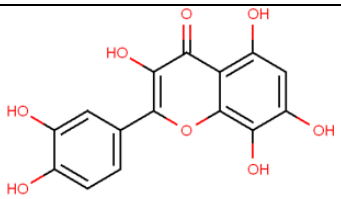
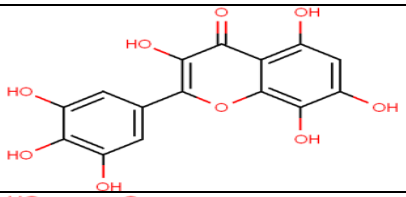
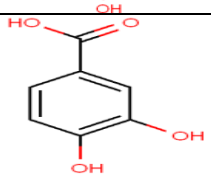
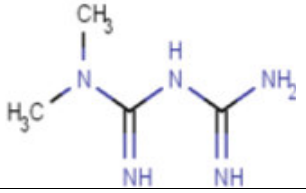
Quercetin	
Hibiscetin	
Gossypetin	
Protocatechuic Acid	
Metformin	

Table 2. Docking result between ligand with the receptor protein enzyme PhosphoenolpyruvatCarboxykinase (PEPCK).

Number	Ligand	Docking Score
1	Quercetin	– 89,2883
2	Hibiscetin	– 85,6101
3	Gossypetin	– 83,7724
4	Protocatechuic Acid	– 70,9521
5	Metformin	– 64,9661

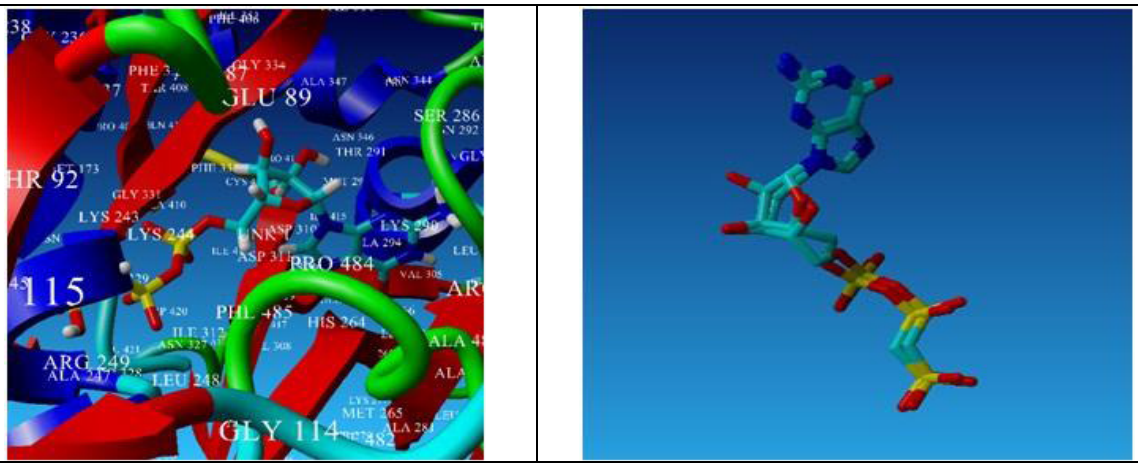


Figure 1. Redocking of GCP704 into the binding pocket 1KHB protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK).

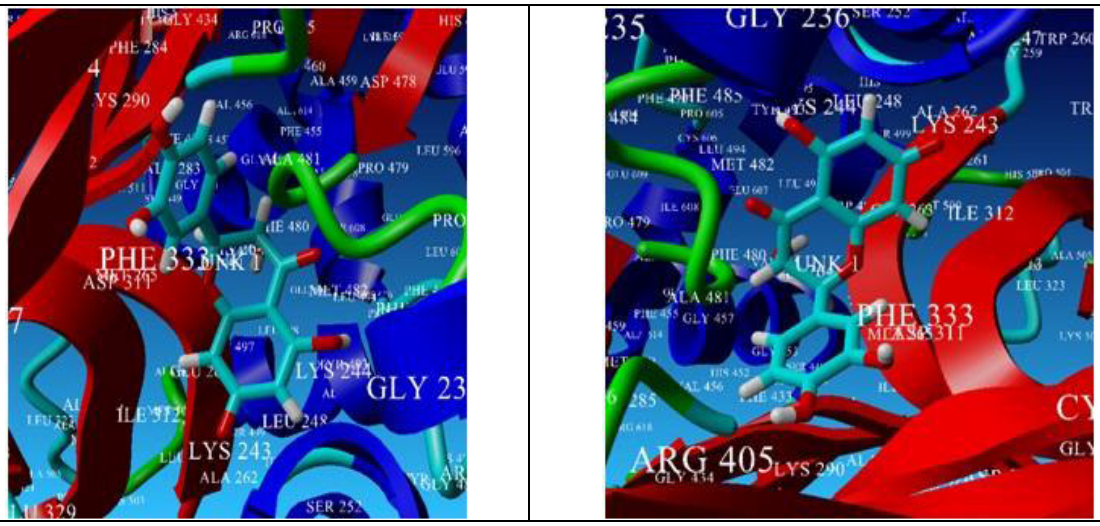


Figure 2. Visualisation of interaction between Quercetin and protein enzyme Phosphoenolpyruvate Carboxykinase (PEPCK).

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RESEARCH ARTICLE

In-silico Analysis of Effects of Ajwain Extract on Tuberculosis

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is Ajwain which has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. Ajwain is full of antioxidants that are essential for living a healthy life. We are using this property of Ajwain to get some new drugs for Tuberculosis. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Tuberculosis and pharmacophores from Ajwain and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Ajwain, Docking, *In silico* Analysis, Tuberculosis, Pharmacophore

INTRODUCTION

Ayurveda is the oldest medicine system originates in the Indian subcontinent about 5000 years ago. In Ayurved herbs play important role. "*Trachyspermum-ammi*" (T.ammi) which is popularly known as "Ajwain" is an annual herb in the family of Umelliferae or Apiaceae. It is also known as bishop's weed or carom. "Ajmoda" is the Sanskrit name of Ajwain this generally cultivated in Iran and India especially in arid and semi-arid region. According to Ayruveda, Ajwain is a powerful cleanser. It is helpful for stimulating the apatite and enhancing digestion. It is recommended to help alleviate gas and discomfort in the stomach. It is easy also helpful for the functioning of the respiratory system

and the kidney. The aromatic plant Ajwain is an annual herbaceous. It height can extend to 30 cm to 70 cm. They are having feathery leaves and red flowers. When the seed are ready to cultivate they are dried and threshed. These seeds are grayish-green in colour with striped and curved. They tastes hot and bitter with leaving the tongue numb for a second. The major oil found in ajwain is Thymol which is strong germicide,anti-spasmodic and fungicide. It contains health benefiting oils like cymene, gamma- terepenine, lupeol, linoeric acid, stearic acid, etc.It is also contain moisture, protein, fat, mineral, fiber, carbohydrates, calcium, etc. The chemical extracted from bishop weeds has antibacterial, antifungal, antitussive,anti-inflammatory,and analgesic effects as well as antioxidant, and antitumor in nature. So, we are trying examining the herb's essential oil and their behavior against hospital-acquired pathogens. Tuberculosis (TB) is one of the most ancient diseases of mankind, with molecular evidence going back to over 17,000 years. In spite of newer modalities for diagnosis and treatment of TB, unfortunately, people are still suffering, and worldwide it is among the top 10 killer infectious diseases, second only to HIV.

According to World Health Organization (WHO), TB is a worldwide pandemic. It is a leading cause of death among HIV-infected people. In India, historically speaking, fight against TB can be broadly classified into three periods: early period, before the discoveries of x-ray and chemotherapy; post-independence period, during which nationwide TB control programs were initiated and implemented; and the current period, during which the ongoing WHO-assisted TB control program is in place. Today, India's DOTS (directly observed treatment-short course) program is the fastest-expanding and the largest program in the world in terms of patients initiated on treatment; and the second largest, in terms of population coverage. Major challenges to control TB in India include poor primary health-care infrastructure in rural areas of many states; unregulated private health care leading to widespread irrational use of first-line and second-line anti-TB drugs; spreading HIV infection; lack of political will; and, above all, corrupt administration. Multidrug-resistant TB (MDR-TB) is another emerging threat to TB eradication and is a result of deficient or deteriorating TB control program.

Although as early as 1689, it was established by Dr. Richard Morton that the pulmonary form was associated with "tubercles," due to the variety of its symptoms, TB was not identified as a single disease until the 1820s and was eventually named "tuberculosis" in 1839 by J. L. Schönlein (News-medical). In 1882, the bacillus causing tuberculosis, *Mycobacterium tuberculosis*, was discovered by Robert Koch; and for this discovery, he was awarded Nobel prize in physiology or medicine in 1905(Kotch,1905) Tuberculosis is caused by a group of closely related bacterial species termed *Mycobacterium tuberculosis* complex. Today the principal cause of human tuberculosis is *Mycobacterium tuberculosis*. Other members of the *M. tuberculosis* complex that can cause tuberculosis include *M. bovis*, *M. microti*and *M. africanum. M. microti* is not known to cause TB in humans; infection with *M. africanum* is very rare, while *M. bovis* has a wider host range and is the main cause of tuberculosis in other animal species. Humans become infected by *M. bovis*, usually via milk, milk products or meat from an infected animal (Prasad et al.,2005, Srivastava et.al., 2008). TB is one of the top three infectious killing diseases in the world: HIV/AIDS kills 3 million people each year, TB kills 2 million and malaria kills 1 million (WHO,2010). Even though tubercle bacilli was identified nearly 130 years ago, a definitive understanding of pathogenesis of this disease is still deficient (Chole et.al, 1998, Brosch et.al., 2002). Although it can affect people of any age, individuals with weakened immune systems, e.g., with HIV infection, are at increased risk. Since the immune system in healthy people walls off the causative bacteria, TB infection in healthy people is often asymptomatic. This bacterium lives and multiplies in the macrophages, thus avoiding the natural defense system in the patient's serum. Infection with TB can result in two stages: asymptomatic latent tuberculosis infection (LTBI) or tuberculosis disease. If left untreated, the mortality rate with this disease is over 50%.

MATERIALS AND METHODS

Various pharmacophores of bael leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Tuberculosis has been taken from

BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

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The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

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A collection of 5 phytocompounds from Cumin were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

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The anti-inflammatory activity of all the 4 phytochemicals reported from Cumin was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Cumin with the selected targets of TB. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Cumin to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 5 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the Cumin and can be commercialized as the natural drug for the Rice Tungro Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from TB

Sl.No	Pharmacophores from Ajwain	Targeted Genes from TB	PDB No of the Genes
1	Thymol	Signaling Protein	2E8O
2	Lupeol	Immune System	4DN3
3	linoleic acid	Membrane Protein	1O77
4	Gamma terpinene	Sugar Binding Protein	2XR5

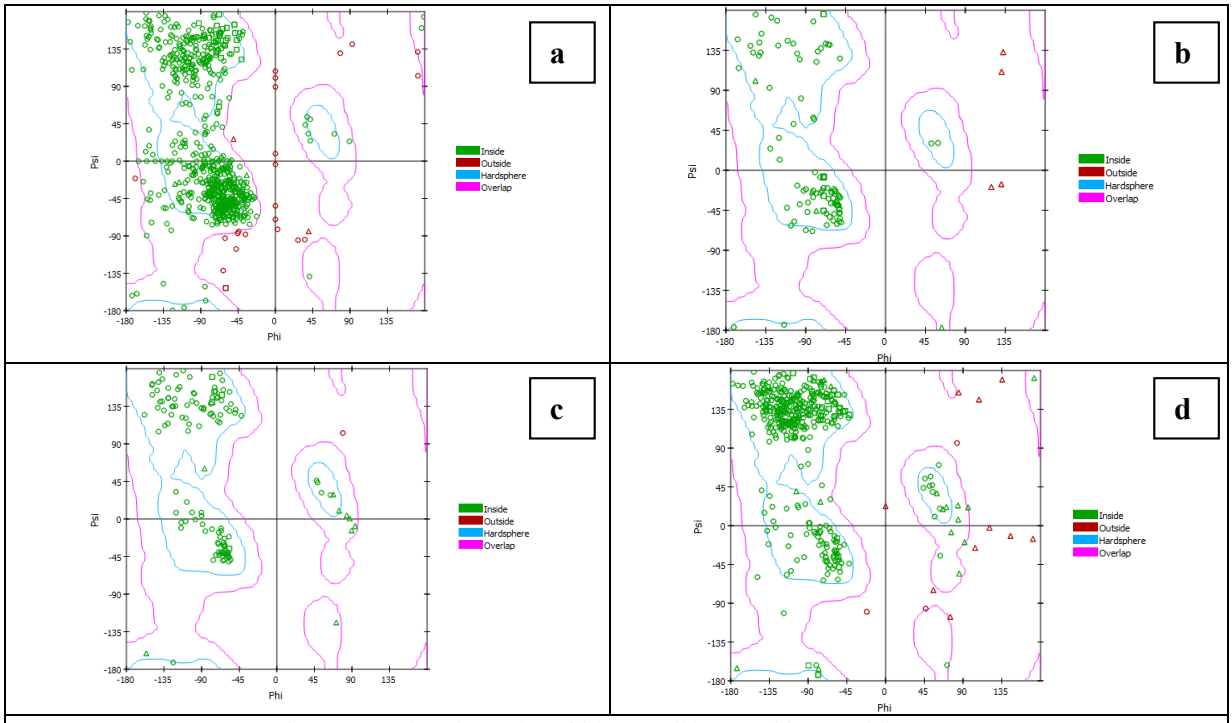


Fig 1: Ramachandran plot of (a) 1O77 (b) 2E8O (c) 2XR5 (d) 4DN3

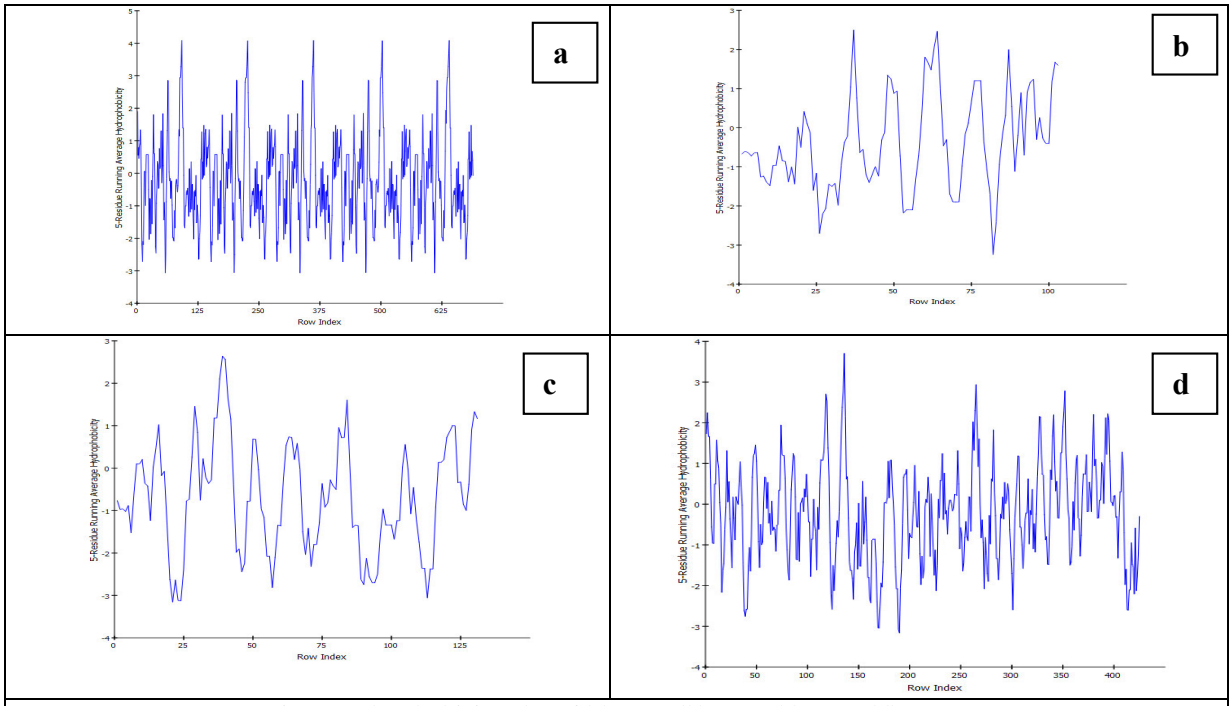


Fig 2: Hydrophobicity Plot of (a) 1O77 (b) 2E8O (c) 2XR5 (d) 4DN3

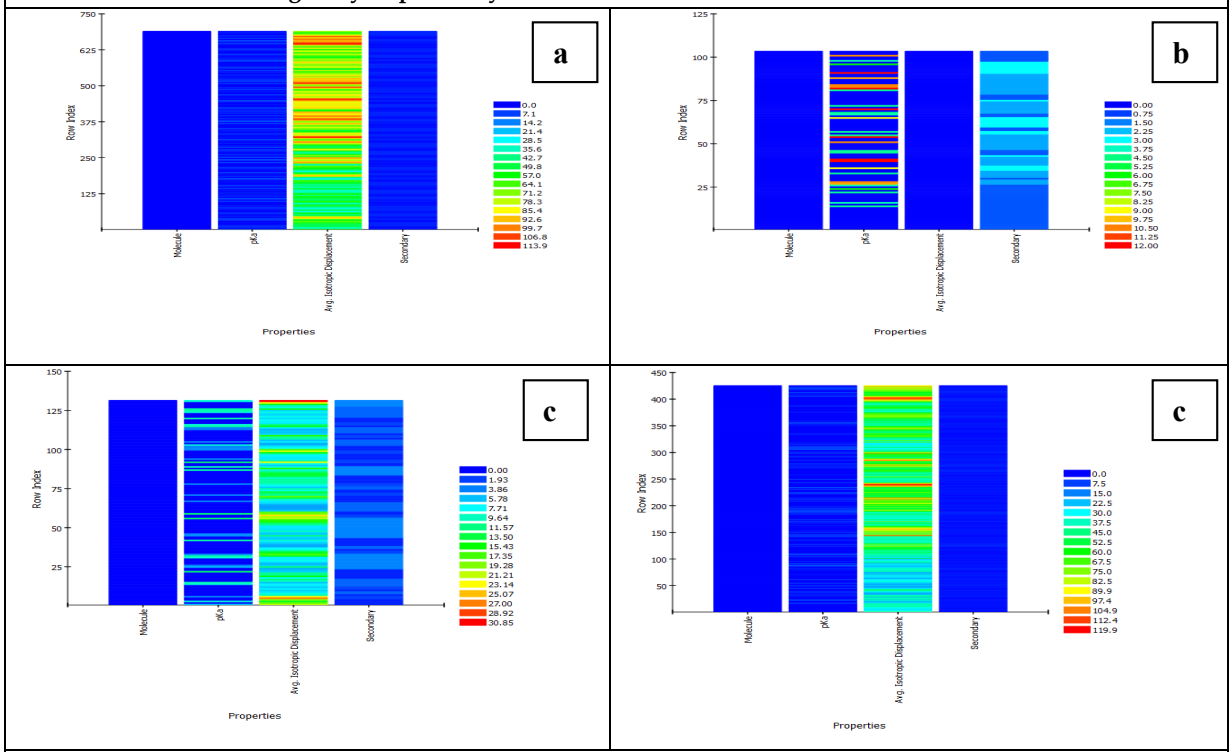


Fig 3: Heat Map Plot of (a) 1O77 (b) 2E8O (c) 2XR5 (d) 4DN3

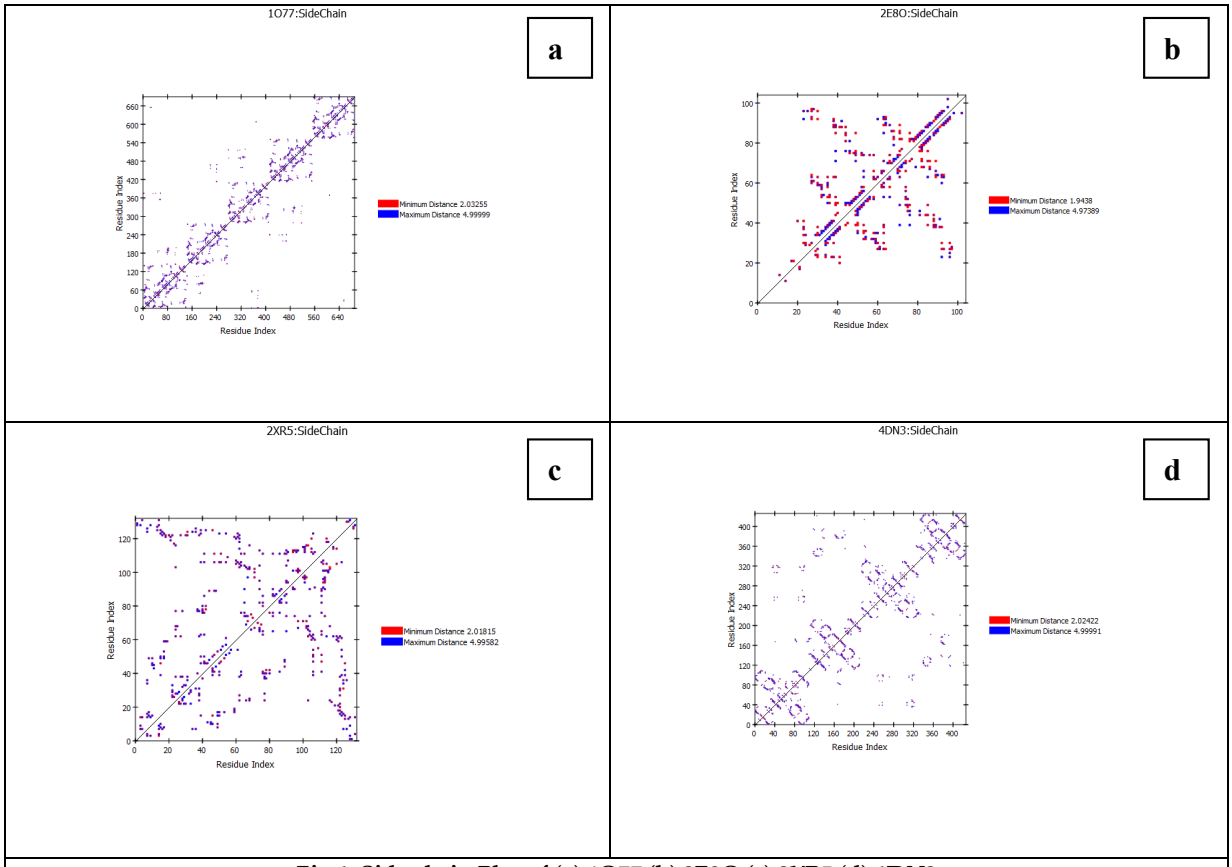
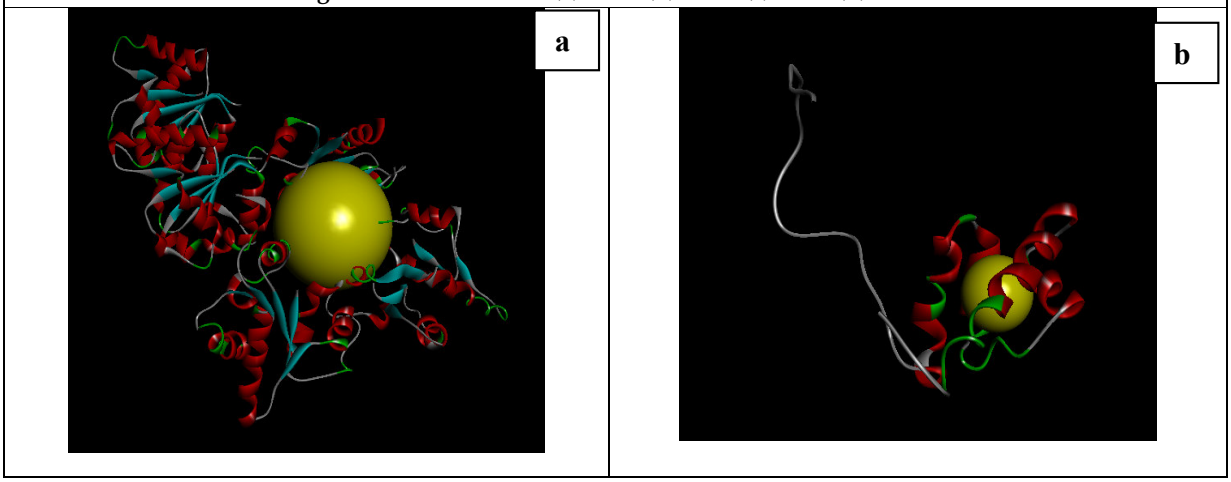
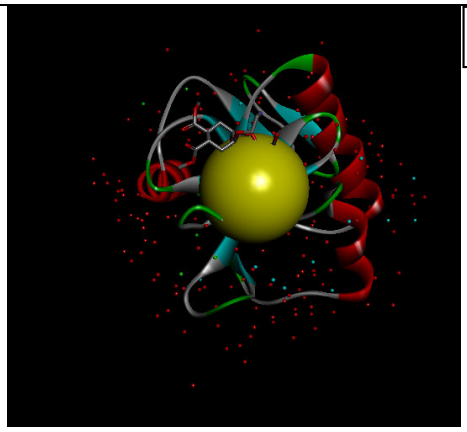


Fig 4: Side chain Plot of (a) 1O77 (b) 2E8O (c) 2XR5 (d) 4DN3





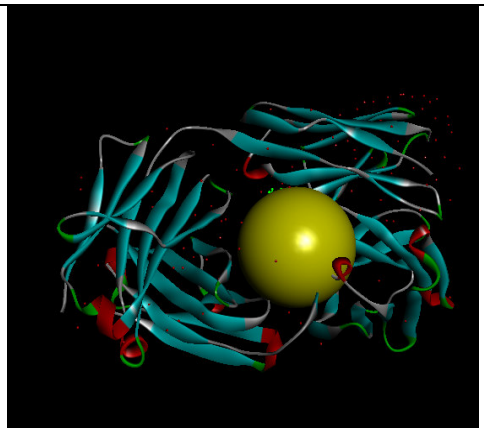
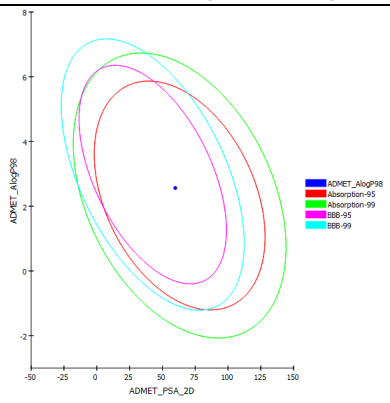


Fig 5: Docking Result of (a) 1O77 (b) 2E8O (c) 2XR5 (d) 4DN3



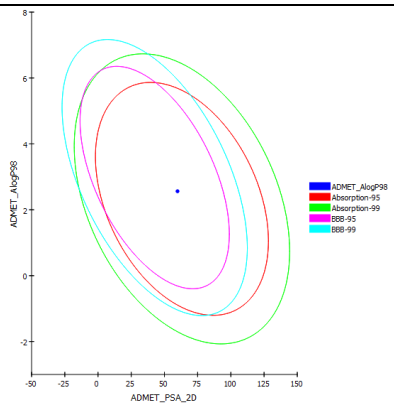


Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

In silico Analysis of Effects of Bael Leaves Extract on Plant Disease

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is Bael which has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. Bael is full of antioxidants that are essential for living a healthy life. We are using this property of Bael to get some new drugs for Tobacco mosaic virus. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Tobacco mosaic virus and pharmacophores from Bael and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Bael, Docking, *In silico* Analysis, Tobacco Mosaic Virus, Pharmacophore

INTRODUCTION

Plants have been used for medicinal purposes long before prehistoric period. Indian vedas and European cultures were using medicinal herbs for over 4000 years as medicine. The uses of medicinal herbs has increased during the past three decades and the screening of plant extracts have been done frequently for discovering new drugs (Rajamanickam et al., 2007). Aeglemarmelos (Bael) is a deciduous shrub or small to medium-sized tree belonging to the family of Rutaceae. It is found in India, Pakistan, Bangladesh and Myaanmar. The medicinal properties of this plant has been described in Ayurveda. The roots, leaves, bark, seeds and fruits consists medicinal values. The bael leaves are used to treat diarrhea, weakness of heart, blood sugar, backache, ulcers(Dutta et al., 2014). Various

compounds such as Skimmianine, Aegelin, Lupeol, Cineol, Citral, Citronellal, Eugenol, Marmesenin have been refined from leaves of bael which shows anticancer,antiulcer,hepatoprotective,antibacterial,cardioactive ,anti-inflammatory, antiseptic, antimalarial, antiallergic, antihyperglycemic, and antioxidant properties (Maity et al., 2009). In 1886, the Director of Agricultural Experiment Station of Netherland, Adolf Mayer described the curling, brittleness , discoloration and deceleration of growth of tobacco leaves which made them unsuitable for making cigar (B. D. Harrison et al., 1999). It was named as Tobacco mosaic and caused by Tobacco mosaic virus which is a rod like,(+)ss RNA virus in the genus tobamovirus. It is known to contaminate many species including tobacco, cucumber, pepper, tomato and a number of decorative flowers. The symptom of this virus is a light green coloration between the layers of leaves and formation of "mosaic" or patterns of dark and light green areas in the leaves. The virus need constant temperature and possible hosts to develop. The leaf extract of bael contains the chemical compound Eugenol which exhibits pharmalogical effects such as antioxidant, antibacterial, hepatoprotective and antiulcer(Maity et al., 2009). Considering the various medicinal properties of bael leaves, the present study was taken on to evaluate the antibacterial properties of bael leaves in Tobacco Mosaic Virus.

MATERIALS AND METHODS

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The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 5 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the Bael and can be commercialized as the natural drug for the TOBACCO MOSAIC VIRUS Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Tobacco mosaic virus

Sl.No	Pharmacophores from Bael	Targeted Genes from Tobacco mosaic virus	PDB No of the Genes
1	aegeline	DEAD-box ATP-dependent RNA helicase 10-like	5GI4
2	skimmianine(1)	protein CHROMATIN REMODELING 35-like	5IKF
3	d-limonene	ATP-dependent DNA helicase homolog RECG, chloroplastic-like	2KYY
4	marmelosin	SNF2 domain-containing protein CLASSY 4-like	1Z5Z

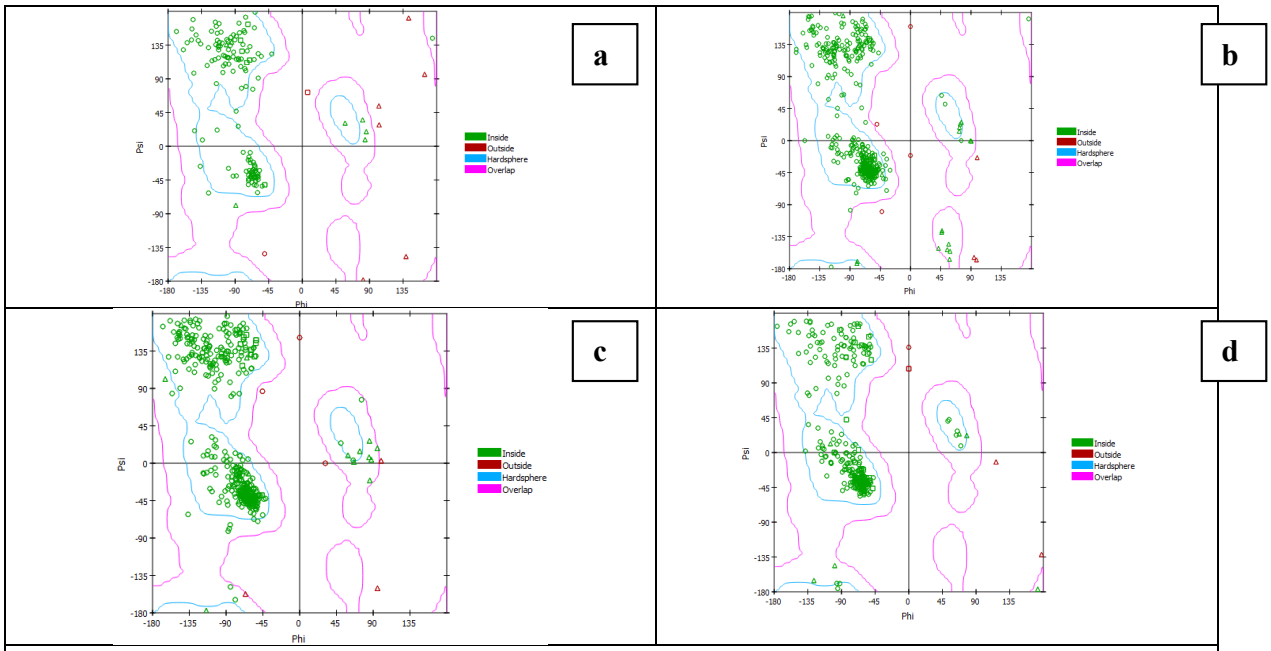

Fig 1: Ramachandran plot of (a) 1Z5Z (b) 2KYY (c) 5GI4 (d) 5IKF

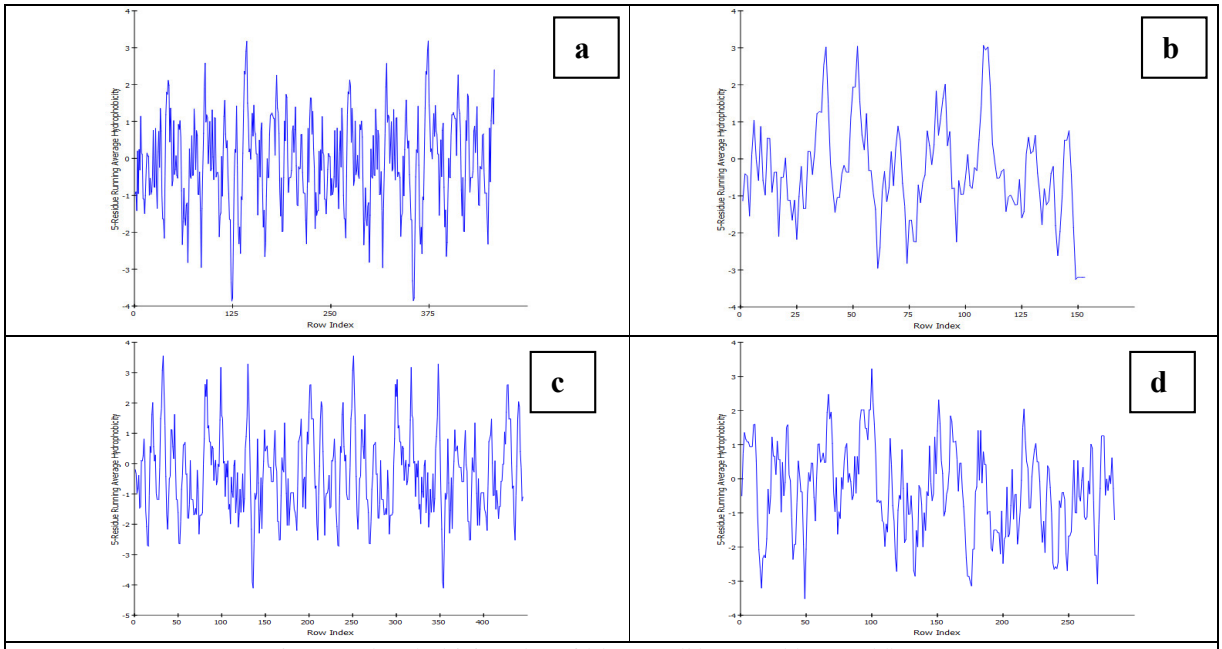

Fig 2: Hydrophobicity Plot of (a) 1Z5Z (b) 2KYY (c) 5GI4 (d) 5IKF

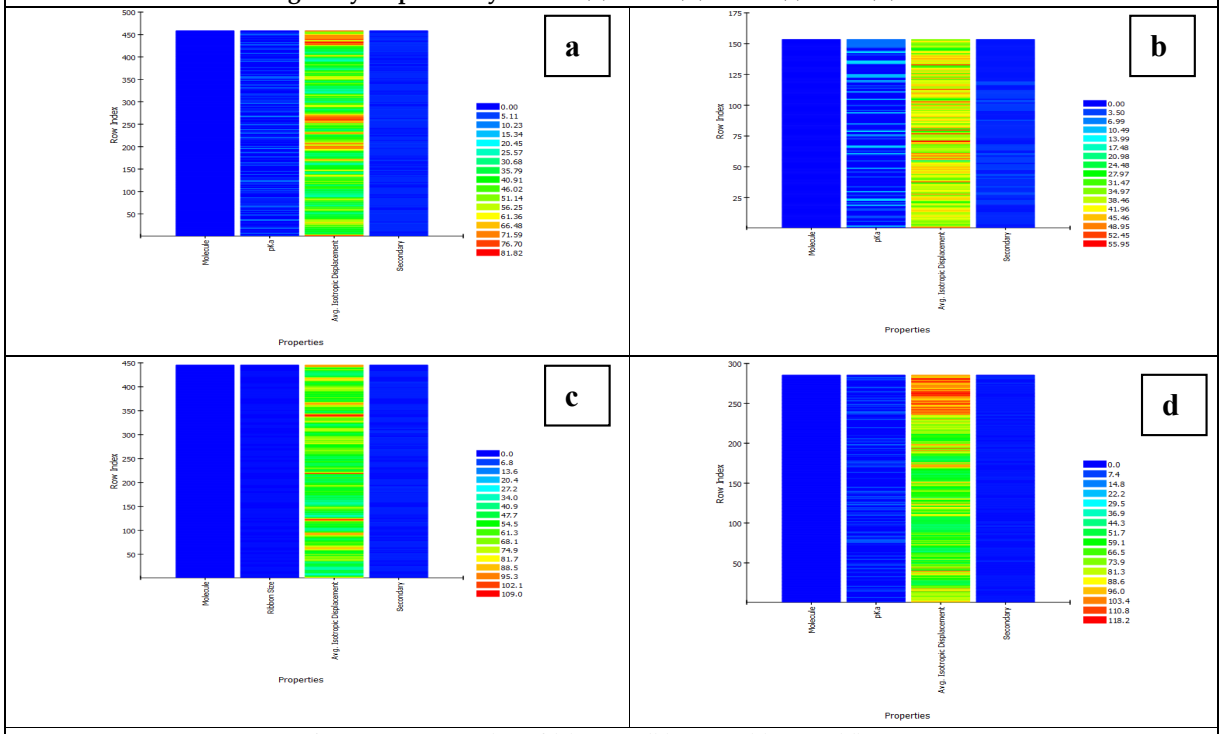

Fig 3: Heat Map Plot of (a) 1Z5Z (b) 2KYY (c) 5GI4 (d) 5IKF

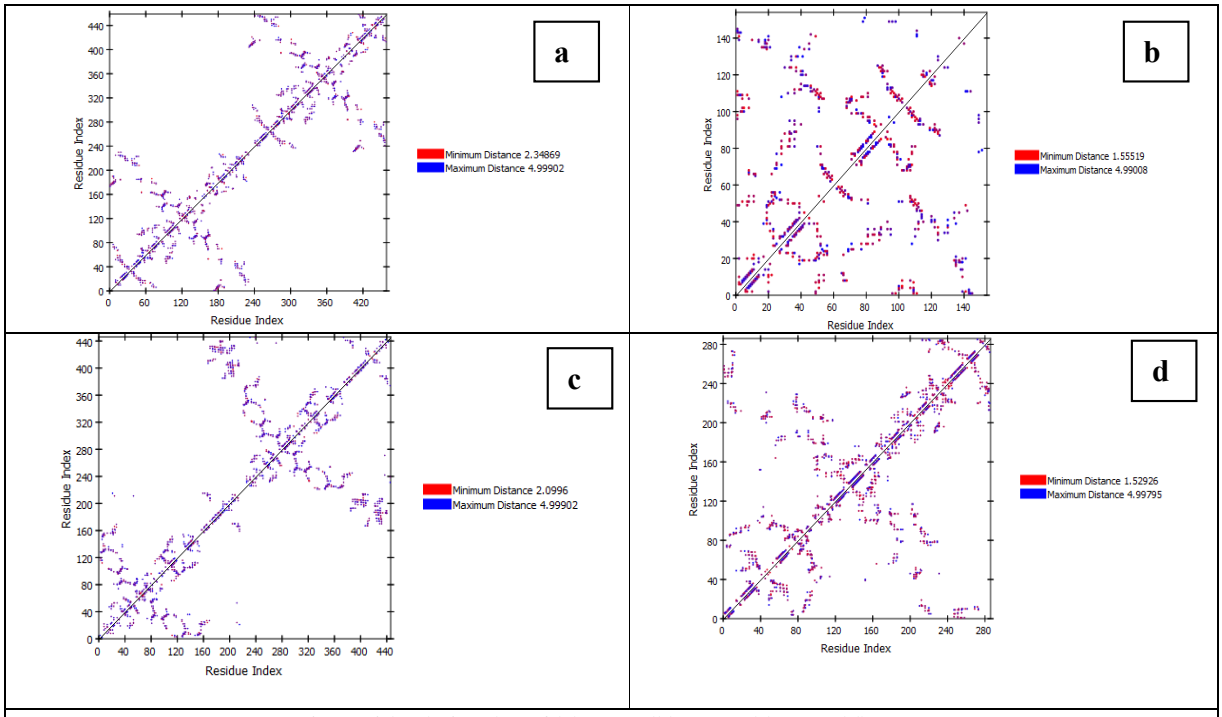

Fig 4: Side chain Plot of (a) 1Z5Z (b) 2KYY (c) 5GI4 (d) 5IKF

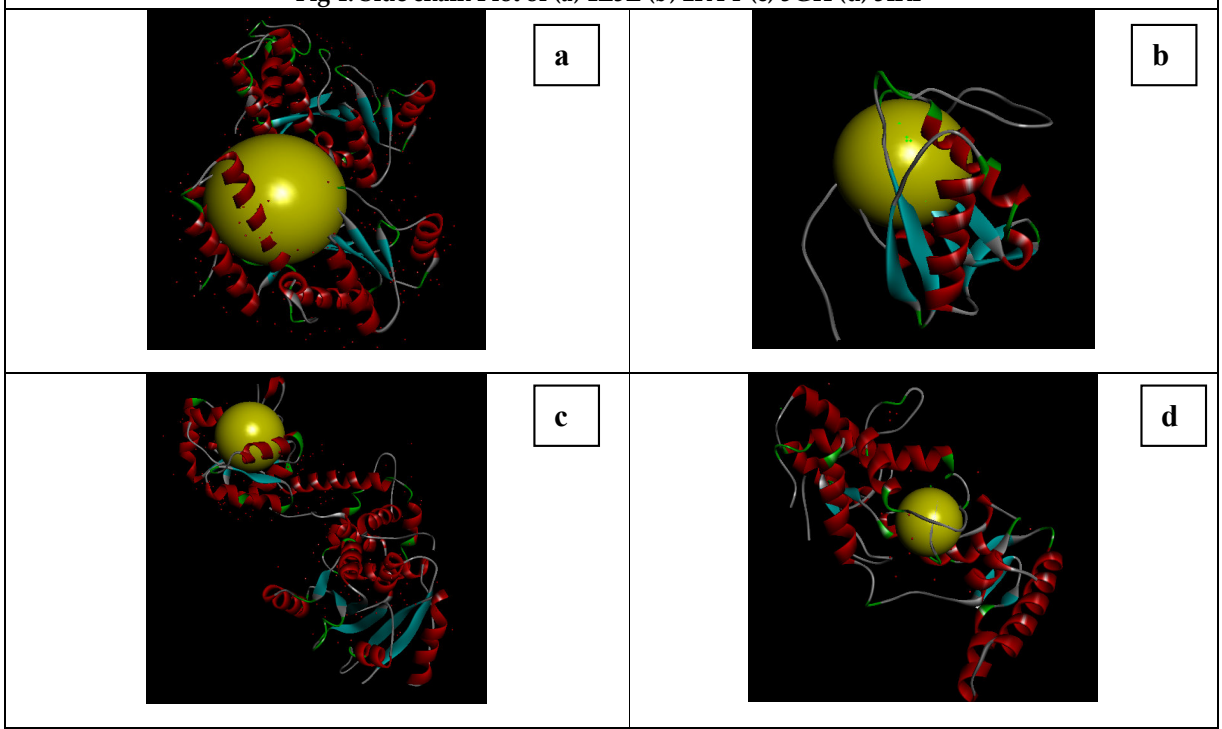

Fig 5: Docking Result of (a) 1Z5Z (b) 2KYY (c) 5GI4 (d) 5IKF

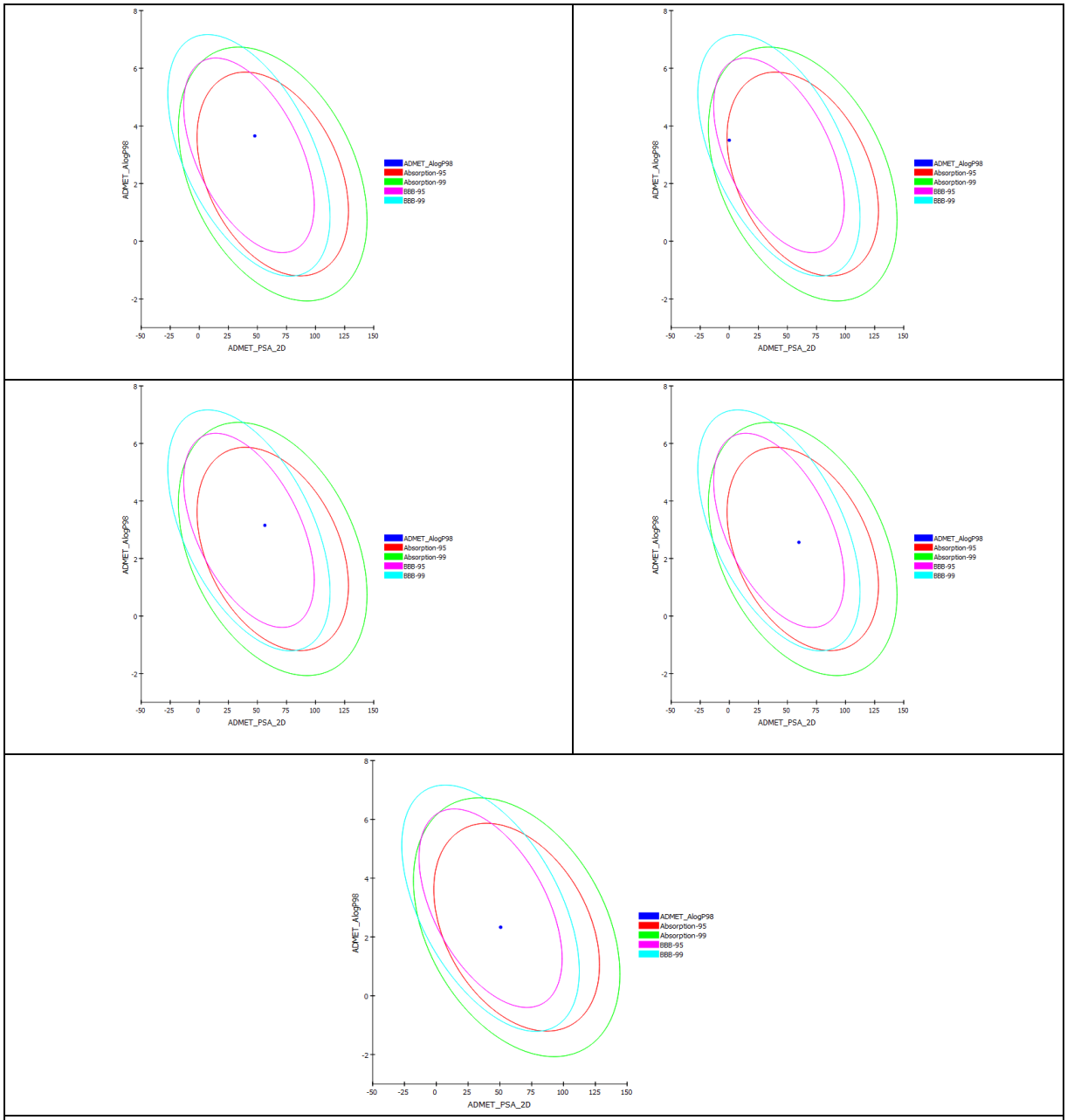

Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

In-silico Analysis of Inhibitory Action of Garlic against Hyperlipidemia by FAS Enzyme

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ABSTRACT

The volatile antimicrobial substance allicin (diallylthiosulphinate) is produced in garlic when the tissues are damaged and the substrate alliin (S-allyl-l-cysteine sulphoxide) mixes with the enzyme alliin-lyase (E.C.4.4.1.4). Allicin is readily membrane-permeable and undergoes thiol-disulphide exchange reactions with free thiol groups in proteins. It is thought that these properties are the basis of its antimicrobial action. Metabolism of lipid into fatty acids and glycerol and the absorption process in the body involves various kinds of enzymes; one of them is Fatty Acid Synthase (FAS). Excess lipid in the body will cause various diseases, such as obesity and cardiovascular diseases. Treatment for excess in lipid level is usually by using synthetic drugs such as statins, but excessive consumption of drug causes various side effects. Single garlic (Allium sativum) (SG) is widely used as an herb that can treat diverse diseases. SG contains organosulfur compounds including Allicin, Alliin, and Ajoene (E-Ajoene and Z-Ajoene). This study aimed to determine the potential of organosulfur compounds in SG as inhibitors of fatty acid synthase (FAS) enzymes which play a role in the process of lipid metabolism.Based on molecular docking results, it is known that the active compounds found in SG could act as an inhibitor for FAS enzymes which play a role in de novo lipogenesis.

Key words: Enzyme Activity, Garlic, Molecular Docking, Pharmacophore

INTRODUCTION

Garlic (*Allium sativum*) is used as a flavouring ingredient in food preparations. Itsthe second most widely used cultivated Allium after onion. It has long been recognized all over the world as a valuable spice for foods and a popular remedy for various ailments and physiological disorders.Garlic grows in temperate and tropical regions all over the world, and many cultivars have been developed to suit different climates.Garlic contains at least 33 sulfur compounds, several enzymes, 17 amino acids, and minerals such as selenium. It contains a higher concentration of sulfur compounds than any other Allium species. The sulfur compounds are responsible both for garlic's pungent odor and many of its medicinal effects. Dried, powdered garlic contains approximately 1% alliin (S-allyl cysteine sulfoxide). One of the most biologically active compounds, allicin (diallylthiosulfinate or diallyldisulfide), does not exist in garlic until it is crushed or cut; injury to the garlic bulb activates the enzyme allinase, which metabolizes alliin to allicin.

MATERIALS AND METHODS

The reported molecular targets responsible for downy mildew of abdiopsis such as salicylic acid,callose, a polysaccharide that is commonly present in these pathogen-induced physical barriers, Multiple independent alleles of dmr1, dmr1-1, dmr1-2, dmr1-3, and dmr1-4, were initially identified. The X-ray crystallised structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. PDB structures include FAS(PDB ID:1DDF) , allinase(PDB ID: 2HOR), Statin(PDB ID: 3LIY), (Z)-Ajoene(PDB ID: 1BWC)etc. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies.

Selection of ligands

The ligands used for docking study were selected from literature. The bioactive compounds that are mainly present in the bulbs of *Allium sativum* were considered for the study. Structures of major compounds present in garlic were retrieved from the PubChem compound database [24] in the SDF file format and followed by conversion in PDB format using the tool Marvin Sketch features an extensive set of functionalities to allow the rapid and precise drawing of chemical compounds, reactions. These structures were used for docking calculation. The reference ligand structure is prepared in prior, using Marvin of ChemAxon by cleaned structure up in two dimension (2D) configurations. Details of bioactive Compounds considered for the study with their 2D structures were represented in Table 1.

Molecular docking

It was found that garlic contains allicin (S-Allyl-L-cysteine sulfoxide). Molecular docking is very necessary step performed to study the receptor-ligand interaction to select potential hits in virtual screening which regarded as the basis for structure based drug discovery. Molecular docking was performed in Yet another Scientific Artificial Reality Application (YASARA) an Auto Dock based tool for molecular docking and virtual screening. Y ASARA was used to gain the docking results of the listed compounds with the indicated target proteins. The energy minimized compounds were imported and the docking conformations were performed twice using genetic evolutionary algorithm and the fitness of the docked structures were calculated. The hydrogen bond, Residues, Dissociation Constant, binding energy was calculated using YASARA Software. Here, the vdW term is van der Waal energy. H-bond and Elect terms are hydrogen bonding energy and electro statistic energy, respectively. The output of docking

run is sorted based on binding energy. Yasara docking gives positive binding energy. So, more the positive energy indicates the higher likeness among the molecules.The results of molecular docking showed that statin had the highest binding affinity for FAS enzymes compared to organosulfur compounds (-5.0 kcal/mol). The visualization of binding position using PyMol software showed that the organosulfur compounds (E-Ajoene, Z-Ajoene, and Allicin) had the same binding site with statin in FAS enzyme. The binding site of ligands and protein is shown in Figure 1. Ligands are shown in red (Alliin), magenta (Allicin), blue (E-Ajoene), orange (Z-Ajoene), and white (Statin).

Pharmacophore

A pharmacophore is an abstract description of molecular features that are necessary for molecular recognition of a ligand by a biological macromolecule.Pharmacophore mapping was carried out in the workspace of mole sign module ofVlife MDS 4.3. Dataset of de navolipogenesis was first aligned with reference to most active molecule as template. The most active molecule statin was selected to set it as the reference. The reference molecule is the molecule on which the other molecules of the align dataset get aligned. All spheres in the snapshot indicate all possible pharmacophoriccenters. This pharmacophore model can serve as an effective search filter for virtual screening.

RESULTS AND DISCUSSION

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. In order to examine the binding capacity of bioactive compounds in Allium sativum on proteins related to de navolipogenesis, we have used Yasara software to dock the ligand data set to the structure of target protein. Since all the natural ligands(inhibitors) were found to be docked in a variety of conformations and with varying binding energy. From the interaction profile numerous interactions including hydrogen bonding interactions, hydrophobic interaction, Van der Waals interactions, and pi–pi interactions were inspected between selected inhibitors and retrieved Hit molecules with target proteins. Through this methodology of computer aided drug interaction, we examine complexes formed between ligands and interesting targets (often many), for dissimilar types of a particular disease. Target proteins docked with different ligands are shown in Fig 2. The best dock pose was chosen on the basis of high docking score. Top two ligands were selected with better score.

CONCLUSION

The results of molecular docking method showed that organosulfur compounds in SG had potential as drug candidates by inhibiting the FAS enzyme. The visualization of the binding site showed that the organosulfur compounds (E-Ajoene, Z-Ajoene, and Allicin) in SG had the same binding site with Statins in FAS enzyme. FAS is an enzyme which plays a role in the biosynthesis of lipid. The inhibition of FAS could reduce the production of fatty acid. Therefore, the SG could be used as an alternative medicine for various diseases caused by hyperlipidemia.

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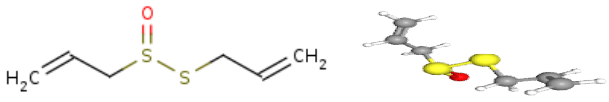
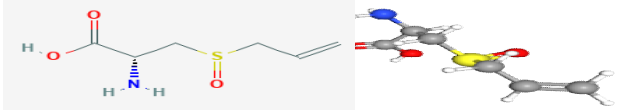
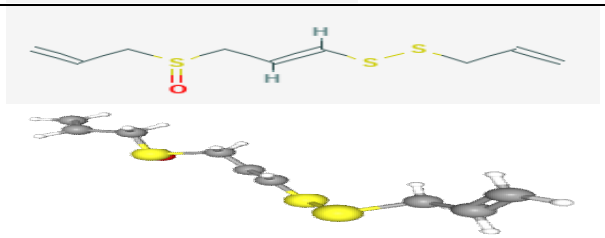
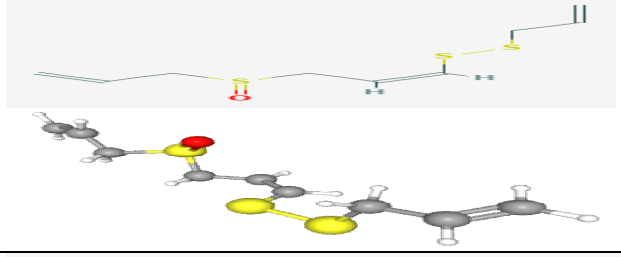
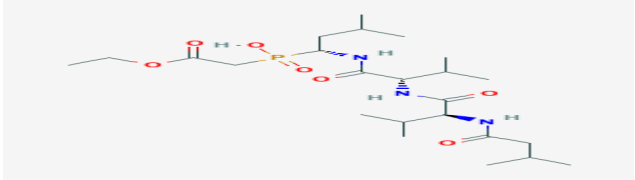
Table 1: List of ligands and their structure

Compound Name	Molecular Weight	Pubchem-Id	Structure
Allicin	162.3g/mol	65036	
Alliin	177.22g/mol	87310	
(E)- Ajoene	234.4g/mol	5386591	
(Z)- Ajoene	234.4g/mol	9881148	
Statin	519.6g/mol	447893	

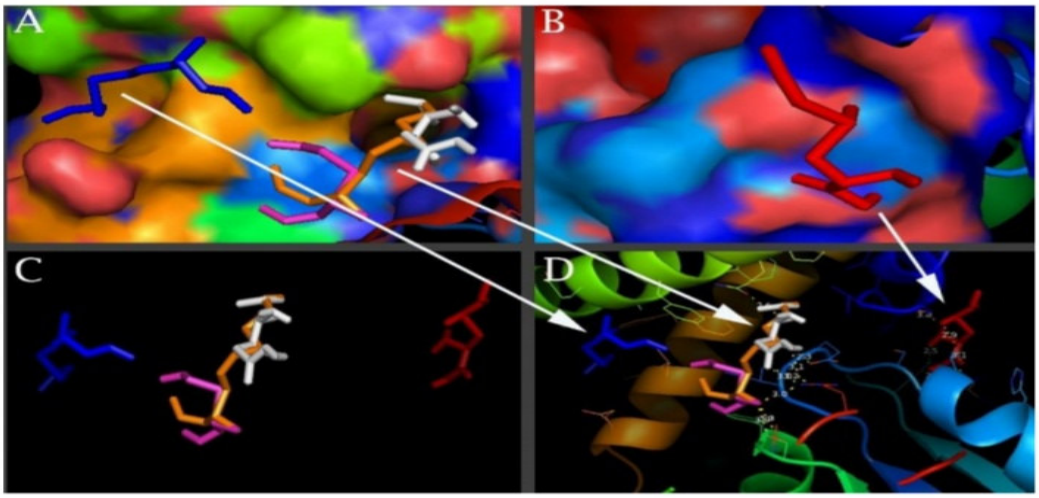


Figure 1.A & B.The visualization of the binding site in organosulfur compounds and statin to FAS enzyme; C.The magnification of the visualization of an organosulfur compound and statin binding site; D.The visualization of all compounds. The white arrow shows the position of organosulfur compounds and statin in the FAS enzyme.

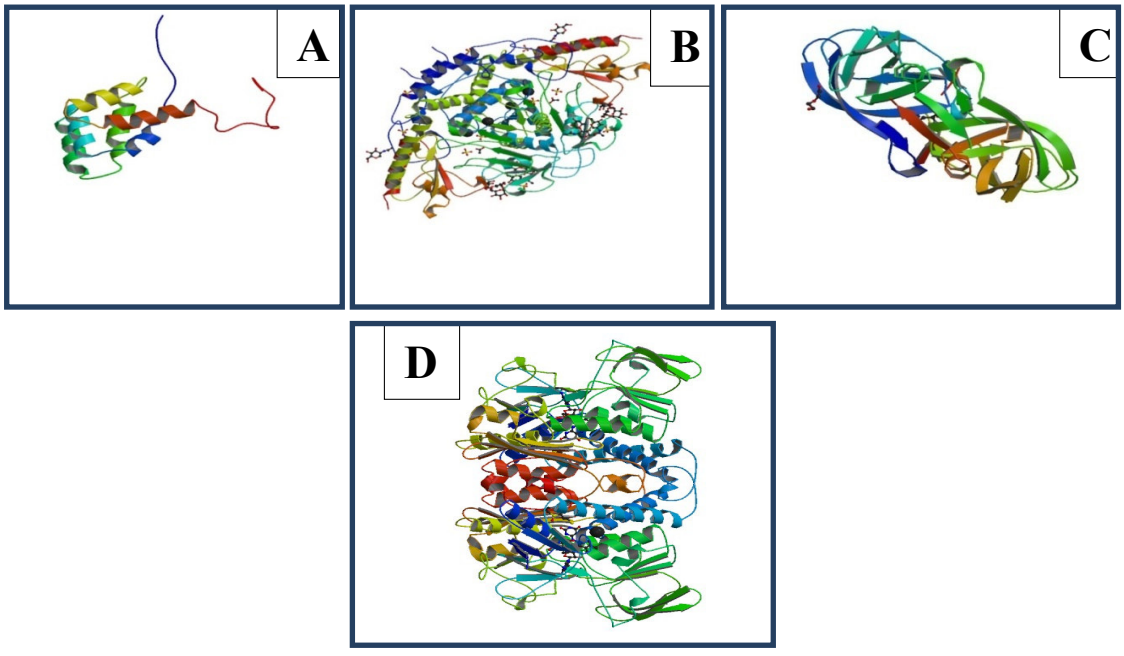
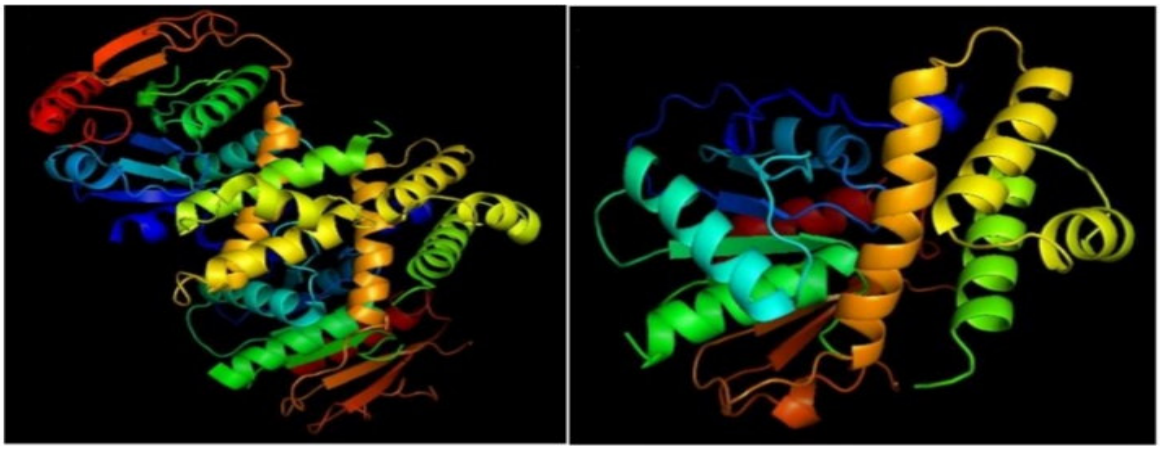


Fig 2. Binding modes and Protein-ligand interaction map of docked complexed ligands with A(FAS), B(Allinase),C(statin), D(Ajoene)



(A) **(B)**

Figure 3. (a) 3D structure of FAS enzyme from RCSB GDP; (b) 3D structure of FAS enzyme after removing water molecules and other ligands.

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RESEARCH ARTICLE

In-silico Analysis of Effects of Ajwain Extract on Plant Disease

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ABSTRACT

Ancient India is one of the pioneers of studies of plants as medicine, i.e. Ayurveda. In our social and economic life we hardly take care of our food we are taking. One such unique herb is Ajwain which has often been regarded as a brain booster. The whole plant including the flowers can be used for medicinal purposes. It has a bitter and sweet taste and is known to impart a cooling energy. Ajwain is full of antioxidants that are essential for living a healthy life. We are using this property of Ajwain to get some new drugs for Aster Yellow. The uses of various pesticides, preservatives, etc. turn the foods into poison. Moreover the side effects of these pesticides and preservatives, etc. are dangerous as because it leads to initiation of different cancer. In this whole world, the number of patients dying from cancer is increasing in a very threatening way. *In-silico* analysis has done using software and we further targeted some of the genes responsible for Aster Yellow and pharmacophores from Ajwain and did some in silico analysis. In this we have found that these two pharmacophores are having better Mol Doc score from any others.

Key words: Ajwain, Docking, *In silico* Analysis, Aster Yellow, Pharmacophore

INTRODUCTION

Ayurveda is the oldest medicine system originates in the Indian subcontinent about 5000 years ago. In Ayurved herbs play important role. "Trachyspermum-ammi" (T.ammi) which is popularly known as "Ajwain" is an annual herb in the family of Umelliferae or Apiaceae. It is also known as bishop's weed or carom. "Ajmoda" is the Sanskrit name of Ajwain this generally cultivated in Iran and India especially in arid and semi-arid region. According to Ayruveda, Ajwain is a powerful cleanser. It is helpful for stimulating the apatite and enhancing digestion. It is

recommended to help alleviate gas and discomfort in the stomach. It is easy also helpful for the functioning of the respiratory system and the kidney. The aromatic plant Ajwain is an annual herbaceous. It height can extend to 30 cm to 70 cm. They are having feathery leaves and red flowers. When the seed are ready to cultivate they are dried and threshed. These seeds are grayish-green in colour with striped and curved. They tastes hot and bitter with leaving the tongue numb for a second. The major oil found in ajwain is Thymol which is strong germicide,anti-spasmodic and fungicide. It contains health benefiting oils like cymene, gamma- terepenine, lupeol, linoeric acid, stearic acid, etc.It is also contain moisture, protein, fat, mineral, fiber, carbohydrates, calcium, etc. The chemical extracted from bishop weeds has antibacterial, antifungal, antitussive,anti-inflammatory,and analgesic effects as well as antioxidant, and antitumor in nature. So, we are trying examining the herb's essential oil and their behavior against hospital-acquired pathogens.

MATERIALS AND METHODS

Various pharmacophores of Ajwain leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Aster Yellow has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for Rice Tungro Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Cumin were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

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Drug likeliness

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The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structures are mentioned in Table 1.

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Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties.

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4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

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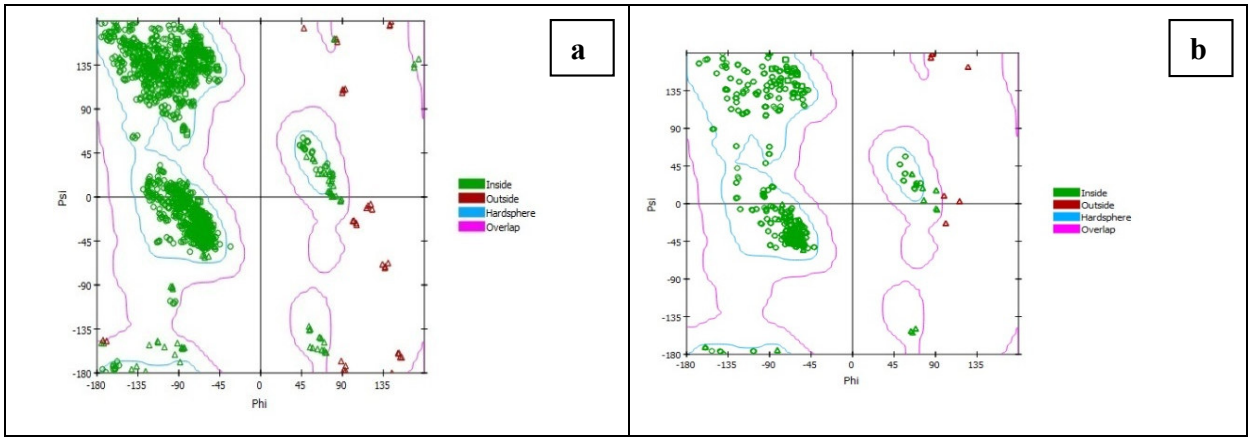
Table 1.The list of pharmacophores and the targeted genes from Aster Yellow

Sl.No.	Pharmacophores from Ajwain	Targeted Genes from Aster Yellow	PDB No of the Genes
1	Thymol	DEAD-box ATP-dependent RNA helicase 10-like	5GI4
2	Lupeol	protein CHROMATIN REMODELING 35-like	5IKF
3	linoleic acid	ATP-dependent DNA helicase homolog RECG, chloroplastic-like	2KYY
4	Gamma terpinene		



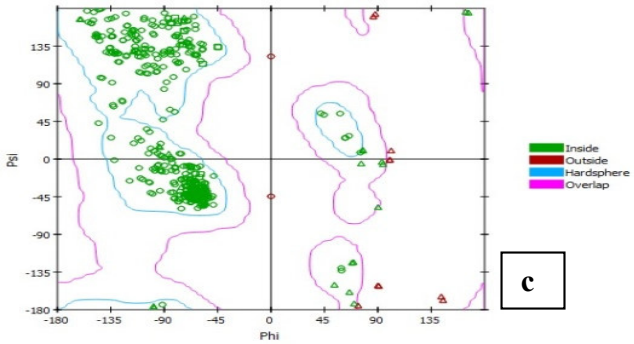


Fig 1: Ramachandran plot of (a) 5GI4 (b) 5IKF (c) 2KYY

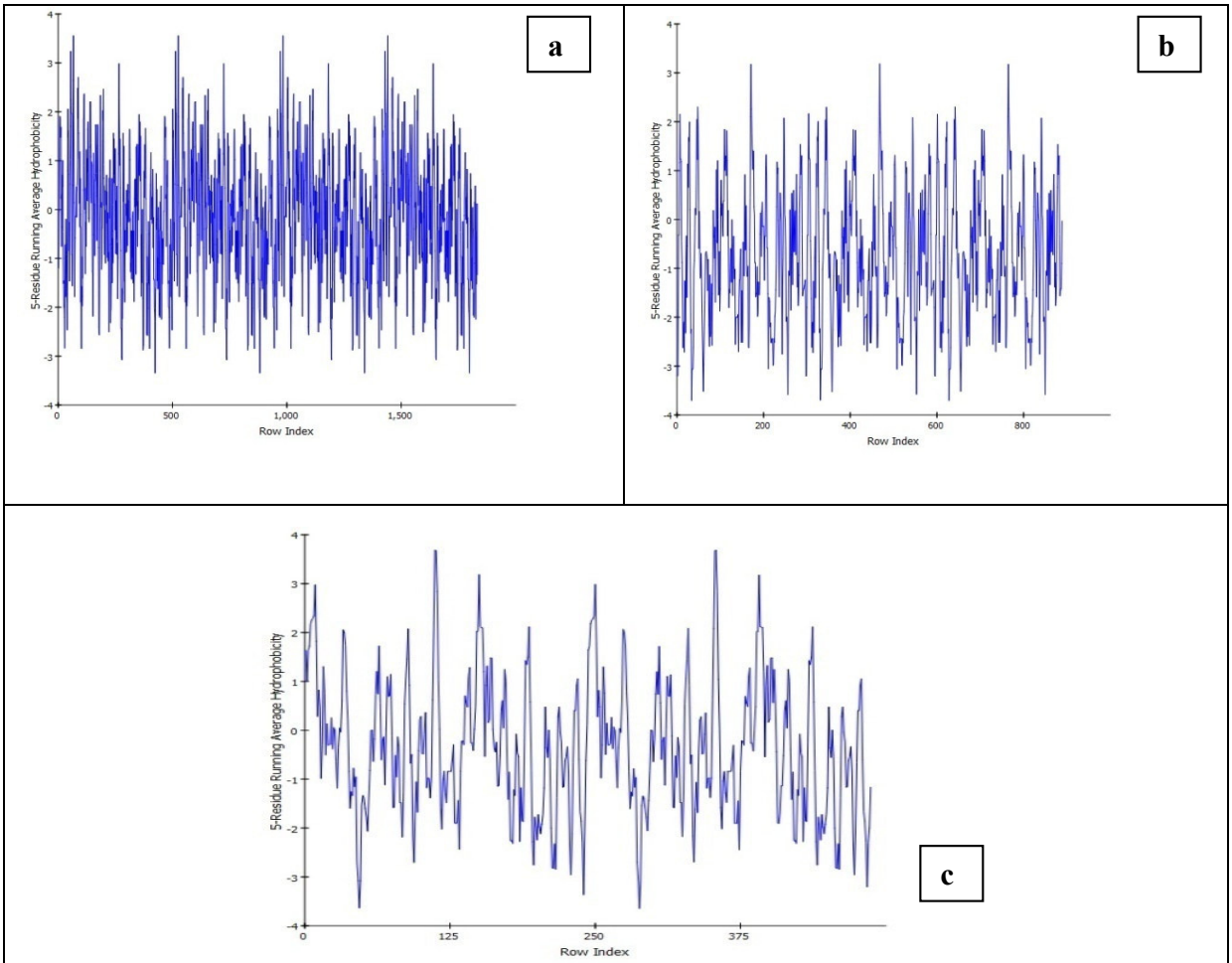


Fig 2: Hydrophobicity Plot of (a) 5GI4 (b) 5IKF (c) 2KYY

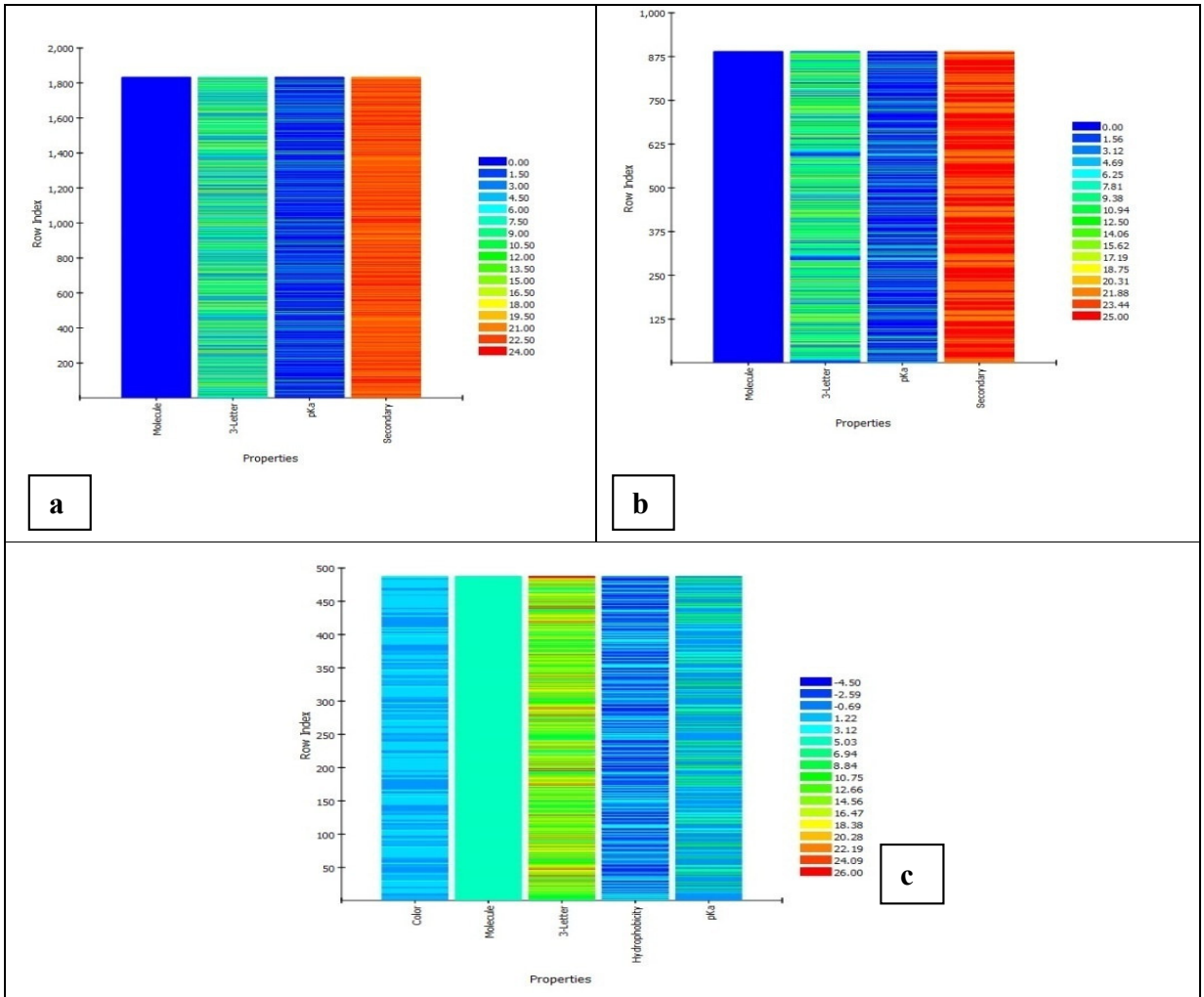
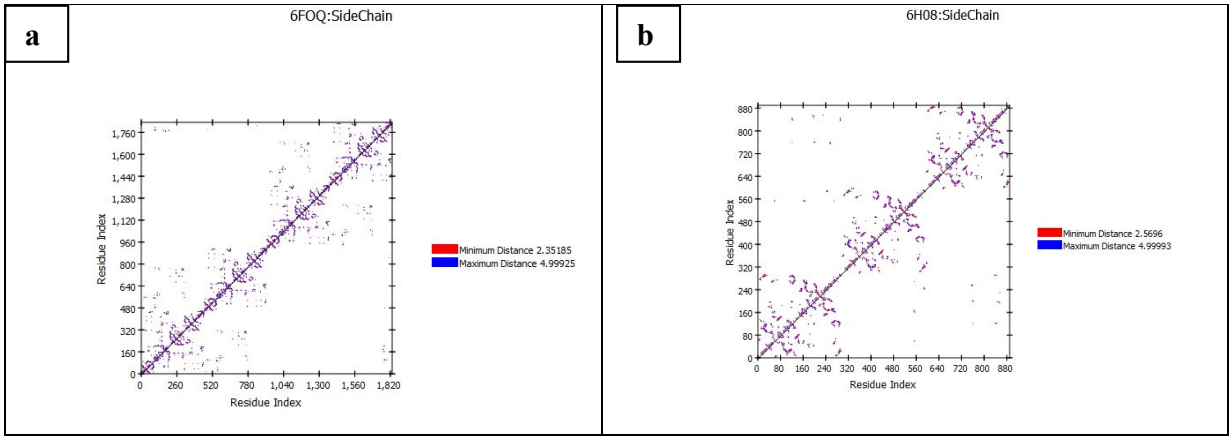


Fig 3. Heat Map Plot of (a) 5GI4 (b) 5IKF (c) 2KYY



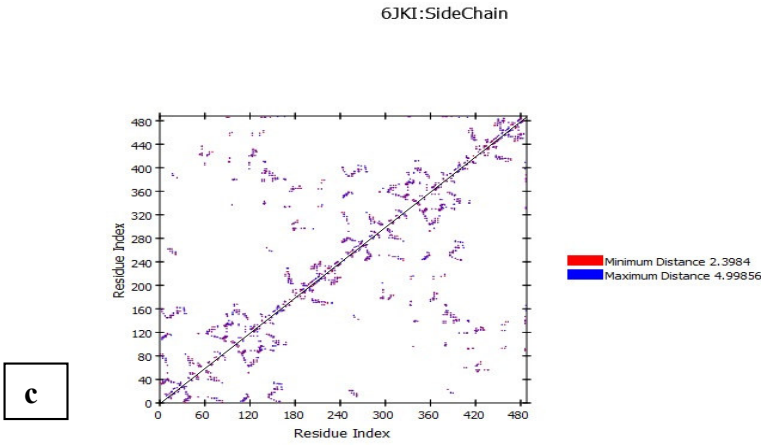


Fig 4.Side chain Plot of (a) 5GI4 (b) 5IKF (c) 2KYY

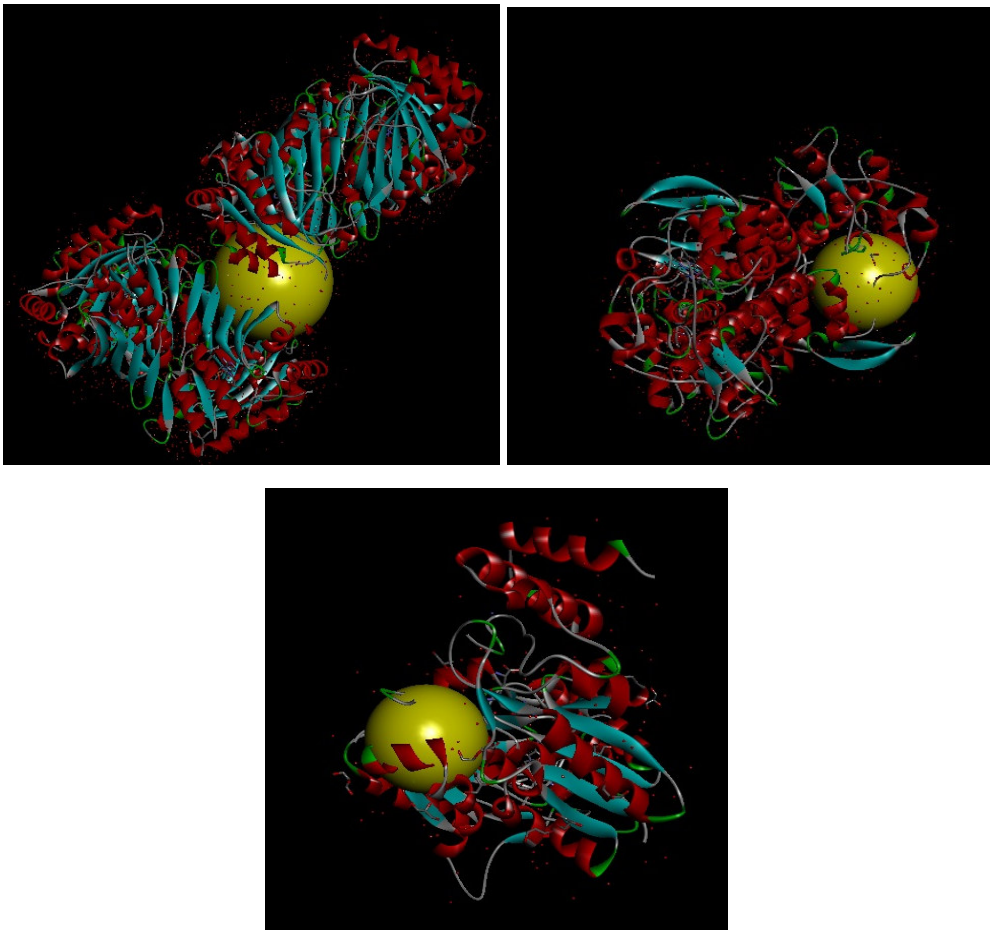


Fig 5: Docking Result of (a) 5GI4 (b) 5IKF (c) 2KYY

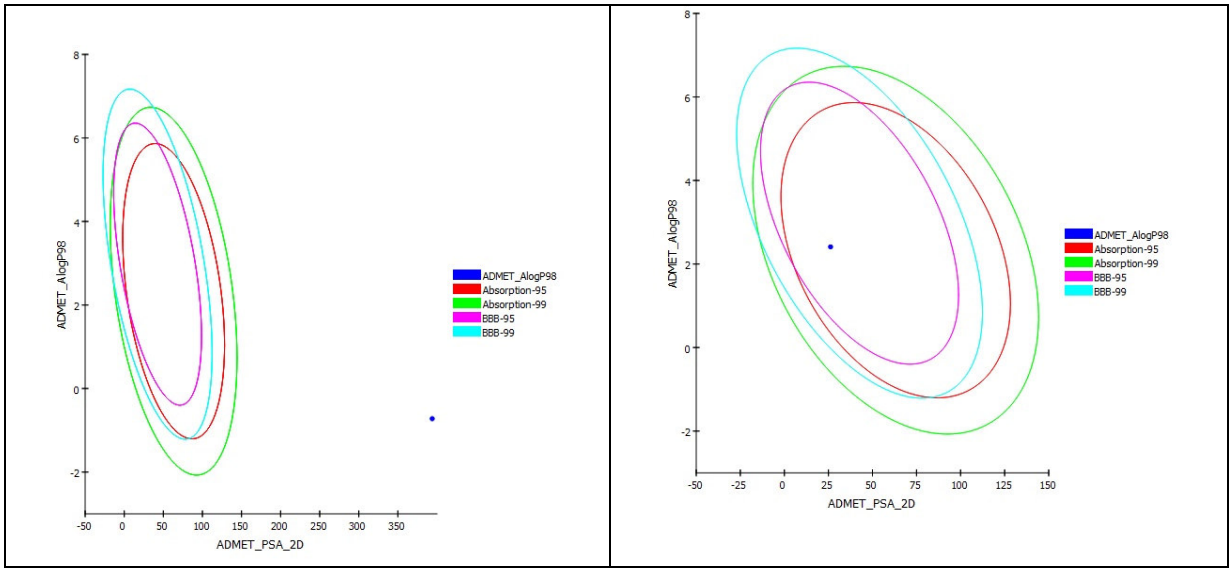


Fig 6: ADMET test analysis report

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RESEARCH ARTICLE

In-silico Analysis of Effects of Black Pepper Extract on Asthma

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ABSTRACT

Black pepper (*Piper nigrum* L.) is the most important spice traded internationally and is cultivated in many tropical regions of the world like India, Brazil, Vietnam, Indonesia, Malaysia and Sri Lanka. A variety of trees species are used as live stakes for supporting black pepper. However, not all are considered ideal. In ancient India spices were mixed along with different solvent and used as medicine to treat different diseases. This spice plants are having extraordinary chemical which we will find as fragrance, taste. We have used these properties of these spice plants and spices to get some targeted medicine for different diseases. We have taken Black Pepper for the targeted therapy for the Asthma, which is a common disease in the topical region of the country.

Key words: Asthma, Black Pepper, Molecular Docking, Pharmacophore

INTRODUCTION

Black Pepper is basically produced in southeast and south Asia and has been known to India cooking since at least 2000 BCE. *Piper nigrum L.* (*P. nigrum;* black pepper) belonging to the family Piperaceae is considered the king of spices due to its spicy savor (Abbasi et al., 2010; Ahmad et al., 2012a, 2013). *P. nigrum* is cultivated throughout the world and is native to tropical and subtropical regions of India (Ahmad et al., 2010, 2012a). High pungency in black pepper fruits indicated the presence of piperine. Piperine, the most active component in the fruits of *P. nigrum* L., denotes the quality and value of spiciness (Ahmad et al., 2011a; Bhat et al., 1995; Philip et al., 1992). Peppercorn from *P. nigrum* can be used in food processing, as crude drugs, and can also be used as food additives (Srinivasan, 2007). Regarding medicinal applications, *P. nigrum* has pronounced antibacterial, antifungal, antiviral, antimutagenic, and

antioxidant activities (Abbasi et al., 2010; Ahmad et al., 2010, 2012a; Dorman and Deans, 2000; Saxena et al., 2007). Nerolidol and b-caryophyllene isolated from *P. nigrum* have anesthetic activity (Santra-Mantra et al., 2005). The fruits of this species are also used to treat respiratory tract diseases and infections such as asthma, cold extremities and sore throat, digestive problems including chronic indigestion, colon toxins, colic, and diarrhea, and fevers including congestion fever and intermittent fever and also control obesity (Ahmad et al., 2011a; Ravindran, 2000). *P. nigrum* also claimed to possess antiapoptotic activity, antidepressant, analgesic, antiinflammatory, antimetastatic, antispasmodic, antispermatogenesis, antithyroid, hepatoprotective, insecticidal, larvicidal, and pesticidal activities (Balkrishna, 1995; Kumar et al., 2007; Li et al., 2007; Mishra and Singh, 2009; Pathak and Khandlewal, 2006; Scott et al., 2008). Plants produced a variety of active metabolites that act as a defense system against various pathogenic agents (Ahmad et al., 2011b, 2012b, 2012c). Black pepper photochemical name is piperine.basically useful for health problems in home. Black pepper properties include for the bioactive and preservative. It uses for spices Worldwide. It is good for improve metabolic rate and inhibits adipose cell growth. It helps for also digestion due to the piperine which stimulate the gastric fluids. The piperine present in black pepper helps body to absorb some of the nutrients found in certain foods. Piperine treatment has also been evidenced to lower lipid peroxidation in vivo and beneficially influence cellular thiol status, antioxidant molecules and antioxidant enzymes in a number of experimental situations of oxidative stress. The chemicals of piperine is C17H19NO3 .

MATERIALS AND METHODS

Various pharmacophores of Black Pepper leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Asthama has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

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Table 1: The list of pharmacophores and the targeted genes

Sl.No	Black Pepper Pharmacophores	Targeted Animal Gene (Asthma)	PDB No of the Genes
1	Beta-pinene	neuropeptide S receptor 1	5ZBH
2	Limonene	thymic stromal lymphopoietin	5J11
3	P- cymene	gasdermin B	6KN0
4	Piperazine	major histocompatibility complex, class II, DQ beta 1	6PX6

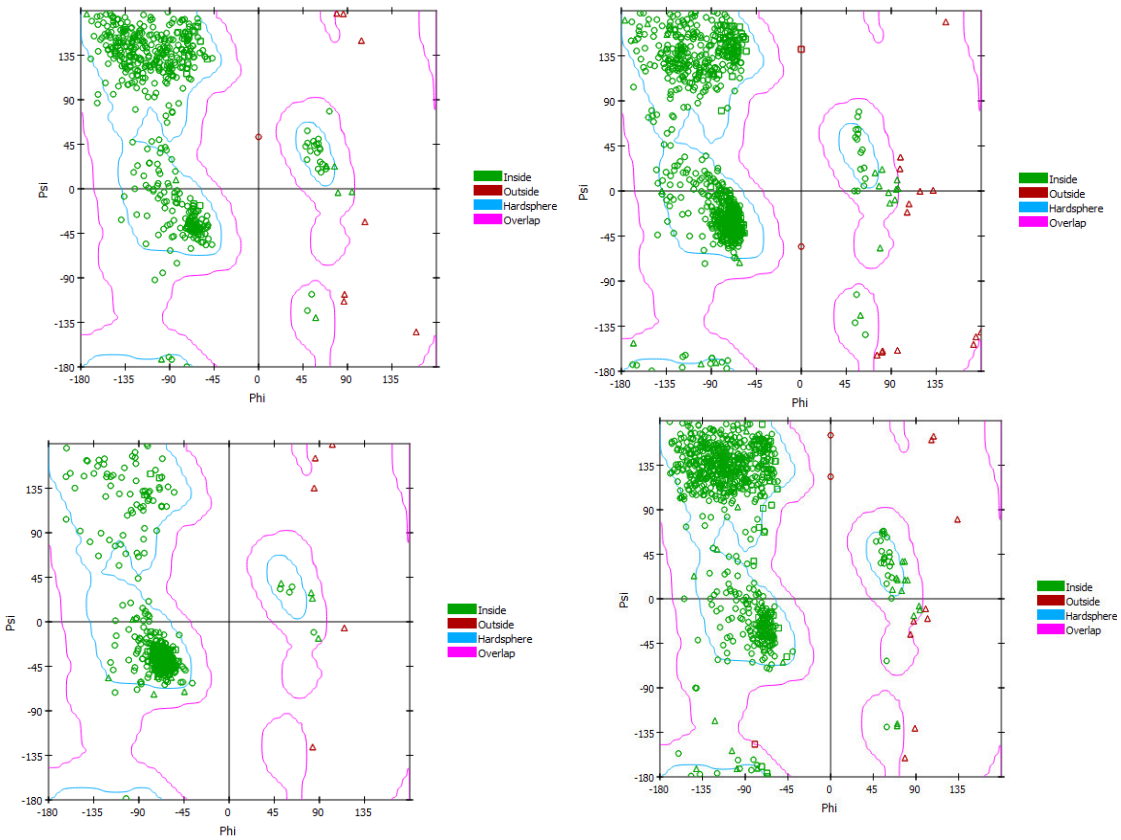

Fig 1. Ramachandran Plot of (a) 5I11, (b) 5ZBH, (c) 6KN0, (d) 6PXP

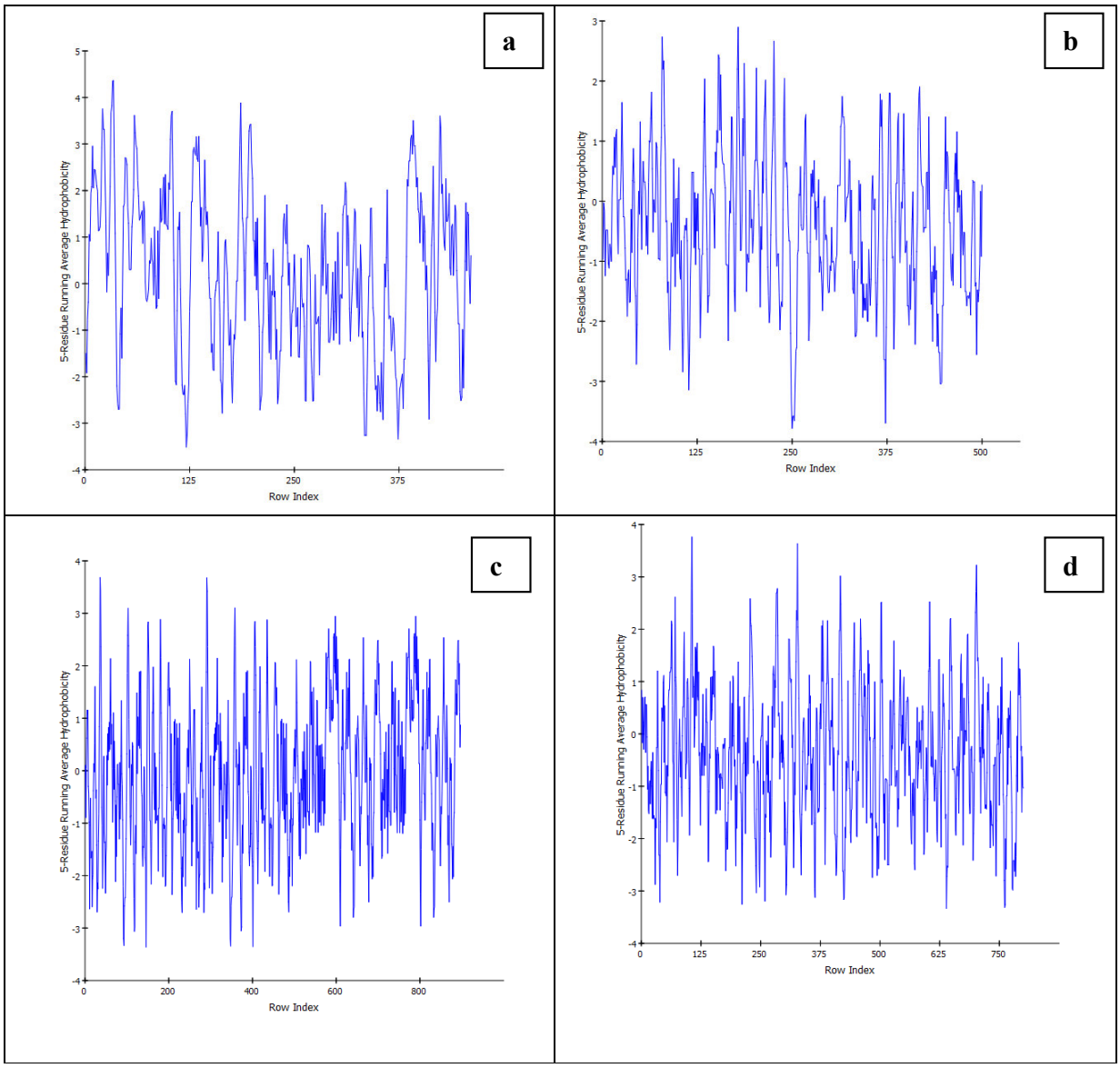

Fig 2. Hydrophobicity Plot of (a) 5I11, (b) 5ZBH, (c) 6KN0, (d) 6PXP

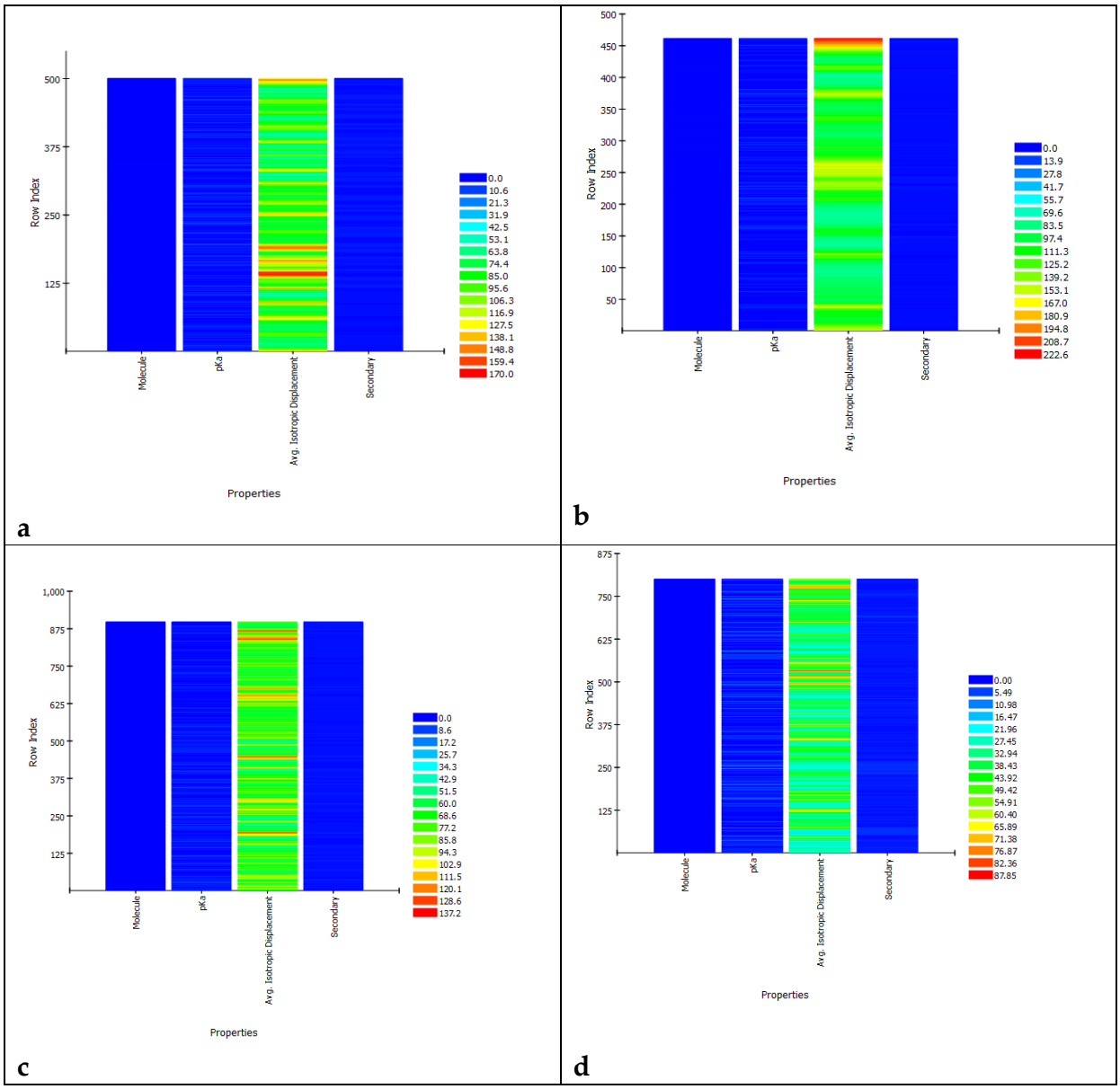

Fig 3.Heatmap of (a) 5I11, (b) 5ZBH, (c) 6KN0, (d) 6PXP

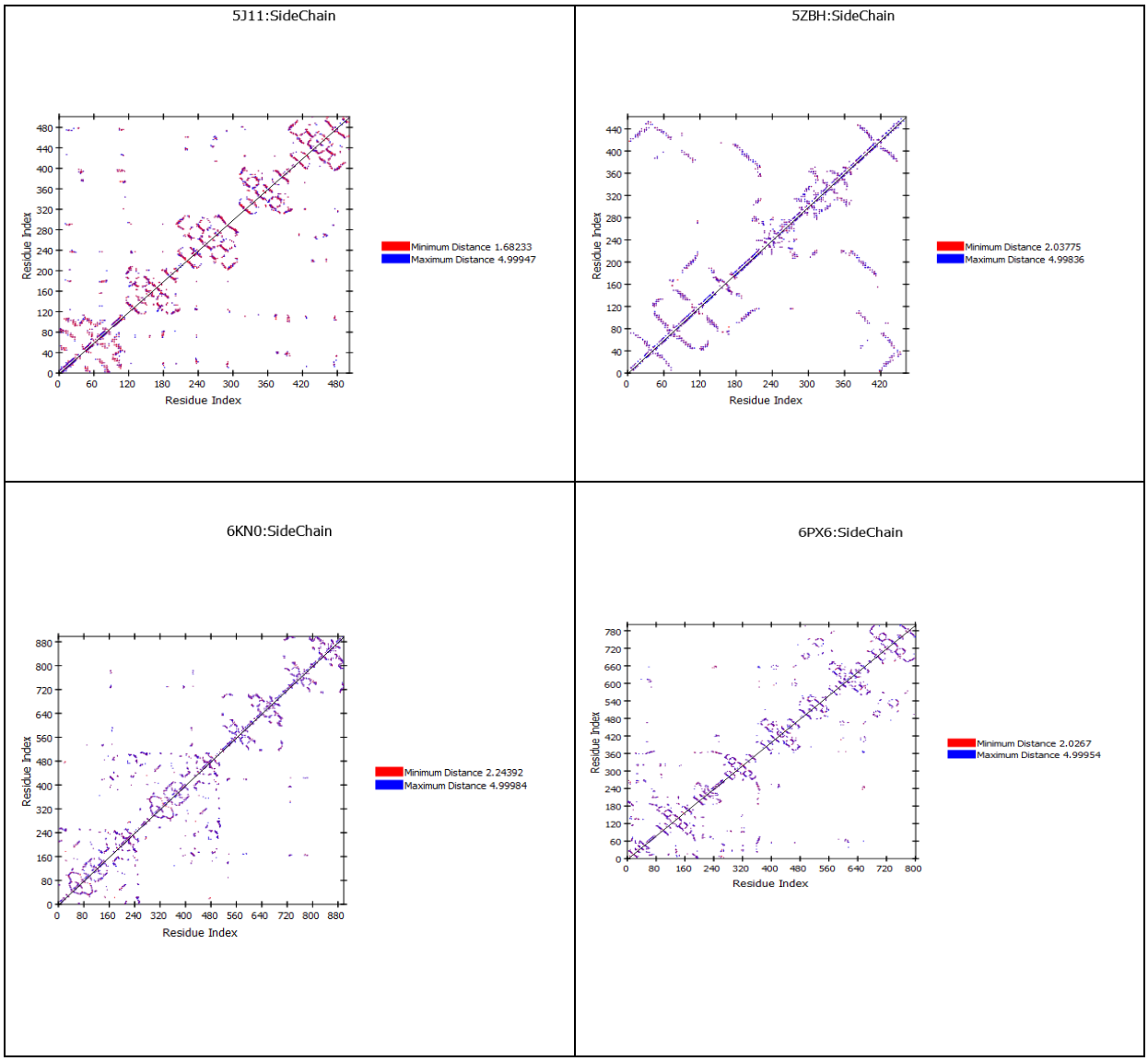

Fig 4.Side chain Analysis Plot of (a) 5I11, (b) 5ZBH, (c) 6KN0, (d) 6PXP

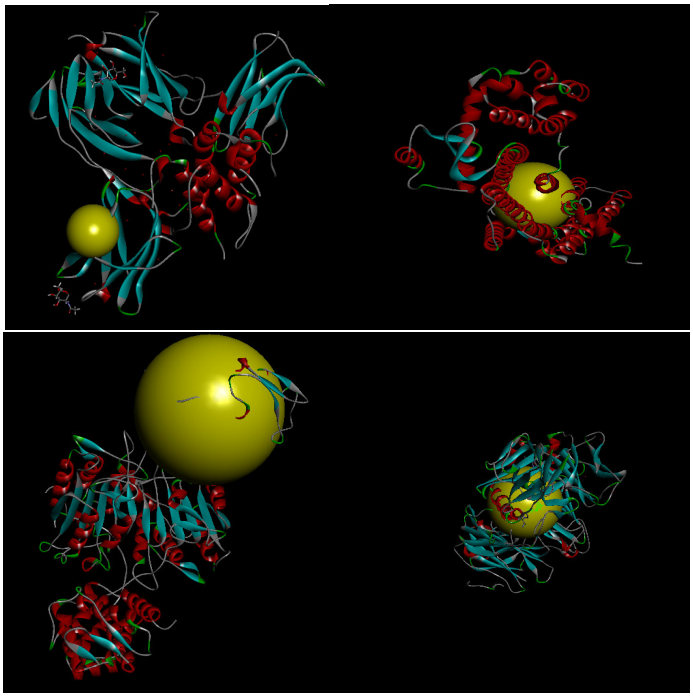

Fig.5.Docking Aaalysis of (a) 5I11, (b) 5ZBH, (c) 6KN0, (d) 6PXP

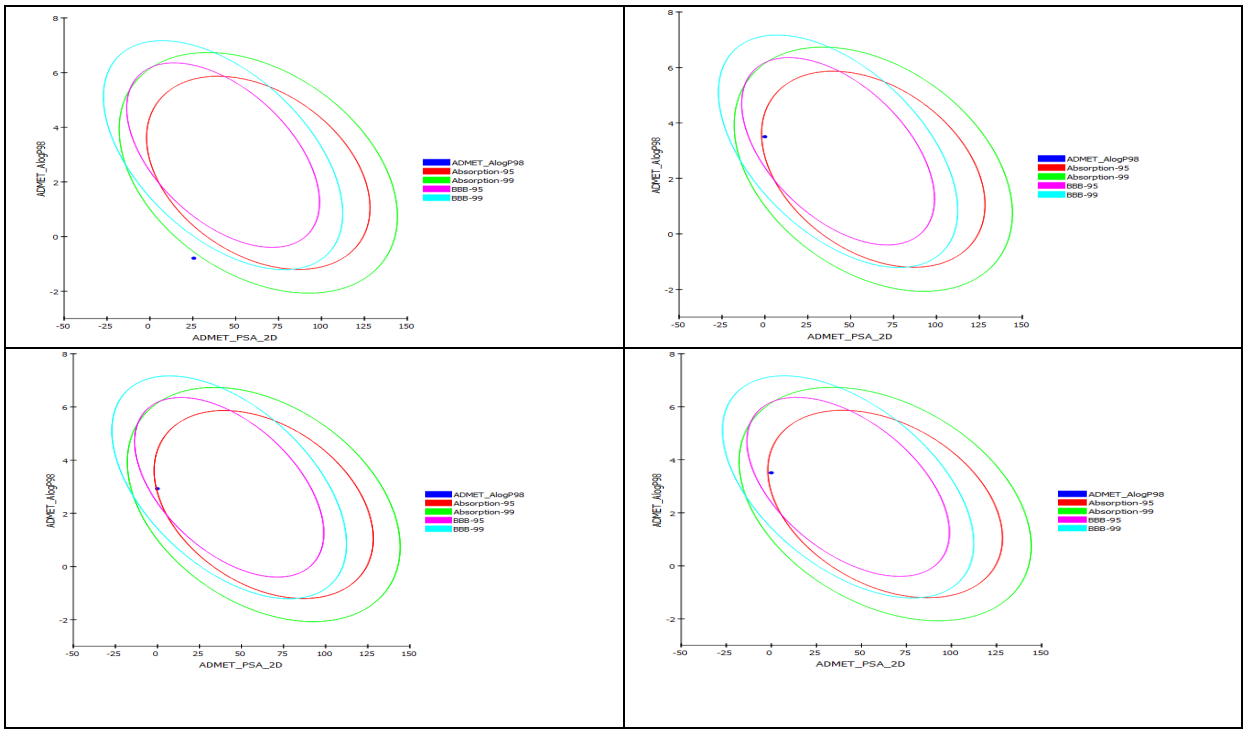

Fig 6. ADMET analysis Report of the Pharmacophores of the Pepper

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RESEARCH ARTICLE

Comparative Study of Different Methods of Reactive Power Compensation in Power System

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ABSTRACT

Reactive power compensation is a technique by which we try to manage the reactive power to improve the performance and quality of AC power. There is always a difference in the rise in loads and the capacity of the transmission line to deliver power. This leads to instability in the case of the transmission system. The reactive power compensation can be achieved by the use of latest optimizing tools that is FACTS. This paper gives an overview about different approaches on sustaining the quality and reliability of power using FACTS devices.

Key words: Reactive power compensation, FACTS, SVCs, and VSCs

INTRODUCTION

Power plays a vital role in the wholesome development and progress of any nation. Power quality has always been a challenging sector since the development of the grid-connected system. There is always a difference between the rise in loads and the capability of the transmissionline to deliver power. This further leads to inefficient transmission lines with more complications.Reactive power is generally denoted by "Q" which signifies the power which is not real in nature and the origin of such type of power is basically from the inductive and capacitive loads. The reactive power is measured in terms of VAR, that is volt ampere reactive. Hence, to maintain the reliability and economical aspects, it is very important to choose the most efficient reactive power compensation technology. The compensation technique is based on administration of reactive power to enhance the quality of AC power in an electrical network.
Power system stability has been a challenge over the years. Thus, it remains the thrust area of research to understand the intricate issues relating to stability and finding cost effective solutions. In the case of power transmission as well as a distribution system, the reactive power needs to compensate [1].Conventional power compensation techniques have no flexibility spatially. In the case of India CEA (Central Electricity Authority) has its guidelines for all domains

of the power system. The most uneven loads are experienced in the case of the distribution system. Reactive power compensation is to be the symbiotic effort of the distribution licensee and bulk consumer and reduce their dependence upon the grid to alleviate the said problem as per the CEA-2019 regulations. It means both the distribution licensee and the bulk consumer are required to compensate the reactive power in their system. The three major areas, which drive the power system analysis, are load flow analysis, transient analysis and short circuit analysis [1]. The performance analysis of reactive power compensators can be done using the ETAP software.

REACTIVE POWER CAUSES AND COMPENSATING TECHNOLOGY

Reactive power systems handle three kinds of power as active, reactive and apparent power. The true power which is beneficial for the system is the ACTIVE POWER. Reactive power production or generation is basically drives by the storage components and the losses.Various reasons for the creation of harmonics in supply source can be broadly classified as switching of power electronics devices, switching of loads and equipment such as transformer and heavy motors, unsymmetrical loading due to uneven loads on each phase of the supply system[9].The reliability of the power system can be assured by use of FACTS devices which ensures balancing the acting and reactive power in AC networks [2],[5]. Another beauty of this technology is that without merging new lines we can also improve the voltage profile and capacity [1]. FACTS are "alternating current transmission systems incorporating power electronics-based and other static controllers to enhance controllability and PTC of transmission lines" [4], [6],[9].The FACTS is a specialized term designated to the application of power electronics based solution for the quality of power in a power system. FACTS controllers can provide compensation both in series and shunt. FACTS controllers attempts compensation by modifying impedance voltage or phase angle.

The concept was first illustrated and defined by N.G.Hingorani in 1988.The FACTS system consists of static equipment's which are used for AC transmission system. FACTS is defined by the IEEE as "a power electronic based system and other static equipment that provide control of one or more AC transmission system parameters to enhance controllability and increase power transfer capability" [3]. The basic advantage of FACTS devices over its conventional counter part is fast control of current, voltage and impedance. The conventional solutions are less expensive but have limited dynamic behavior.Apart from that they are less optimal in nature.FACTS has always been advantageous to power sector.In the past few years it has gain its popularity a lot for its dynamic nature and versatility. Series controllers, shunt controllers, series-shunt controllers and series-series controllers are major four types of FACTS devices with different working principles[2],[3],[7].

SERIES CONTROLLERS

Series controllers can be broadlyclassified as-

1. **TCSC:** It is a capacitive reactance controller and it is made up of series capacitor bank in shunt with the thyristor-controlled reactor. This gives smooth series capacitive reactance which is variable in nature.

2. **SSSC:** The underlying working principle can be expressed as series controller whose output voltage is in quadrature with the line and control the increasing or decreasing overall reactive voltage drop across the line. It operates without an external energy source i.e. a static synchronous generator.

3. **TSSC:** It is a capacitance reactance controller. In this a series capacitor bank is in shunt with a thyristor. There is also a switched reactor, which helps to provide the control in a stepwise manner of series capacitive reactance.

SHUNT CONTROLLERS

Shunt controllers maintain the voltage profile through its optimal placement in the power system network. It works with the principle by injecting the current in the line that supplies the reactive power. The injected current gets in the phase quadrature and sustained line voltage while managing the active power.

SVS AND STATCOMS

SVCs (Static Var Compensators) are known as 1st generation devices and which is in use for many years to improve transmission line economics by solving dynamic voltage problems. It helps to combine the traditional methods of compensating elements [2], [8].Voltage Source Converters (VSC) based FACTS controllers are the STATCOMS. These have generally faster operating time as compared to that of SVCs.

CONCLUSION

With the latest emerging technology, we should also update the traditional methods of compensation with the new one. This paper generalises the different types of FACTS devices along with its features.The comparative study of FACTS devices is also discussed in it. FACTS devices has been serving Indiain power sector more than a decade . But now a days it is becoming more and more popular. As everyone needs power with quality, reliability, safety and security, so the Indian Power Sector for its better upliftment is adapting such methodologies. The use of this FACTS technology our power system is becoming more and more efficient day by day.

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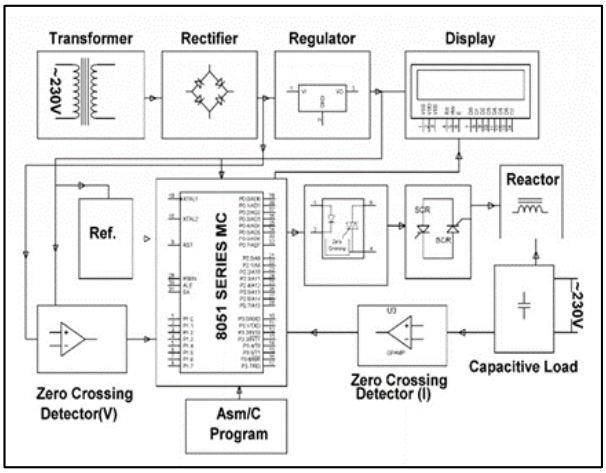

Fig.1.Generalised picture for FACTS

Table 1. Comparative study of different types of FACTS devices

S.NO	CONTROL ATTRIBUTES	FACTS CONTROLLERS					
		TCSC	SSSC	TSSC	STATCOM	SVC	
1.	Power flow control	✓	✓	✓			
2.	Voltage profile improvement				✓	✓	
3.	Line commutated	✓		✓		✓	
4.	Forced commutated		✓		✓		
5.	Voltage source converter		✓		✓		
6.	Current source converter	✓	✓	✓	✓	✓	
7.	Transient and dynamic converter	✓	✓	✓		✓	
8.	Damping oscillation	✓	✓	✓	✓	✓	
9.	Fault current limiting	✓		✓			
10.	Voltage stability	✓	✓	✓	✓	✓	

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REVIEW ARTICLE

Phenomenon of Molecular Gastronomy or Physiology of Digestion in Insects

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ABSTRACT

Molecular gastronomy is a subdiscipline of food science that seeks to investigate the physical and chemical transformations of ingredients (edible materials) that occur during cooking and the sensory phenomena associated with their consumption. In insects, however, these transformations are done by the sundry enzymes secreted in the salivary gland and midgut epithelial cell. For normal growth, development and reproduction, carbohydrates, proteins and fats are the main alimental components consumed by insects to engender energy which can be procured from a wide variety of animals, vegetables and dead organic matters. Insects ingest food in macro molecular form, which cannot be used directly by body ergo they must be broken down into more minuscule components. Depending on the insect and its mode of life, various mechanisms are exploited for finding and recognition of such food. However, vision and olfaction are of widespread paramountcy. In biting and chewing insects, contact chemoreceptors are present in all the mouthparts except the mandibles, additionally on the dorsal and ventral walls of the cibarium and have immensely colossal numbers of sensilla in groups with especially sizably voluminous numbers on the tips of the maxillary and labial palps. The victualing comportment shown by the insects are due to the presence of such sensilla and this comportment is governed by two components, one is phagostimulants and other alimenting or feeding deterrents. Information from all the sensilla is integrated in the central nervous system and whether or not the insect feeds depends on the

balance between phagostimulants and deterrents. The knowledge on molecular gastronomy or physiology of digestion can be exploited for development of different stomach poisons and antifeedants for the management of various pests of economic consequentiality. The conception of utilizing entomopathogens for the management of insect pests is primarily based on the principles of physiology of digestions in insects.

Key words: deterrents, digestion, molecular gastronomy and phagostimulants

INTRODUCTION

Molecular gastronomy is a subdiscipline of aliment science that seeks to investigate the physical and chemical transformations of ingredients (edible materials) that occur during cooking and the sensory phenomena associated with their consumption (Schenkelaars *et al*., 2010). Corresponding to other organism, insects additionally require victuals as a source of energy to perform various functions like growth, development and reproduction. However, these transformations are done by the sundry enzymes secreted in the salivary gland and midgut epithelial cell present in insect body. This source of energy customarily consumed in the form of carbohydrates, proteins and fats and is present in a wide array of animals, vegetables and dead organic matter. The study of the victuals requisites of organisms is termed as nutrition and these studies may include the constituents of the normal diet, or the studies may be expanded to include substances that engender energy in the most efficient way. The aliment constituents may be further relegating into essential and non-essential constituents. Essential constituents are those that must be included in the diet because they cannot be synthesized by either the metabolic system of the animal or the mundane compliment of symbionts e.g., vitamins, amino acids and certain mineral salts whereas the non-essential betokens aliment materials that may have to be consumed to produce energy that can be converted into form in which they can be utilized through metabolic processes e.g., carbohydrates, proteins and fats. Most insects have qualitatively homogeneous alimental requisites since the rudimental chemical composition of their tissues and their metabolic processes are generally homogeneous but differences in alimental requisites do subsist. These may be the result of evolutionary changes associated with alimenting on substrates with quantitatively and sometimes qualitatively. The pabulum ingested by the insects for their normal growth and development are in macro molecules consequently they have to be broken down into more diminutive molecules so that they can be facilely absorbed by insect's body which is kenned as digestion. Digestion is carried out by digestive enzymes and these enzymes are present in the saliva and in the secretions of the midgut. After digestion, the products are absorbed in the midgut and hindgut of the insects.

Nutrition and its importance

Carbohydrates

Carbohydrates play a fundamental role in the life of animals and plants. They are the major source of energy and additionally act as a structural function (Insects cuticle contains chitin, a polysaccharide). The utilization of the carbohydrate depends upon the competency of the insect species to convert the intricate polysaccharides and oligosaccharides into assimilable simple sugars. The carbohydrates in the order of utilization by insects generally include: dextrin, fructose, glucose, lactose, maltose, mannitol, raffinose, sorbitol, starch, sucrose and trehalose. Glucose and fructose are facilely utilized by insects but pentose is not utilized at all.

Results from the study of the locusts *Schistocerca gregaria* (Forsk) denote the quantitative requisites, for carbohydrate. These insects grew poorly and failed to consummate development when carbohydrate other than indigestible cellulose was omitted from their diet. Mundane magnification was obtained when glucose or sucrose composed 13

per cent of the diet, but some experiments designated that this percentage was inadequate for good development beyond the third instar. Copacetic growth and development occurred with 26% carbohydrate (Dadd, 1960).

Siekmann *et al*., 2001, additionally reported that sugar consumption can increment the longevity and lifetime fecundity of many species of parasitic wasps. After a single honey repast differing in sugar concentration (25, 47, 86 %) and timing (day of emergence and 24 h, later) the researchers had quantified the longevity of the parasitoid *Cotesia rubecula*. Survival was analysed with Cox's Proportional Hazards Model. The jeopardy of starving to death in sugar-victualed wasps was truncated by 0-73% in comparison to unfed wasps, depending on sugar concentration and timing. Longevity was significantly incremented by sugar concentration.

Proteins and Amino acids

Amino acids are conventionally present in the diet as proteins and the value of any ingested protein to the insect depends on its amino acid content and the facility of the insect to digest it. Amino acids are required for the engenderment of proteins which are utilized for structural purposes, as enzymes, for convey and storage and as receptor molecules. They are withal involved in morphogenesis. Tyrosine is essential for cuticular sclerotization and tryptophan for the synthesis of visual screening pigments. γ-aminobutyric acid and glutamate, are neurotransmitters and, in some tissues and some insects, proline is a consequential energy source. Albeit proteins contain some 20 different amino acids, customarily only 10 of these are essential *viz*., arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine in the diet (Dadd, 1977).

In general, the absence of any one of these amino acids obviates growth. Some insects have essential requisites for adscititious amino acids. Proline is the most prevalent of these, e.g., it is essential for the development of the mosquito (*Culex*), and for several other dipterans as well as the silkworm (*Bombyx*). In some other insects, it is obligatory for good growth and survival, albeit it is not absolutely essential. Aspartic acid or glutamic acid is additionally essential for *Phormia* and the silkworm.Wilkinson and Douglas, 2003, withal reported that certain clones of *Aphis fabae* Scop. reared on diets destitute of histidine, methionine, threonine and valine, showed despondence on larval survival, larval growth rate and adult fecundity.

Lipids

Molecules that helps in constituting the building blocks that contributes to structure and function of living cells are known as lipids which include fats, waxes, sterols, fat soluble vitamins viz., A, D, E and K, monoglycerides, diglycerides, triglycerides, phospholipids and others. Lipids have biological functions like storing energy, signaling, and acting as structural components. Major types of lipid found in plants are monogalactosyl diglycerides, digalactosyl diglycerides and triacylglycerols whereas in animals are triacylglycerols, phospholipids and cholesterol.

Lipids are absorbed in the form of adipose acids and sterols. The polyunsaturated adipose acids are essential for development of many lepidopterans, dipterans and orthopterans, more concretely in connection with wing expansion and prosperous emergence from the pupal cuticle. For example, shortage of linoleic acid in the diet of *Ephestia* sp. results in the moth emergence without scales on the wings because the scales do not disunite from the pupal cuticle. Larval mosquitoes additionally required linoleic acid in their dietary source, without them the emerging adults are impotent and unable to fly (Stanley-Samuelson *et al*., 1992; Dadd, Kleinjan and Stanley-Samuelson, 1987).Generally, insects are unable to synthesize sterols. As a consequence, they customarily require a sterol in the diet, albeit some may obtain their sterols from symbiotic micro-organism. Insects alimenting on the animal tissues obtain cholesterol directly from their victuals and some plant victualing insects, process the prevalent plant sterols to engender cholesterol. In most species, cholesterol is a compulsory precursor in the synthesis of ecdysone and withal essential structural components of cell membranes (Bernays, 1992).

Mouthparts and its Sensilla

Alimenting or feeding in insects is facilitated by the mouthparts which comprises of unpaired labrum in front, a median hypopharynx behind the mouth, a pair of mandibles and maxillae laterally, and a labium forming the lower lip. The form of the mouthparts is cognate to diet, but two rudimental types can be apperceived: one habituated for biting and masticating solid victuals, and the other acclimated for sucking up fluids. Most of the sensilla on the mouthparts are contact chemoreceptors, but mechanoreceptors are withal prevalent and olfactory sensilla are often present on the palps. Biting and masticating insects have contact chemoreceptors on all the mouthparts except the mandibles. They withal have chemoreceptors on the dorsal and ventral walls of the cibarium, often called epipharyngeal and hypopharyngeal sensilla, respectively. Orthoptera and Blattodea have astronomically immense numbers of sensilla in groups with especially astronomically immense numbers on the tips of the maxillary and labial palps. For example, *Gryllus bimaculatus*, has over 3000 sensilla on each maxillary palp. Because each sensillum contains at least four neurons, the potential chemosensory input to the central nervous system is considerable; an adult locust has about 16000 chemosensory neurons on the mouthparts. The number of chemosensory neurons increases in case of orthopteroid insects each time the insect molts. By contrast, caterpillars have only about 100 neurons in mouthpart receptors and the proximately associated antennae; the number does not increment during larval life. Fluid-victualing insects conventionally have chemoreceptors at the tip of the labium, on the palps when these are present, and in the walls of the cibarium. In integration, at least some planthoppers have an olfactory sensillum towards the tip of the rostrum. No chemoreceptors are present on the mandibular and maxillary stylets. Aphids have only mechanoreceptors at the tip of the labium; their only chemoreceptors on the mouthparts are in the cibarium. In perforating and sucking insects (Hemiptera and Culicidae) only the cibarial sensilla come directly into contact with the pabulum as it is ingested; the labium does not enter the tissues of the host so that its sensilla can only monitor the outer surface of the pabulum, either plant or animal. The axons of contact chemoreceptors and mechanoreceptors on the mandibles, maxillae and labium end in arborizations in the corresponding neuromeres of the subesophageal ganglion, but the axons from olfactory sensilla on the palps run directly to the olfactory lobes. The axons of sensilla on the labrum arborize in the tritocerebrum (Backus, 1988 and Chapman, 1982).

Behaviour of feeding

Afore an insect commences to aliment or feeding, it exhibits a series of behavioural activities which may lead to acceptance or rejection of the food. A grasshopper first physically contacts the surface of the plant with the sensilla at the tips of its palps. This demeanor enables the insect to monitor the chemicals on the surface of the plant wax and perhaps withal the odour of the plant. This may lead the insect to repudiate the plant without further investigation or to make an exploratory bite, presumably relinquishing chemicals from within the plant which in turn, may result in rejection, or acceptance. Essentially homogeneous behaviours are optically discerned in caterpillars and leaf-orally consuming beetles.

These comportments are governed by two factors; phagostimulants and feeding deterrent. Phagostimulants are the principal chemicals present in the plants that induced victualing. For example, sucrose and hexose sugars are the phagostimulants of leaf-eating insects. However, the compounds that inhibit feeding are kenned as feeding deterrents. For example, azadirachtin in neem and karanjin and pongamol in *Pongamia pinnata* acts as antifeedants to lepidopteran pests. Information from all the sensilla is integrated in the central nervous system. Whether or not the insect aliments depends on the balance between phagostimulants and deterrents.

Insects that aliment only on categorical plant taxa may require the presence of a compound that is characteristic of the plant species, or group of species. For example, many caterpillars and beetles that feed on plants in the family Brassicaceae, which includes cabbage, are stimulated to aliment by mustard oil glucosides (glucosinolates) that are characteristic of this plant family (Bernays and Chapman, 1994). In the larvae of *Bombyx*, Hamamura *et al*., (1962) analysed the factors promoting feeding and have isolated disunited factors which lead to attraction, biting and

perpetuated swallowing. The chemical β- sitosterol and morin have been isolated as biting factors, and cellulose as swallowing factor whose effect is enhanced by a number of co-factors such as sucrose, inositol, inorganic phosphate and silica. In case of fluid feeding insects, e.g., in aphids, host plant selection occurs mainly after alighting when the insect probes the plant with its proboscis, testing the physical and chemical properties of sap. In predators, visual and mechanoreceptors play a very paramount role in capturing their prey.

Alimentary canal

The alimentary canal of insects is divided into three main regions *viz*., the foregut or stomodeum, the midgut or mesenteron and the hindgut or proctodeum. The foregut and hindgut are ectodermal in inception while midgut is endodermal. The epithelium of all components of the gut consists of a single layer of cells. Since the foregut and hindgut are ectodermal in inception, the cells secrete cuticle which is perpetual with that covering the outside of the body. The lining cuticle is kenned as the intima. It is shed and renewed at each molt. Albeit the midgut is not responsible for secreting the cuticle, however, it is known to secrete a delicate peritrophic envelope around the victuals in some insects. Customarily the gut is a perpetual tube running from the mouth to the anus, but in some insects that aliment on a fluid diet containing little or no solid waste material, the connection between the midgut and the hindgut is occluded. In certain plant-sucking heteropterans, the occlusion is in between the different components of the midgut, whereas larval neuropterans digest their prey extra-orally. A homogeneous modification occurs in the larvae of gregarious Hymenoptera with the result that the larvae never foul the nest. In these insects a pellet of fecal matter is deposited at the larval-pupal molt (Chapman, 1985; Poisson and Grassé, 1976).

After recognizing the host plants by various sensilla, the insects have to ingest the aliment materials and transform or digest them into micro molecules with the help of various digestive enzymes in the gut. These enzymes are secreted in the salivary glands and in midgut epithelial cell. Salivary glands are present in the foregut region just beneath the alimentary tract. These glands are of two types, acinous (alveolar) and tubular glands. In acinous glands, the central, or zymogen, cells have extensive endoplasmic reticulum and golgi bodies and probably engender the enzymes. The peripheral or parietal cells have an extensive microvillar border to the channel leading to the lumen of the duct. These cells are responsible for the kineticism of dihydrogen monoxide into the lumen of the gland. In tubular glands both functions appear to be performed by the same cells. The kineticism of dihydrogen monoxide results from the engenderment of an osmotic gradient across the cells by H+-ATPase pumps in the microvillar plasma membrane. The pumps move protons into the lumen, and the protons are then exchanged for sodium or potassium at cation/H+ antiporters resulting in a high ionic concentration in the lumen. The duct cells of acinous glands, or the cuboid cells of tubular glands, abstract cations from the salivary secretion, and those of the cockroach have sodium/potassium pumps in the basal plasma membrane (Just and Walz, 1994).

Acinous glands are innervated by axons from the subesophageal ganglion and from the stomatogastric system. In both cockroach and locust, one of the innervating neurons engenders dopamine, another serotonin. Dopamine stimulates the secretion of fluid, while serotonin causes the central cells to engender and secrete the enzymes (Just and Walz, 1996). In additament, a network of branches of an octopaminergic neuron is proximately associated with the salivary glands of *Locusta*. Tubular glands are not directly innervated albeit in the female mosquito, *Aedes aegypti*, a plexus of nerves proximately circumvents part of the gland. In both *Aedes* and *Calliphora*, serotonin, acting directly on the gland, regulates the engenderment and relinquish of saliva. In *Aedes*, the serotonin is relinquished from the neural plexus adjacent to the gland, while in *Calliphora* it emanates from neurohemal organs on the ventral nerves in the abdomen. In most insects, engenderment and relinquish occur together, but in insects with a salivary reservoir the two processes may be discretely controlled. Engenderment ceases when sensory input is abstracted. In *Calliphora* it takes less than two minutes to clear the serotonin from the hemolymph when alimenting ceases and the interpseudotracheal pegs are no longer stimulated (Ali, 1997; House and Ginsborg, 1985).

Functions of Salivary Glands

Salivary glands moisten food, lubricate mouthparts, contain digestive enzymes, non-digestive functions includes toxins of predators that affect CNS of prey, anti-coagulants and Silk production. Salivary glands are also involved in disease transmission.

Mechanisms of Digestive Enzyme Secretion

Mechanisms of digestive enzyme secretory and their control are probably the least understood areas in insect digestion. Studies of secretory mechanisms have only described major differences, which seem to include unique aspects not optically discerned in other animals. The digestive enzyme, as with all animal proteins, are synthesized in the rough endoplasmic reticulum and processed in the golgi intricate, and are packed into secretory vesicles. There are several mechanisms by which the contents of the secretory vesicles are liberated in the midgut lumen. In holocrine secretion, secretory vesicles are stored in the cytoplasm until they are relinquished, during which the whole secretory cell is disoriented to the extracellular space. During exocytic secretion, secretory vesicles fuse with the midgut cell apical membrane, vacating their contents without any loss of cytoplasm. In contrast, apocrine secretion involves the loss of at least 10 per cent of the apical cytoplasm following the relinquishment of secretory vesicles. These have aforetime undergone fusions, leading to more sizably voluminous vesicles that, after release, ineluctably free their contents by solubilization. When the loss of cytoplasm is diminutively minuscule, the secretory mechanism is called microapocrine. Release of budding double-membrane vesicles or, at least in insect midguts, pinched-off vesicles are included in microapocrine secretion which may contain a single or several secretory vesicles. In both cases, the secretory vesicle contents are released by membrane fusion and/or by membrane solubilization caused by high pH contents or by luminal detergents (Terra and Ferreira, 1994; Lehane *et al*., 1996). Secretion by midgut cells of hemipterans exhibit special features, as seen in Immunocytolocalization data due to the presence of perimicrovillar membranes in addition to microvillar ones (Silva *et al*., 1995).

Digestion

A large part of the food ingested by insects is macromolecular, in the form of polysaccharides and proteins, while lipids are present as glycerides, phospholipids and glycolipids. Generally, only small molecules can pass into the tissues and the larger molecules must be broken down into smaller components before absorption can occur. Enzymes concerned with digestion are present in the saliva and in the secretions of the midgut. In addition, digestion may be facilitated by micro-organisms in the gut (Applebaum, 1985). Digestion may be classified into two types *viz*., extra-intestinal digestion and digestion in the gut lumen. In extra- intestinal digestion, the insects inject saliva into their food before starting to ingest and as it contains enzymes, considerable digestion may occur. Such extra-intestinal (or extra-oral) digestion may constitute a major part of the total digestion. This is true in case of some hemipterans at all stages of their development, in adult Asilidae and Empididae amongst the Diptera, and in the larvae of Neuroptera and some beetles such as *Dytiscus* and the Lampyridae. Extra-intestinal digestion is probably also significant in some adult carabid beetles, although the bulk of digestion occurs in the gut. Amongst the plant-sucking Hemiptera, extra -intestinal digestion is most significant amongst seed feeding species such as *Oncopeltus* and *Dysdercus*, although it may also be important in species feeding from the parenchyma of plants. However, it is amongst the predaceous Heteroptera that extra-intestinal digestion is most widespread. Predaceous larval beetles and Neuroptera have biting mandibles with which they capture their prey and through which enzymes are injected into the prey and the digested contents withdrawn. Beetles have no salivary glands so it must be presumed that, in this case, the enzymes originate in the midgut. Adult carabids in the tribes Carabini and Cychrini masticate their prey before ingesting the fluid contents. Some extra-intestinal digestion occurs and may be considerable (Cohen, 1995).

Digestion in the gut lumen

Regardless of their feeding habits, most insects must digest proteins, carbohydrates and lipids and so they have a similar array of enzymes in the midgut. Nevertheless, the enzymes produced do reflect the type of food eaten by each species and stage.

Digestion of Proteins

The digestion of proteins involves endopeptidases, which attack peptide bonds within the protein molecule, and exopeptidases, which remove the terminal amino acids from the molecule. Within these general categories, the enzymes are classified according to the nature of their active sites and the sites at which they cleave protein molecules. The principal endopeptidases in the majority of insects are the serine proteases, trypsin and chymotrypsin, which have serine at the active site. Trypsin cleaves peptide linkages involving the carboxyl groups of arginine and lysine residues. Chymotrypsin is less specific, cleaving bonds involving the carboxyl groups of tyrosine, phenylalanine and tryptophan preferentially, and bonds involving other amino acid residues more slowly. Usually both types of enzyme are present in any insect with serine proteases. However, in many Coleoptera and in blood-sucking Hemiptera, the main endopeptidases have cysteine or aspartic acid at their active centers (Murdock *et al*., 1987). They are called cathepsins. Carboxypeptidases that attack peptides from the -COOH end, and aminopeptidases that attack the chain from the -NH_2 end comes under exopeptidases.

Keratin : Keratin is a protein occurring in wool, hair and feathers. Hard keratins contain 8–16% cystine, and disulfide linkages between cystine residues render the protein very stable. Nevertheless, a number of insects normally feed on keratinous materials. These include larvae of the clothes moth (*Tineola*), carpet beetles (Dermestidae) and numerous biting lice (Ischnocera). *Tineola* larva has a complex mixture of proteolytic enzymes. In addition to those normally present in caterpillars, it possesses a highly active cysteine desulfhydrase which produces hydrogen sulfide from cysteine. This contributes to the strong reducing conditions in the gut which promote the breaking of disulfide bonds in the keratin (Yoshimura *et al*., 1988).

Digestion of carbohydrates

Carbohydrates are generally absorbed as monosaccharides so disaccharides and polysaccharides in aliment require digestion. The polysaccharide cellulose is a major constituent of green plants, but albeit many insects are phytophagous, relatively few of them are able to utilize cellulose. Those that do, proximately always depend on micro-organisms to digest it. However, starch and glycogen, the main storage polysaccharides of plants and insects, respectively, are digested by amylases that hydrolyse 1-4-α-glucosidic linkages. There may be discrete endo- and exo-amylases, acting on starch internally or terminally. The common disaccharides sucrose and maltose contain a glucose residue linked to another sugar by an α-linkage and are digested by α-glucosidases. As with the proteolytic enzymes, α-glucosidases may exhibit different substrate specificities. For example, a trehalase is often present, though it is not pellucid why this should occur in insects that feed on plants where trehalose is not found. The naturally occurring β-glucosides (e.g., salicin and arbutin) are conventionally of plant inception and the highest β-glucosidase activity is found in phytophagous insects. Cellobiose is a product of cellulose digestion and a cellobiase is often present even in insects where cellulose digestion is not known to occur.

Cellulose is polymer of glucose in which the glucose molecules are joined by β-1, 4 linkages. The chains of cellulose are unbranched and may be several thousand units long. Hydrogen bonds occur within and between cellulose molecules, resulting in a crystalline state which contributes to the resistance of cellulose to digestion. Three classes of enzyme are involved in its hydrolysis: endoglucanases, which assailment the bonds between glucose residues within the chain, exoglucanases that attack bonds near the terminuses of the cellulose molecule and β-glucosidases that

hydrolyze cellobiose. Exoglucanases are conventionally more active against crystalline cellulose than endoglucanases.

Cellulose digestion with endosymbiotic microorganism

Amongst the termites, species in all the families except Termitidae have huge numbers of flagellate protozoans in the paunch. These organisms may constitute more than 25% of the wet weight of the insect. Many different species of flagellate may be present in one species of termite, but the species are, in general, only found in termites. The protozoans engulf fragments of plant material and ferment the cellulose, producing acetate and other organic acids, carbon dioxide and hydrogen. Fermentation is an anaerobic process and conditions in the paunch are highly reducing. The organic acids are absorbed in the hindgut and provide a large proportion of the respiratory substrate used by the insect. These insects probably do produce cellulose-digesting enzymes themselves, but their activity is insufficient for the termites to sustain themselves without the aid of the symbionts. Flagellates also occur in the hindgut of the wood-eating cockroach, *Cryptocercus*. Other termites use fungi to digest cellulose. Species of the subfamily Macrotermitinae cultivate fungi of the genus *Termitomyces* in fungus gardens. The fungus grows on this comb, producing cellulolytic enzymes, and the termites then feed on the fungus and the comb. While doing so they ingest the cellulases produced by the fungus. These may contribute to cellulose digestion in the termite gut, but probably only to small extent.

Bacteria are responsible for cellulose digestion in larval scarab beetles and in some crickets and cockroaches. The former commonly feed in decaying wood and they acquire the bacteria with the food. Digestion of the wood occurs in the fermentation chamber of the hindgut where it is retained by branched spines arising from the intima.Termites in the family Termitidae, other than Macrotermitinae, probably do produce their own cellulose digesting enzymes, but whether or not other insects do so is open to question. It is likely that in most cases, as in grasshoppers, small quantities of cellulose are digested by micro-organisms ingested with the food **(**Breznak and Brune, 1994; Martin, 1987, 1991; Wood and Thomas, 1989).

Digestion of lipids

Lipids that contain fatty acids comprise storage lipids and membrane lipids. Storage lipids, such as oils present in seeds, and fats in adipose tissue of animals, are triacylglycerols (triglycerides), and are hydrolyzed by lipases. Phospholipids and glycolipids, such as mono- and digalactosyldiglycerides are included under membrane lipids. Phospholipids are digested by phospho-lipases. Phosphate moieties need to be removed from phosphorylated compounds prior to absorption. This is accomplished by non-specific phosphatases. The phosphatases may be active in an alkaline or acid medium (Terra *et al.,* 1996).

Absorption

The products of digestion are absorbed in the midgut, but some absorption, especially of salts and water, also occurs in the hindgut. The cells in the midgut concerned with absorption are often the same cells that produce enzymes in a different phase of their cycle of activity. Absorption may be a passive or an active process. Passive absorption depends primarily on the relative concentrations of a compound inside and outside the gut, diffusion taking place from the higher to the lower concentration. In addition, in the case of electrolytes, the tendency to maintain electrical equilibrium inside and outside the gut epithelium will interact with the tendency to diffuse down the concentration gradient. These two factors together constitute an electrochemical potential. Certain metabolic processes are involved in moving a substance against its concentration gradient in case of active absorption. In the midgut of caterpillars, and probably of other insects, the energy for these processes is derived from a V (vacuolar) - type ATPase in the apical plasma membranes. This pumps protons from the cells into the gut lumen and the protons are exchanged for potassium, or perhaps sometimes, another ion. Movement of potassium down its electrochemical gradient into the

cell is coupled with that of amino acids, and perhaps other compounds, at symports (Dow, 1986; Harvey and Nelson, 1992; Lepier *et al*., 1994).

Absorption of amino acids: If amino acids are present in high concentration in the gut lumen they diffuse across the epithelium down a concentration gradient and at low concentrations, amino acid absorption occurs at symports coupled with the movement of a cation, usually potassium, into the cell.

Absorption of carbohydrates: It is a passive process depending on diffusion from a high concentration in the gut to a low one in the hemolymph.

Absorption of lipids: Lipids appear to be absorbed primarily as fatty acids. In *Stomoxys sp.,* fatty acids are absorbed in the posterior zone of the midgut and then incorporated into phospholipids and triacylglycerides. In caterpillars, the turnover of triacylglycerides is rapid and it appears that they are transported to the basal parts of the cell where they are actively exported as diacylglycerides. Sterols appear to be absorbed unchanged, but, in some caterpillars, sterols are esterified in the gut cells.

CONCLUSION

By applying the cognizance of molecular gastronomy or the physiology of digestion, different stomach poisons and antifeedants have been developed for the management of various pests of economic consequentiality. Further exploitation of this concept may helps in designing new modified tactics under Integrated Pest Management. The conception of utilizing entopathogens for the management of insect pests is primarily predicated on the principles of physiology of digestions in insects.

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RESEARCH ARTICLE

In-silico Analysis of Effects of *Cardamom* Extract as Targeted Therapy for Lung Cancer

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ABSTRACT

Antiquated India is one of the pioneers of investigations of plants as medication, for example Ayurveda. In our social and monetary life we barely deal with our food we are taking. One such novel herb is *Cardamom* which has frequently been viewed as a mind supporter. The entire plant including the blossoms can be utilized for restorative purposes. It has a harsh and sweet taste and is known to give a cooling vitality. *Cardamom* is loaded with cancer prevention agents that are basic for carrying on with a sound life. We are utilizing this property of *Cardamom* to get some new medications for Aster Yellow. The employments of different pesticides, additives, and so on transform the nourishments into poison. Also the reactions of these pesticides and additives, and so on are perilous as on the grounds that it prompts commencement of various malignant growth. In this entire world, the quantity of patients kicking the bucket from malignant growth is expanding in a compromising manner. In-silico investigation has done utilizing programming and we further focused on a portion of the qualities answerable for Lung cancer and pharmacophores from *Cardamom* and destroyed some silico examination. In this we have discovered that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Cardamom, Docking, *In silico* Analysis, Pharmacophore

INTRODUCTION

According to review, the cardamoms are the compartments of dried natural items in different genera of the Zingiberaceae family, in a general sense *Elettaria*, *Amomum* and *Aframomum*. Among them, *Elettaria cardamomum* (L.) Maton is commonly huge and is grown overwhelmingly in southern India (Govindarajan et al., 1982). The counterfeit cardamom, huge cardamom, or dim *cardamom* from the banded together class *Amomum* is nearby to

Nepal, Sikkim, Bengal and southeast Asian countries. African cardamom, which is naturally known as *Aframomum* danielli (Hook.f.) K. Schum., is neighborhood to south east Africa especially in Tanzania, Cameroon, Madagascar and Guinea (Govindarajan et al., 1982; Adegoke et al., 1998). Little *cardamom* is comprehensively evolved in Nepal and Sikkim and to a compelled degree with the gigantic *cardamom* (*Amomum* subulatum Roxb.). Regardless, all inclusive trade is by and by compelled to Asian countries most certainly because of critical costs. Around the globe, *cardamom* is seen as the "sovereign of flavors" for its flawless scent and taste, and is the third most expensive get-up-and-go after saffron and vanilla.

Elettaria cardAmomum (L.) Maton is ordinarily known as meager cardamom, green cardamom, or certifiable *cardamom* and is created in India, Guatemala, Sri Lanka, Nepal, Indonesia, Costa Rica, Mexico and Tanzania (Garg et al., 2016). In India, *cardamom* is created in heights running from 900 to 1400 m above msl (mean sea level) covering three southern Indian states (Kerala, Karnataka and Tamil Nadu). In Kerala, it is produced generally in the Indian *Cardamom* Hills covering a region of 1050 square kilometers alloted as *Cardamom* Hill Reserves, (Madhusoodanan et al., 2002). The home grown name of cardamom, Elettaria cardamomum, began from the Tamil word "Elettari" which insinuates the seeds of *cardamom* (Mahindru, 1982).

For a significant long time, *cardamom* holders have been used for culinary and regular drug applications including controlling asthma, teeth and gum ailments, stomach related and kidney issue (Hamzaa et al., 2012; Saeed et al., 2014), cascades, disorder, free entrails and cardiovascular issue (Gilani et al., 2008; Khan et al., 2011). The essential oil and other bioactive metabolites accumulated in *cardamom* cases add to their trademark smell and utility as an utilitarian food, pharmaceutical, and nutraceutical (Hamzaa et al., 2012). The essential oil (EO) substance of *cardamom* cases changes from 6 to 14% dependent upon the sort and dealing with procedures (Menon, 2000). EO of *cardamom* cases have fantastically monoterpene constituents, for instance, 1,8-cineole, α-pinene, α-terpineol, linalool, linalyl acidic corrosive induction and nerolidol and the ester constituent α-terpinyl acidic corrosive deduction (Kaskoos et al., 2006; Yashin et al., 2017; Ashokkumar et al., 2019b), all of which have supportive focal points including malignancy anticipation operator, anticancer, antidiabetic, relieving, antifungal, antiviral and gastroprotective activities (Nirmala, 2000; Marongiu et al., 2004; Hamzaa et al., 2012; Winarsi et al., 2014). Continuous reports attested that flavonoids, terpenoids, anthocyanins, alkaloids and other phenolic constituents from *cardamom* were being used for controlling cardiovascular, pneumonic, kidney and lung related disperses (Vaidya and Rathod, 2014). The purpose of this review is to include the essential phytochemicals and valuable effects of *cardamom* fundamental oil (CEO) and focuses on human prosperity.

MATERIALS AND METHODS

Various pharmacophores of Methi leaves have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Aster Yellow has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for Rice Tungro Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using 'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy

their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 5 phytocompounds from Cumin were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 4 phytochemicals reported from Cumin was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Cumin with the selected targets of Lung cancer. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Cumin to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the Cumin and can be commercialized as the natural drug for the Wilt Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Lung cancer

Sl.No	Pharmacophores from Cardamom	Targeted Animal Gene (Lung cancer)	PDB No of the Genes
1	Threonine	telomerase reverse transcriptase	5UGW
2	1,8- Cineole	tumor protein p63	6FGN
3	limonene	cholinergic receptor nicotinic alpha 5 subunit	5HBT

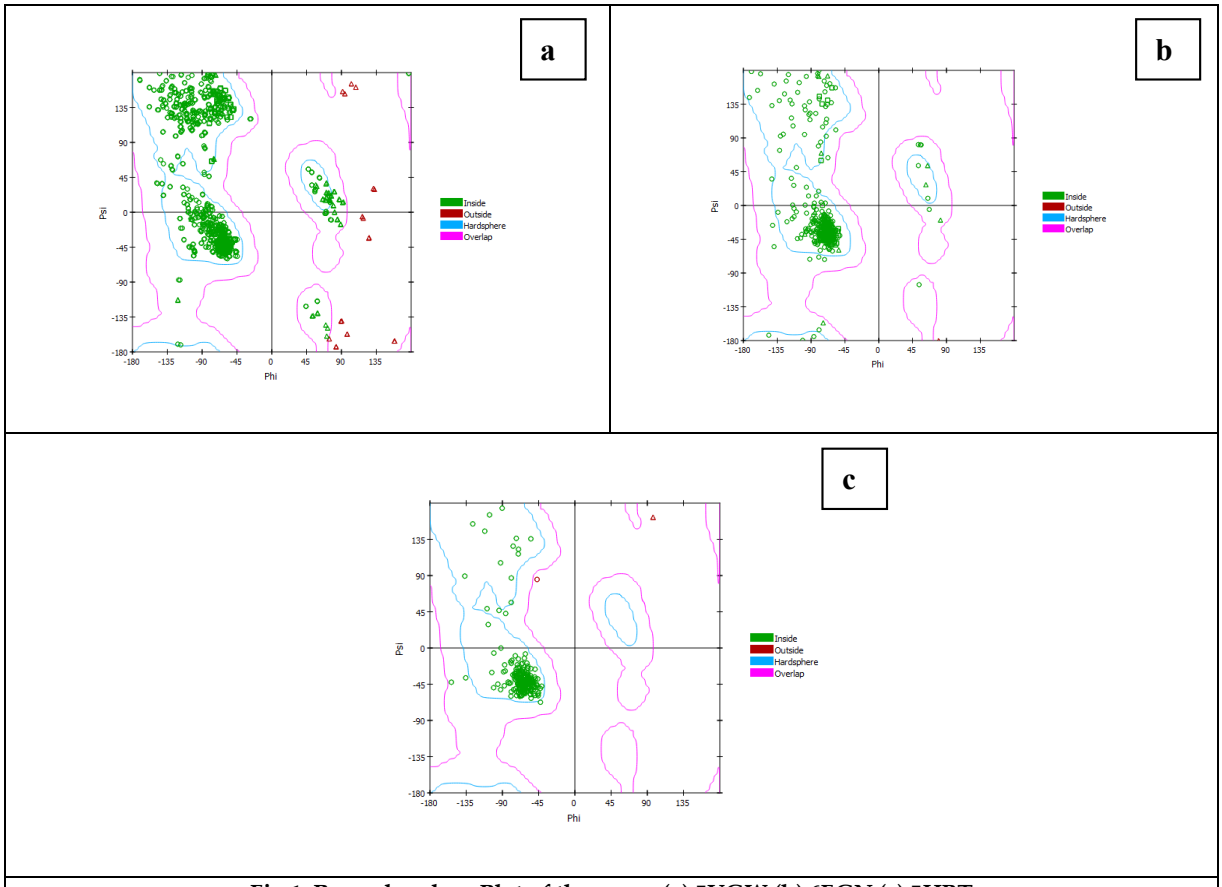

Fig 1: Ramachandran Plot of the genes (a) 5UGW (b) 6FGN (c) 5HBT

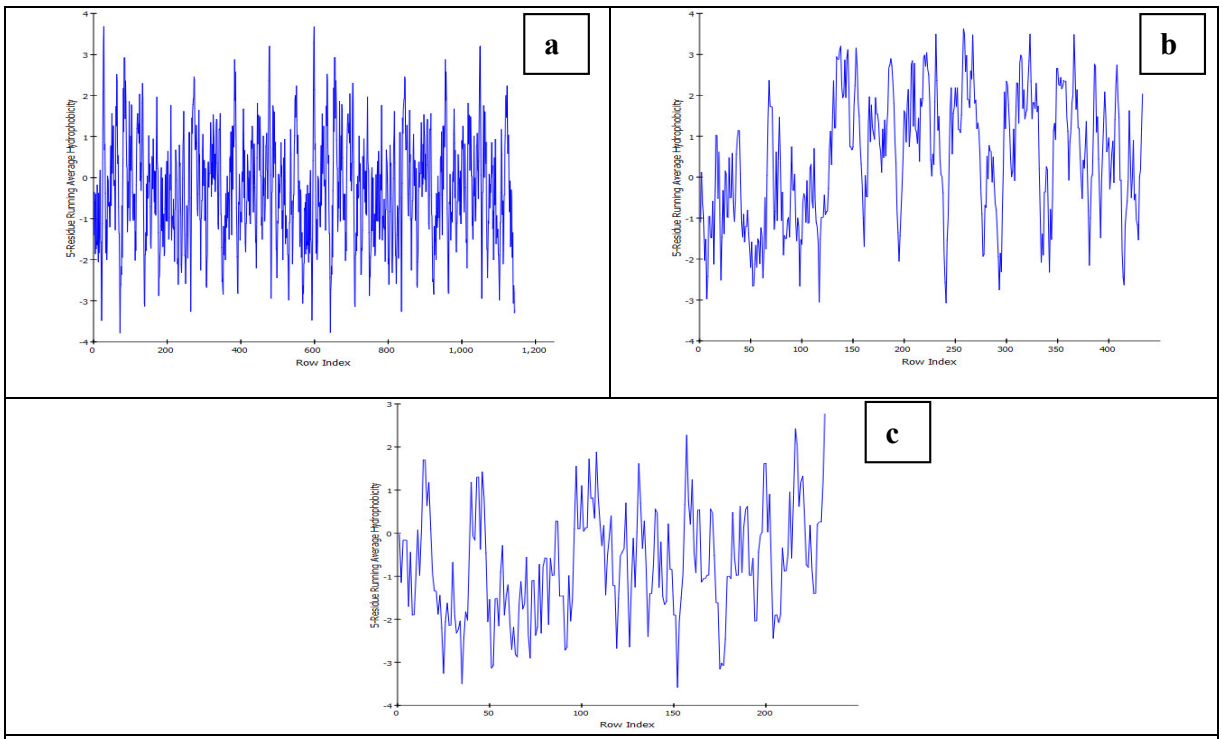

Fig 2: Hydrophobicity Plot of the genes (a) 5UGW (b) 6FGN (c) 5HBT

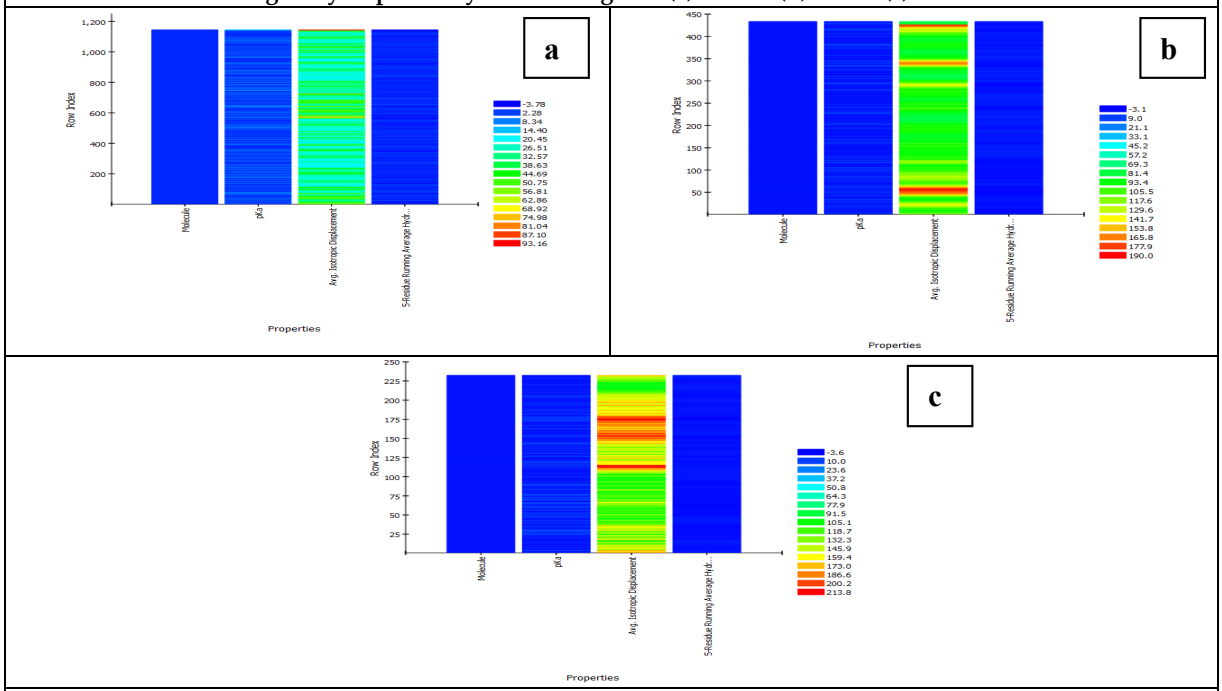

Fig 3: Heat Plot of the genes (a) 5UGW (b) 6FGN (c) 5HBT

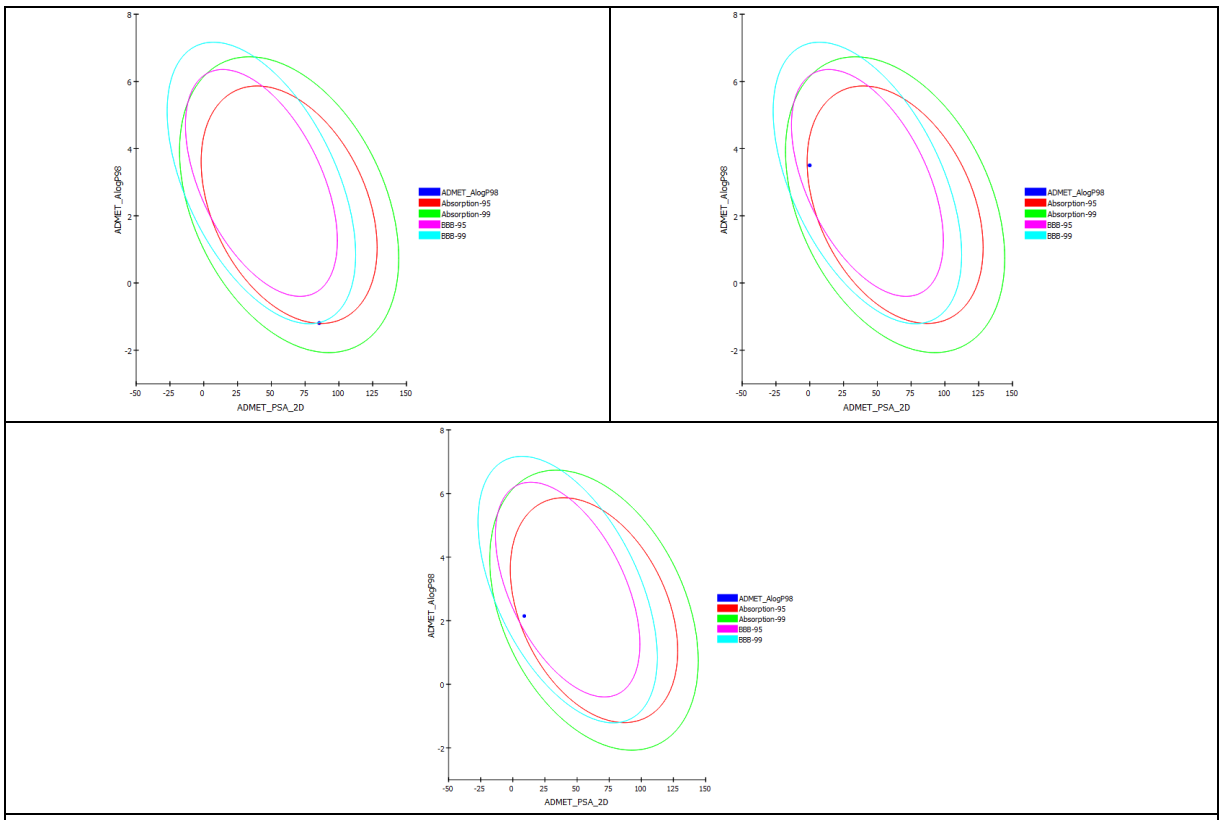

Fig 5: ADMET analysis Plot

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RESEARCH ARTICLE

Efficacy of Some Compounds Isolated from *Nyctanthes arbor-tristis* Linn. on Human and Plant Diseases as Revealed from *In silico* Analysis

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ABSTRACT

Molecular docking analysis is used as an important tool in designing new drugs for different diseases. In the present study, GC-MS analysis of methanol extract of *Nyctanthesarbor-tristis*leaf yielded five compounds namely astragalin, nicotiflorin, nyctanthic acid, friedeline and lupeol. These molecules were subjected to molecular docking analysis against protein S-adenosyl-L-methionine decarboxylase involved in human liver cancer and against β-1,3-glucanase involved in wheat leaf rust diseases. Astragalin was the best inhibitory ligand for the enzyme S-adenosyl-L-methionine decarboxylase and friedeline was the best forβ-1,3-glucanase. Further in vivo study can confirm candidate molecules to be used in reality.

Key words: *Nyctanthesarbor-tristis*, Phytochemicals, anticancer, anti-leaf rust, docking

INTRODUCTION

A plethora of knowledge regarding the benefits of herbal drugs was stored in ourearliest treatise of Indianmedicine, the CharakaSamhita (1000 B.C.), wherein the useof over 2000 herbs for medicinal purpose was mentioned (Cragg*et al*., 1997). According to a survey of WHO, 80% of the population living in the developingcountries depend almost exclusively on the traditional medicine fortheir primary health care needs.Exploration of the chemicalconstituents of the plants and pharmacological screening mayprovide us the basis for developing the leads for synthesis of novel

agents. Among theestimated 400,000 plant species, only 6% have till now beenstudied for biological activity (Goyal*et al*., 2007).

*Nyctanthesarbor-tristis*Linn. (popularly known as nightjasmineor *parijaat*or *sephalika*)of familyOleaceae is a small tree, with a gray or greenish, rough and peeling bark. The shrub grows to a height of 10 meters. The simple leaves are opposite, with an entire edging about 6 to 12 cm long and 2 to 6.5 cm wide. The flowers are having snow white petals, fragrant with a five-to-eight lobed corolla and orange-red center, often seen in a cluster of two to seven. The fruit is plane, brown and heart-shaped to round capsule, around 2 cm in diameter with two sections, each containing a single seed (Bordoloi*et al*., 2016). It is traditionally used due to its extensive medicinal properties by the tribal rural people of India and also in Ayurveda, Siddha, and Unanimedicine systems (Sasmal*et al*., 2007). The whole plant and its parts are used for its effects in treating sciatica, arthritis, malaria, enlargement of spleenand as blood purifier; and the white flowers are used as stomachic, carminative,astringent, anti-bilious, expectorant, hair tonic and in the treatment of various skindiseasesandpiles; and in recent findings have been found to possess anti-spasmodic, anthelmintic,cytoprotective, anti-diabetic, anti-leishmanial, CNS depressant activity (Sandhar*et al*., 2011).
A number of bioactive compounds including flavanol glycosides, astragalin, nicotiflorin, oleanolic acid, nyctanthic acid, tannic acid,friedeline, lupeol, nyctanthin, nyctanthic acid, 3,4-secotriterpene acid, etc. have been isolated from the plant (Wikipedia, 2020). But reliable study on their efficacy against different human and plant diseases have not been carried out till date. In the present investigation molecular docking technology has been employed to find the effect of somecompoundsin controlling human and plant diseases.

MATERIALS AND METHODS

Plant collection and extract preparation

The leaves of *N. arbor-tristis*(Fig. 1. a) were collected from the campus of CUTM, Paralakhemundi, Odisha and were cleaned and dried under shade overnight. Then these were subjected to further drying in hot air oven at 40°C for 24 hours and subsequently ground into powder with Bajaj Maximix grinder. The powdered leaves were then extracted repeatedly with hot methanol (CH_3OH) using Soxhletapparatus(Fig. 1. b) fitted on a heating mantle keeping temperature set at 55°Cfor 12 hours following the method of Arulmozhi*et al.* (2019). The solvent was then removed at reduced pressure and temperature (50°C) with a rotary vacuum evaporator to yield methanolic leaf extract to be used for further analysis.

Sample preparation for GC-MS analysis

The dried leaf extract (5 mg) was dissolved in 10 mL HPLC-grade methanol and was filtered through 0.22 μm PTFE membrane filter (Milipore, USA) and 1 mL of this was further diluted to 5 mL for GC-MS analysis.

GC-MS analysis

Thegas chromatography-mass spectrometry (GC-MS) analysisfor identification of the compounds was done as follows(Hemamalini*et al*., 2014). The GC-MS usedwas Varian CP 3800 GC coupled with Saturn 2200 MS andCombiPAL auto-sampler. The column used was Factor-Fourcapillary column (VF 5ms, 30m, 0.25 μm). The carrier gaswas helium at a flow rate of 1.0 mL min^{-1} and injection volumewas 1 μL. The temperature programming was as follows:injector temperature: 260°C, column oven temperatureprogramme: 50°C (1 min) to 270°C ramp at 10°C min^{-1}, heldfor 10 min.

Identification of compounds

Interpretation of mass spectrum in GC-MS was conducted using data base of National Institute Standard and Technology (NIST) and Wiley spectra libraries. Spectrum of the unknown component was compared with the

spectrum of known components stored in the NIST library. A total of five compounds were identified. The molecular weight, molecular formula, and the number of hits used to identify the name of the compound from NIST and Wiley spectra libraries were recorded.

Ligand preparation

The compounds identified in the GC-MS analysis of methanolic extract of *N. arbor-tristis*leaf were used in the present study. The structures of the five compounds to be used as ligands were retrieved from PUBCHEM database.

Selection of enzymes with elevated activity during disease

In case of human beings, the activity of the enzyme S-adenosyl-L-methionine decarboxylase is found to be elevated in persons with liver cancer(Hemamalini*et al*., 2014). So the anticancer activity of these five compounds with S-adenosyl-L-methionine decarboxylase wasanalysed with molecular docking study. The same compounds were used to study the fungicidal efficacy against the fungal pathogen *Pucciniatriticina*,the causal organism of wheat leaf rust. This pathogen,an obligatory biotrophic parasite, is a severe fungal disease ofwheat causing substantial yield loss over a large part of theworld (Kolmer, 2005). Activity of one of the several pathogenesisrelated(PR) proteins, β-1,3-glucanase, is modulated due to *Puccinia* infection(Naz*et al*., 2014). So antifungal activity of the same five compounds isolated from *N. arbor-tristis*leaf was studied with this protein by utilizing molecular docking analysis.

Protein preparation

The target proteinsS-adenosyl-L-methionine decarboxylaseand β-1,3-glucanasewere retrieved from Protein Data Bank (www.rcsb.org), the ribbon structures of which are presented in Fig. 2.

Molecular docking analysis

Molecular docking continues to hold a great promise in the field of computer based drug design which screens small molecules by orienting and scoring them in binding site of a protein. The interaction study was carried out in Ligandfit of Accelrys Discovery Studio software. The binding sites of the protein were predicted using find cavities from the receptor site parameter of the tool. The determination of the ligand binding affinity was calculated using Dock scores, the Dock score for each ligand is calculated by the software itself. The number of hydrogen bondsinvolved in the interaction along with amino acids involved in the hydrogen bonding and the distance between the hydrogen bonds were also estimated using LigandfitAccelrys Discovery Studio software. Here, the five phytochemicals identified in GC-MS analysis is docked with the target proteins S-adenosyl-L-methionine decarboxylase and β-1,3-glucanase.

RESULTS AND DISCUSSION

GC-MS identification of compounds

The results of GC-MS analysisof the active principles with their molecular formula and molecular weight are presented in Table 1. Here, five compounds were identified which are reported as astragalin, nicotiflorin, nyctanthicacid, friedeline and lupeol; structures of which are given in Fig. 3.

Lipinski properties

Lipinski's rule of five also known as the Pfizer's rule is applied to evaluate drug-likeness or determine if a chemical compound with a certain pharmacological or biological activity has properties that would make it a likely orally

active drug in humans. All the ligands satisfy Lipinski rule as shown in Table 2. Lipinski rule of five is used as the first step filter to perform virtual screening of compound libraries in an effort to quickly eliminate lead candidates that have poor physico-chemical properties, but satisfactorily all the five compounds identified as ligand passed the initial screening test.

Validation of docking result

Docking describes a process by which two molecules fit together in three-dimensional space. Molecular docking has contributed important inputs to drug discovery for many years. Here, the five phytochemicals identified through GC-MS analysis is docked with the target proteins S-adenosyl-L-methionine decarboxylase and β-1,3-glucanase. The validation process consists of two parts: (i) prediction of binding energy between the docked ligand and the protein using various score calculated using Discovery Studio (PLP1, PLP2, JAIN, Ligand internal energy and PMF), and (ii) hydrogen bond details of the top ranked docked pose(Hemamalini*et al*., 2014). The summary of docking information of the top ranked poses in each compound is given in Table 3 and Table 4 for the target proteins S-adenosyl-L-methionine decarboxylase and β-1,3-glucanase respectively. The score values include PLP1 and PLP2 (steric and H-bonding intermolecular function);higher PLP scores indicate stronger receptor-ligand binding (Gehlhaar*et al*., 1995), JAIN (sum of five interaction terms),lower internal energy means better docking stability. Scores are calculated by summing pairwise interaction terms over all interatomic pairs of the receptor-ligand complex (higher score indicates stronger receptor-ligand binding affinity, Muegge, 2006) and Dockscore (candidate ligand poses are evaluated and prioritized according to the Dock score function).

The order of ligands based on Dock score for the enzyme S-adenosyl-L-methioninedecarboxylase is: astragalin>nicotiflorin>nyctanthic acid >lupeol>friedeline; and that for β-1,3-glucanase is: friedeline >astragalin >nicotiflorin>nyctanthic acid >lupeol.So, astragalinwas observed to have maximum score (45.87) with S-adenosyl-L-methionine decarboxylase in molecular docking study and friedeline has maximum score (48.65) withβ-1,3-glucanase. The docking model of the five ligands with the protein S-adenosyl-L-methioninedecarboxylase is shown in Fig. 4.

By studying the interaction between protein and the ligands and also considering the H-bond interaction it was found that out of the five molecules under study, astragalinisthe best ligand that can successfully inhibit S-adenosyl-L-methionine decarboxylase, and thus can be taken as one candidate anticancer agent. In case of β-1,3-glucanase,friedeline showed maximum possible interaction with the protein and so this molecule can be considered as a candidate fungicide for controlling the wheat leaf rust.

CONCLUSION

Molecular docking analysis is used as an important tool in designing new drugs for different diseases. It saves expenses, manpower and time to a very good extent and so has become popular among the concerned scientists. In the present study astragalinwas found to be the best ligand that could inhibit the enzyme S-adenosyl-L-methionine decarboxylasesuccessfully and friedeline was the best one to inhibit the function of β-1,3-glucanase. So these two compounds can be considered as candidate molecules for drug of human cancer and wheat leaf rust respectively. Further *in vitro*and *in vivo*analysis will confirm the possibilities to be real.

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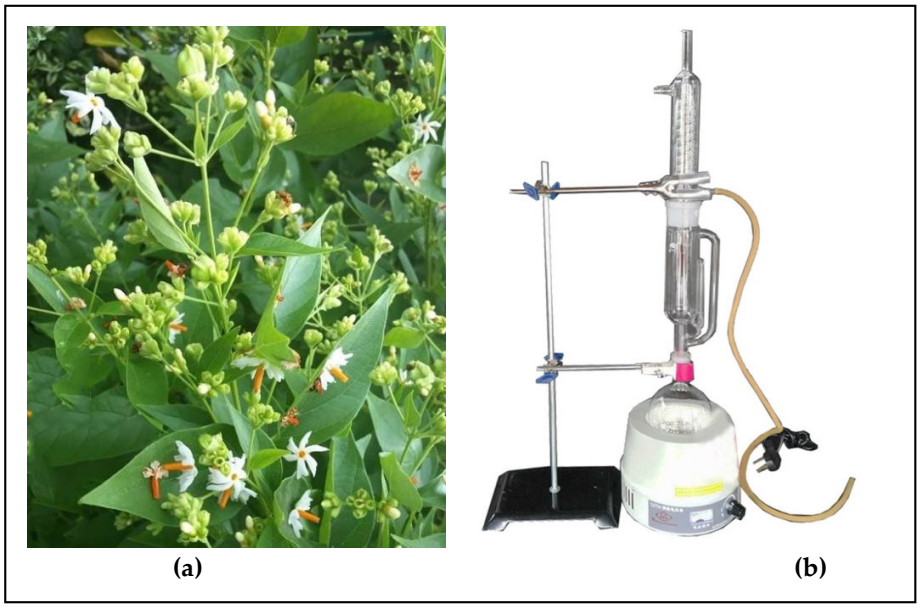


Fig. 1. (a) *N. arbor-tristis*plant, (b) Soxhlet extractor apparatus

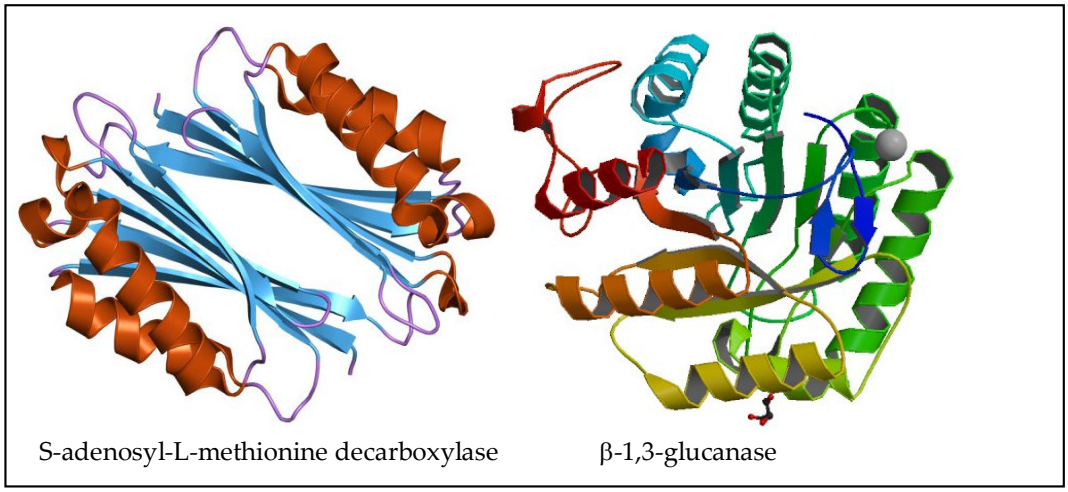


Fig. 2. Ribbon structures of the two enzymes under study retrieved from RCSB PDB

Table 1.Compounds identified from *N. arbor-tristis* by GC-MS

Sl. No.	Name of compound	Molecular formula	Molecular weight (g/mol)
1.	Astragalin	$C_{21}H_{20}O_{11}$	448.4
2.	Nicotiflorin	$C_{27}H_{30}O_{15}$	594.5
3.	Nyctanthicacid	$C_{30}H_{48}O_2$	440.7
4.	Friedeline	$C_{30}H_{50}O$	426.7
5.	Lupeol	$C_{30}H_{50}O$	426.7

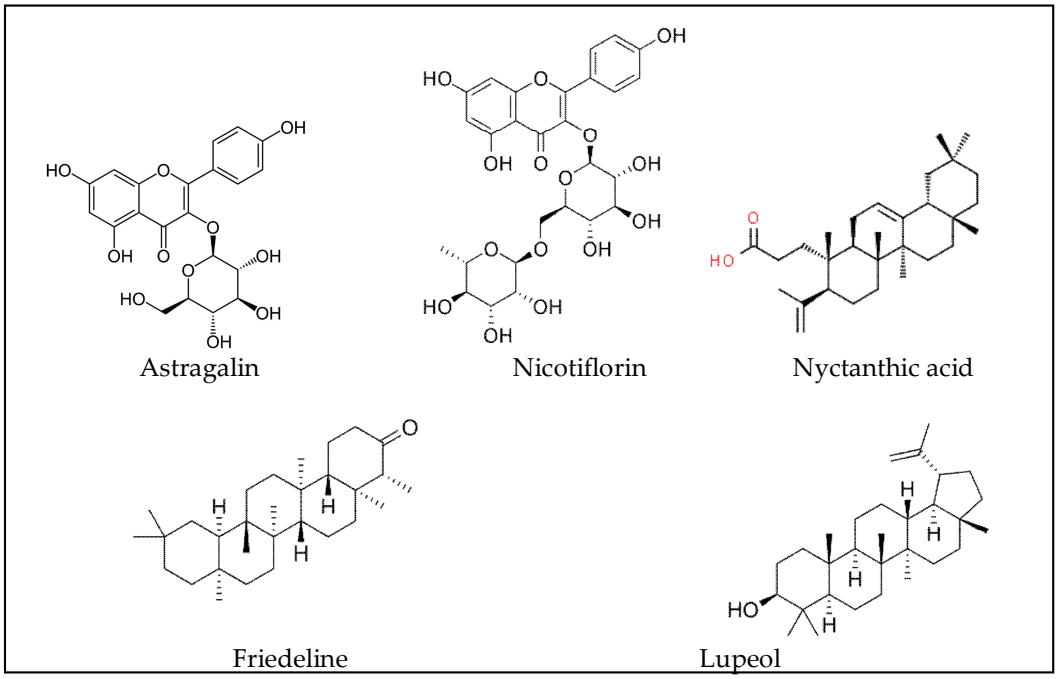


Fig. 3.Structures of the compounds identified by GC-MS analysis from *N. arbor-tristis*Linn.

Table 2.Properties of ligands following Lipinski rule

Sl. No.	Name of compound	Molecular weight (g/mol)	H bond donor ≤ 5	H bond acceptor ≤ 10	log p < 5
1.	Astragalin	448.4	1	4	2.3
2.	Nicotiflorin	594.5	0	2	1.8
3.	Nyctanthicacid	440.7	2	3	3.4
4.	Friedeline	426.7	0	6	1.7
5.	Lupeol	426.7	1	3	3.1

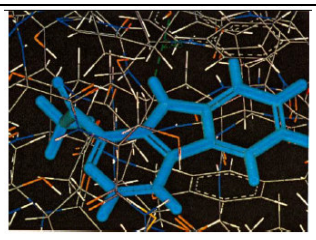
Table 3. Summary of docking information of the compounds for S-adenosyl-L-methionine decarboxylase enzyme

Sl. No.	Compound name	PLP1	PLP2	JAIN	Ligand internal energy	PMF	Dock Score
1	Astragalin	40.81	40.53	1.83	-0.93	54.32	45.87
2	Nicotiflorin	48.47	59.27	2.65	-2.95	94.58	42.26
3	Nyctanthicacid	51.68	49.75	-1.74	-1.77	60.59	36.47
4	Friedeline	68.43	67.39	1.88	-1.83	74.28	26.85
5	Lupeol	31.28	37.74	-0.85	-0.89	37.71	29.04

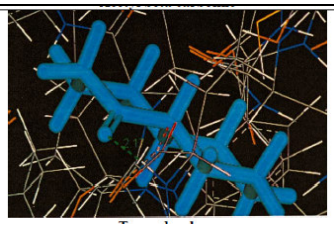
Table 4. Summary of docking information of the compounds for β-1,3-glucanase

Sl. No.	Compound name	PLP1	PLP2	JAIN	Ligand internal energy	PMF	Dock Score
1	Astragalin	38.63	41.37	1.74	-0.91	56.47	43.565
2	Nicotiflorin	47.52	58.87	2.55	-2.76	92.63	41.226
3	Nyctanthicacid	52.49	48.56	-1.78	-1.83	61.46	37.276
4	Friedeline	67.34	66.59	1.72	-1.37	75.33	48.65
5	Lupeol	33.82	38.45	-0.83	-0.87	39.46	28.24

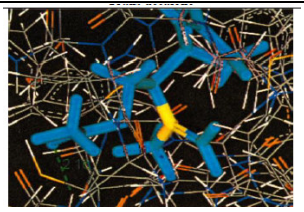
Astragalin



Nicotiflorin



Nyctanthicacid



Friedeline

Fig. 4.Docking model of five ligands with S-adenosyl-L-methioninedecarboxylase

Lupeol

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RESEARCH ARTICLE

In-silico Ananlysis of Effects of Cardamom Extract on Plant Disease

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ABSTRACT

Antiquated India is one of the pioneers of investigations of plants as medication, for example Ayurveda. In our social and monetary life we barely deal with our food we are taking. One such novel herb is Cardamom which has frequently been viewed as a mind supporter. The entire plant including the blossoms can be utilized for restorative purposes. It has a harsh and sweet taste and is known to give a cooling vitality. Cardamom is loaded with cancer prevention agents that are basic for carrying on with a sound life. We are utilizing this property of Cardamom to get some new medications for Aster Yellow. The employments of different pesticides, additives, and so on transform the nourishments into poison. Also the reactions of these pesticides and additives, and so on are perilous as on the grounds that it prompts commencement of various malignant growth. In this entire world, the quantity of patients kicking the bucket from malignant growth is expanding in a compromising manner. In-silico investigation has done utilizing programming and we further focused on a portion of the qualities answerable for Aster Yellow and pharmacophores from Cardamom and destroyed some silico examination. In this we have discovered that these two pharmacophores are having better Mol Doc score from any others.

Key Words: Cardamom, Docking, *In silico* Analysis, Pharmacophore

INTRODUCTION

As per review, the cardamoms are the containers of dried organic products in various genera of the *Zingiberaceae* family, fundamentally Elettaria, Amomum and Aframomum. Among them, *Elettaria cardamomum* (L.) Maton is

generally significant and is developed overwhelmingly in southern India (Govindarajan et al., 1982). The bogus cardamom, enormous cardamom, or dark cardamom from the partnered class Amomum is local to Nepal, Sikkim, Bengal and southeast Asian nations. African cardamom, which is organically known as *Aframomum* danielli (Hook.f.) K. Schum., is local to south east Africa particularly in Tanzania, Cameroon, Madagascar and Guinea (Govindarajan et al., 1982; Adegoke et al., 1998). Little cardamom is broadly developed in Nepal and Sikkim and to a constrained degree with the huge cardamom (Amomum subulatum Roxb.). Notwithstanding, universal exchange is presently constrained to Asian nations most definitely as a result of significant expenses. Around the world, cardamom is perceived as the "sovereign of flavors" for its lovely fragrance and taste, and is the third most costly zest after saffron and vanilla. .

Elettaria cardamomum (L.) Maton is normally known as little cardamom, green cardamom, or genuine cardamom and is developed in India, Guatemala, Sri Lanka, Nepal, Indonesia, Costa Rica, Mexico and Tanzania (Garg et al., 2016). In India, cardamom is developed in elevations running from 900 to 1400 m above msl (mean ocean level) covering three southern Indian states (Kerala, Karnataka and Tamil Nadu). In Kerala, it is developed for the most part in the Indian Cardamom Hills covering a territory of 1050 square kilometers assigned as Cardamom Hill Reserves, (Madhusoodanan et al., 2002). The herbal name of cardamom, *Elettaria cardamomum*, started from the Tamil word "Elettari" which alludes to the seeds of cardamom (Mahindru, 1982).

For quite a long time, cardamom containers have been utilized for culinary and conventional medication applications including controlling asthma, teeth and gum diseases, stomach related and kidney issue (Hamzaa et al., 2012; Saeed et al., 2014), waterfalls, sickness, loose bowels and cardiovascular issue (Gilani et al., 2008; Khan et al., 2011). The basic oil and other bioactive metabolites gathered in cardamom cases add to their trademark smell and utility as an utilitarian food, pharmaceutical, and nutraceutical (Hamzaa et al., 2012). The basic oil (EO) substance of cardamom cases changes from 6 to 14% contingent on the sort and handling strategies (Menon, 2000). EO of cardamom cases have transcendently monoterpene constituents, for example, 1,8-cineole, α-pinene, α-terpineol, linalool, linalyl acetic acid derivation and nerolidol and the ester constituent α-terpinyl acetic acid derivation (Kaskoos et al., 2006; Yashin et al., 2017; Ashokkumar et al., 2019b), all of which have helpful advantages including cancer prevention agent, anticancer, antidiabetic, mitigating, antifungal, antiviral and gastroprotective exercises (Nirmala, 2000; Marongiu et al., 2004; Hamzaa et al., 2012; Winarsi et al., 2014). Ongoing reports asserted that flavonoids, terpenoids, anthocyanins, alkaloids and other phenolic constituents from cardamom were being utilized for controlling cardiovascular, pneumonic, kidney and lung related scatters (Vaidya and Rathod, 2014). The point of this audit is to feature the primary phytochemicals and useful impacts of cardamom basic oil (CEO) and concentrates on human wellbeing.

MATERIALS AND METHODS

Various pharmacophores of Cardamom fruit have been listed and their respective SDF were taken accordingly from Pubchem, Molinstincts, and Chebi. The enzyme corresponding to microbe of Aster Yellow has been taken from BRENDA (Braunschweig Enzyme Database). Then, the PDB (Protein Data Bank) code was found from RCSB (Research Collaboratory for Structural Bioinformatics). The above mentioned information was then processed in Discovery Studio to initiate Docking. The following screenshots are taken from Discovery Studio, showing positive results of docking;

Protein identification and preparation

The reported molecular targets responsible for Aster Yellow Gene are taken (Table 1) and the X-ray crystallographic structures of these target proteins were retrieved from protein data bank (PDB). The retrieved PDB structures contain water molecules, heavy atoms, cofactors, metal ions etc. and these structures do not have information about topologies, bond orders and formal atomic charges. Hence the downloaded PDB structures were prepared using

'prepare protein' protocol of Discovery Studio 4.0. The target proteins were prepared by removing all water molecules, ligands and other hetero atoms from the structures. Hydrogen atoms were added to the atoms to satisfy their valencies. The structures were then energy minimized by applying CHARM force field to remove the steric clashes between the atoms in order to get stable conformation.

Active site identification

The binding sites of the receptor proteins were predicted based on 'receptor cavity method' using Accelry's Discovery Studio 4.0. Using this protocol, active sites of the target receptor were identified based upon the inhibitory property of the amino acid residues present in the binding sites.

Ligand preparation and filtration

A collection of 3 phytocompounds from Cardamom were taken as ligands for docking analysis. The 3D structures of these compounds were downloaded from PubChem database. These ligands were then cleaned up, calculated 3D coordinates and generated ligand conformations by applying 'prepare ligand protocol' of Discovery Studio 4.0. After preparation, the compounds were filtered based on the molecular properties for predicting their solubility and permeability in drug discovery. The best known of the physical property filters is Lipinski's "rule-offive", which focuses on bioavailability. The rule states that the compounds have molecular mass less than 500 daltons, not more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors and an octanol-water partition coefficient log P not greater than 5 (Lipinski et al.,2001). The filtered compounds were then used for docking analysis.

Docking

The anti-inflammatory activity of all the 3 phytochemicals reported from Cardamom was assessed by docking these compounds against the respective active sites of the target proteins. Discovery studio 4.0 was used in this study to find the interacting compounds of Cardamom with the selected targets of Leaf Blister. Strategies of Discovery Studio 4.0 are to exhaustively dock or score possible positions of each ligand in the binding site of the proteins. Docking study of the target proteins was done with natural compounds derived from Cardamom to find the preferred orientation and binding affinity of the compounds with each target protein using scoring functions. A molecular dynamics (MD) simulated-annealing-based algorithm, namely, CDOCKER was used to score the interacting compounds. This method uses a gridbased representation of the protein-ligand potential interactions to calculate the binding affinity (Wu et al., 2003). CDOCKER uses soft-core potentials, which are found to be effective in the generation of several random conformations of small organics and macromolecules inside the active site of the target protein. Ligands were docked to the proteins followed by scoring them for their relative strength of interaction to identify candidates for drug development. The final poses were then scored based on the total docking energy, which is composed of intramolecular energy of ligand and the ligand-protein interaction. The lowest energy structure was taken as the best fit. Interpretation of the values was done using standards provided by Discovery Studio such as CDOCKER energy, CDOCKER interaction energy, hydrogen bonds, binding energy etc.

Drug likeliness

Drug-likeness is a qualitative concept used in drug design to evaluate how the substance acts like drug with respect to factors like bioavailability. The molecular properties which influence absorption, distribution, metabolism, excretion and toxicity are recognized as a long side therapeutic potency as key determinants of whether a molecule can be successfully developed as a drug (Zhang et al., 2012). These parameters are responsible for about 60 percent failures of all drugs in the clinical phases and so the prediction of ADMET properties plays a significant role in new drug discovery process (Hire et al., 2012). Thus, it has become imperative to design lead compounds which would be easily Gastricly absorbed, easily transported to their targeted site of action, not easily converted into toxic metabolic products and easily eliminated from the body before accumulating in sufficient amounts. The ADMET properties of the compounds were analyzed for drug like candidates.

RESULT AND DISCUSSION

Protein preparation and active site identification

The three dimensional structures of the identified target proteins were retrieved from the protein data bank. PDB ID of the targeted protein structure are mentioned in Table 1.

Ramachandran Plot of the targeted gene

The Ramachandran plot is among the most central concepts in structural biology, seen in publications and textbooks alike. However, with the increasing numbers of known proteinstructures and greater accuracy of ultra-high resolution protein structures, we are still learning more about the basic principles of protein structure. The use of torsion angles to describe polypeptide and protein conformation was developed by Sasisekharan as part of his studies of the structure of collagen chains during his work as a graduate student in the research group of G.N. Ramachandran. The power of this approach was readily apparent and its use quickly became widespread. Using revised definitions, this so-called Ramachandran plot or φ, ψ-plot has remained nearly unchanged in the ensuing fifty years and continues to be an integral tool for protein structure research and education.

Hydrophobicity Plot of the Genes

Protein–protein interactions (protein functionalities) are mediated by water, which compacts individual proteins and promotes close and temporarily stable large-area protein–protein interfaces. In their classic article, Kyte and Doolittle (KD) concluded that the "simplicity and graphic nature of hydrophobicity scales make them very useful tools for the evaluation of protein structures." In practice, however, attempts to develop hydrophobicity scales (for example, compatible with classical force fields (CFF) in calculating the energetics of protein folding) have encountered many difficulties

Ligand preparation

4 of the pharmacophores are satisfied Lipinski rule and are expected to be active compounds after Gastric administration. The ligand molecules with least binding energy are considered as compounds with highest binding affinity. This binding affinity indicated a focused interaction between the above compounds with the targets compared to others. The parameters for finding the best inhibitors such as CDOCKER energy, CDOCKER interaction energy and number of hydrogen bonds were also evaluated. CDOCKER energy is the combined energy produced by the sum of internal ligand strain energy and receptor-ligand interaction energy where, CDOCKER interaction energy is the interaction energy between the protein and ligand and the values of these two parameters indicate the strength of interaction between the proteins and the ligands. Besides least binding energy, compounds with least atomic energy difference between CDOCKER energy and CDOCKER interaction energy were analyzed. Based on CDOCKER energy and CDOCKER interaction energy, Fig 4 is showing the result.

ADMET Evaluation

Considering the comparable CDOCKER energy, interaction energy and binding energy, three compounds were forwarded for ADMET analysis. These studies are based on the ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties of the compounds. These properties provide insights in to the pharmacokinetic properties of the compounds and were checked using Discovery Studio's built in ADMET protocol. The various parameters tested in this study were aqueous solubility, Blood Brain Barrier (BBB) level, Hepatotoxicity, Absorption level, AlogP and CYPD26. Pharmacokinetic properties of the best fit phytochemicals showed that two of the compounds had passed all the pharamacokinetic parameters. The compounds that passed the parameters were N-methyltyramine and dalbergioidin. These compounds were thus selected as the best compounds in this study as they had good interaction scores along with ADMET properties.

CONCLUSION

The identified pharmacophores can be isolated from the Cardamom and can be commercialized as the natural drug for the Aster Yellow Gene which is having lesser harmful side effect from the chemotherapeutic drug available in the market. This drug will also be very cheaper from the available drugs and these drugs are also not harmful for the normal cells as they are derived from the natural products. The unique feature of the study is to targeted gene therapy for a particular cancer. This will help our future medicine to be completely allied to the Pharmachophores and the uses of synthetic and carcinogenic drug will reduce.

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Table 1: The list of pharmacophores and the targeted genes from Leaf Blister

Sl.No	Pharmacophores from Cardamom	Targeted Plant Disease Causing Microbial (leaf blister) Gene	PDB No of the Genes
1	Threonine	BLISTER	6PRK
2	1,8- Cineole	NADH dehydrogenase subunit 1	6HL2
3	limonene	Cytochrome b	6LW5

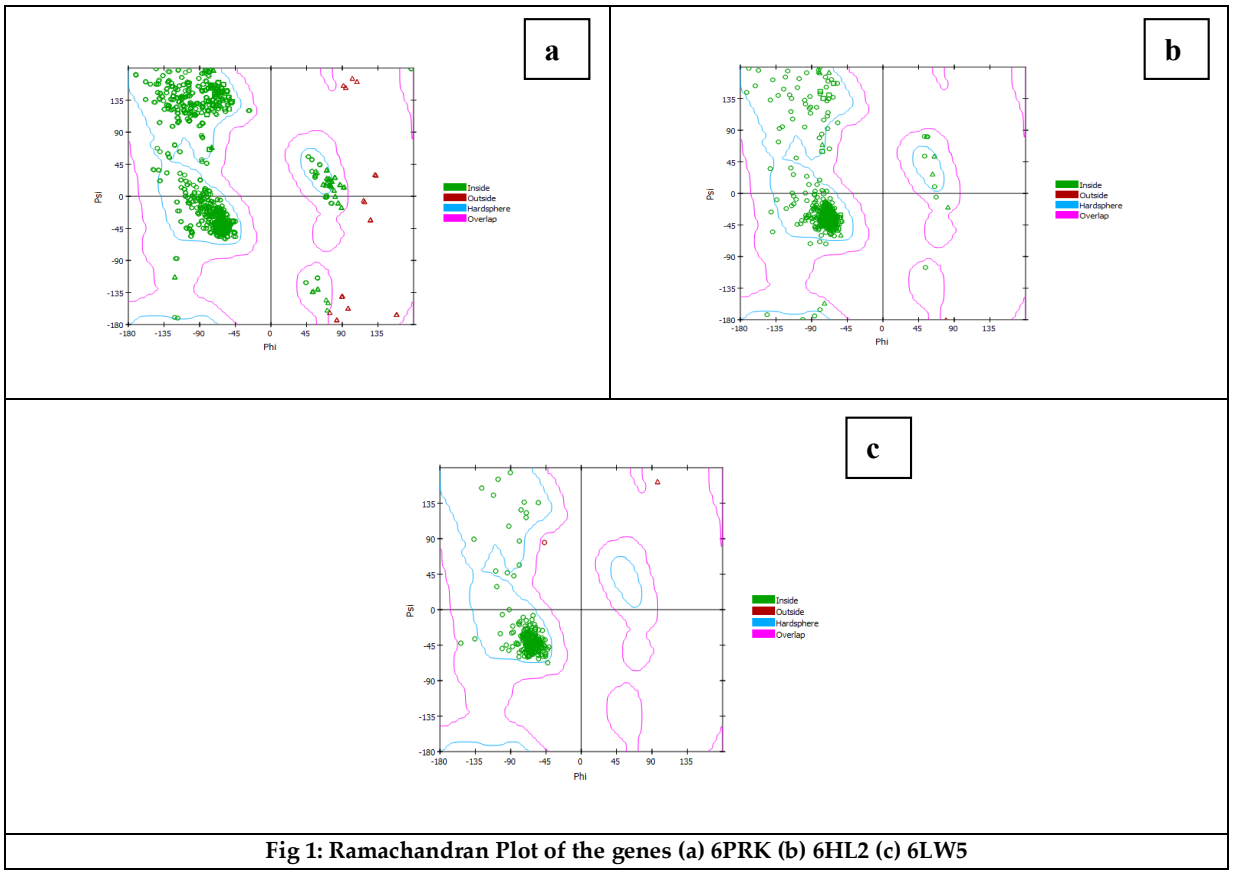

Fig 1: Ramachandran Plot of the genes (a) 6PRK (b) 6HL2 (c) 6LW5

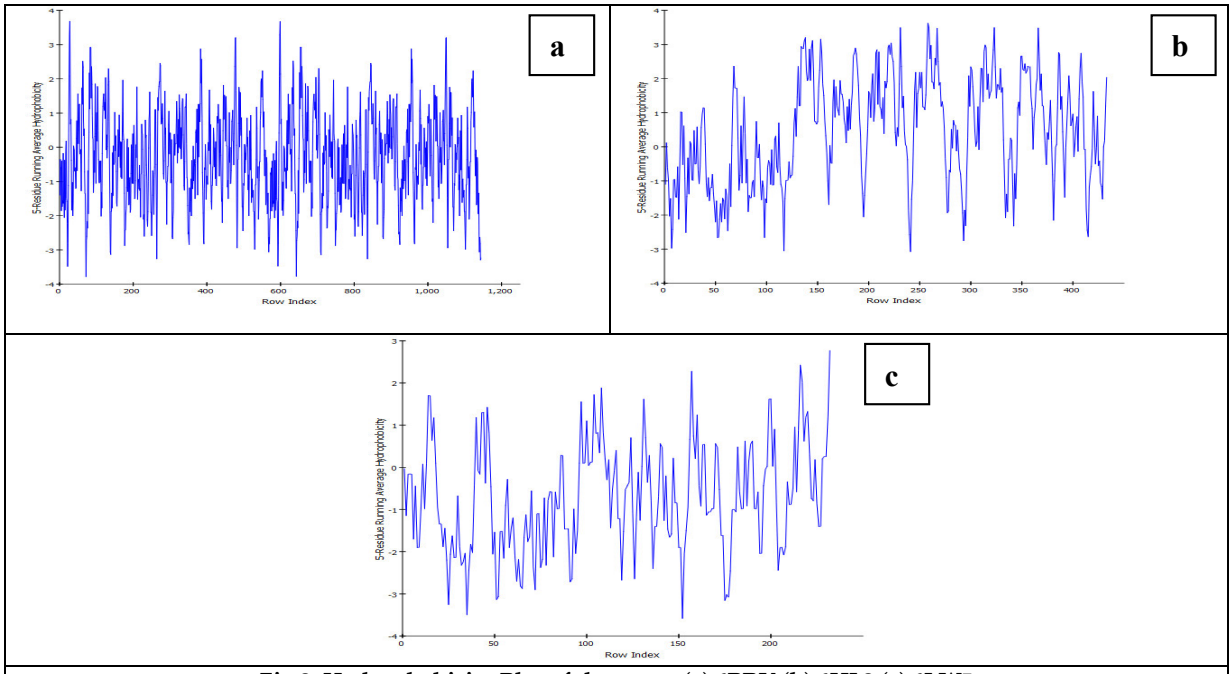

Fig 2: Hydrophobicity Plot of the genes (a) 6PRK (b) 6HL2 (c) 6LW5

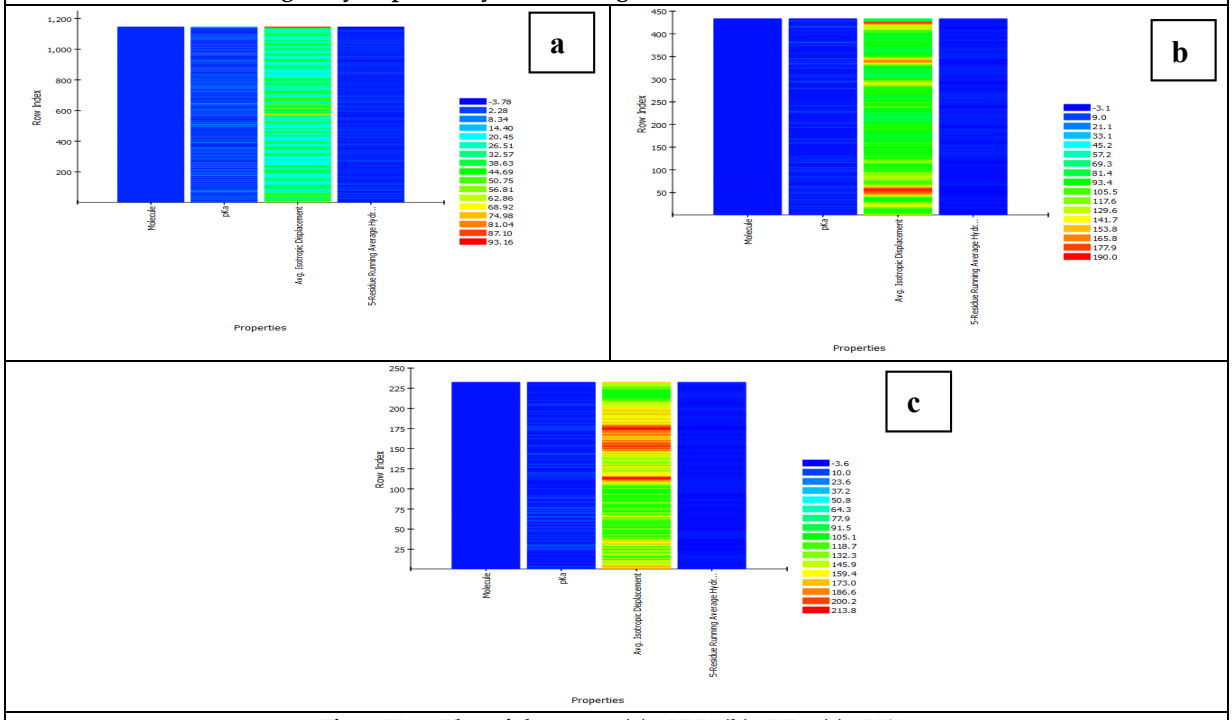

Fig 3: Heat Plot of the genes (a) 6PRK (b) 6HL2 (c) 6LW5

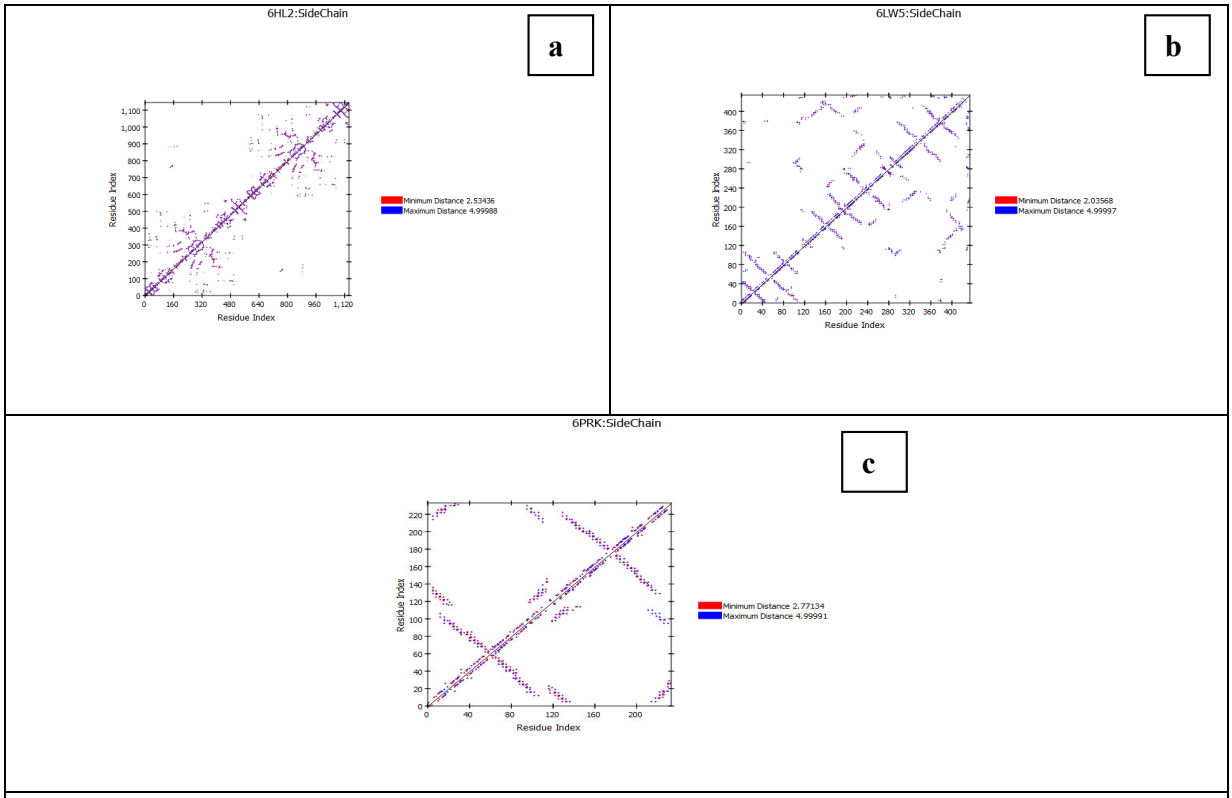

Fig 4: Side chain graph of the genes (a) 6PRK (b) 6HL2 (c) 6LW5

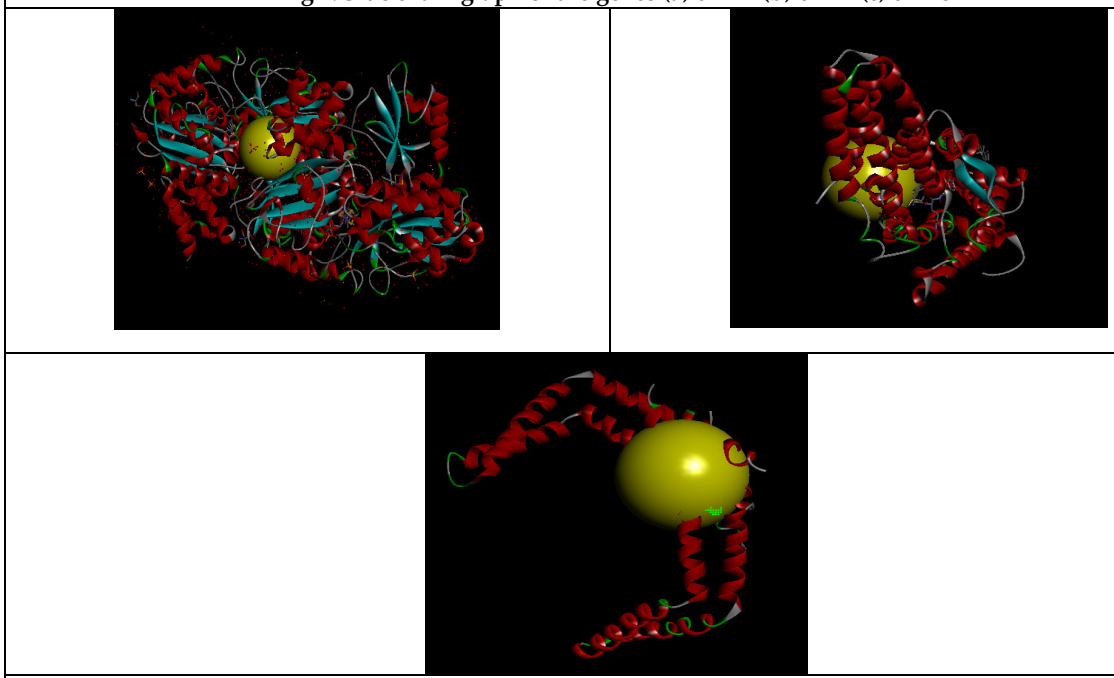

Fig 5: Docking analysis

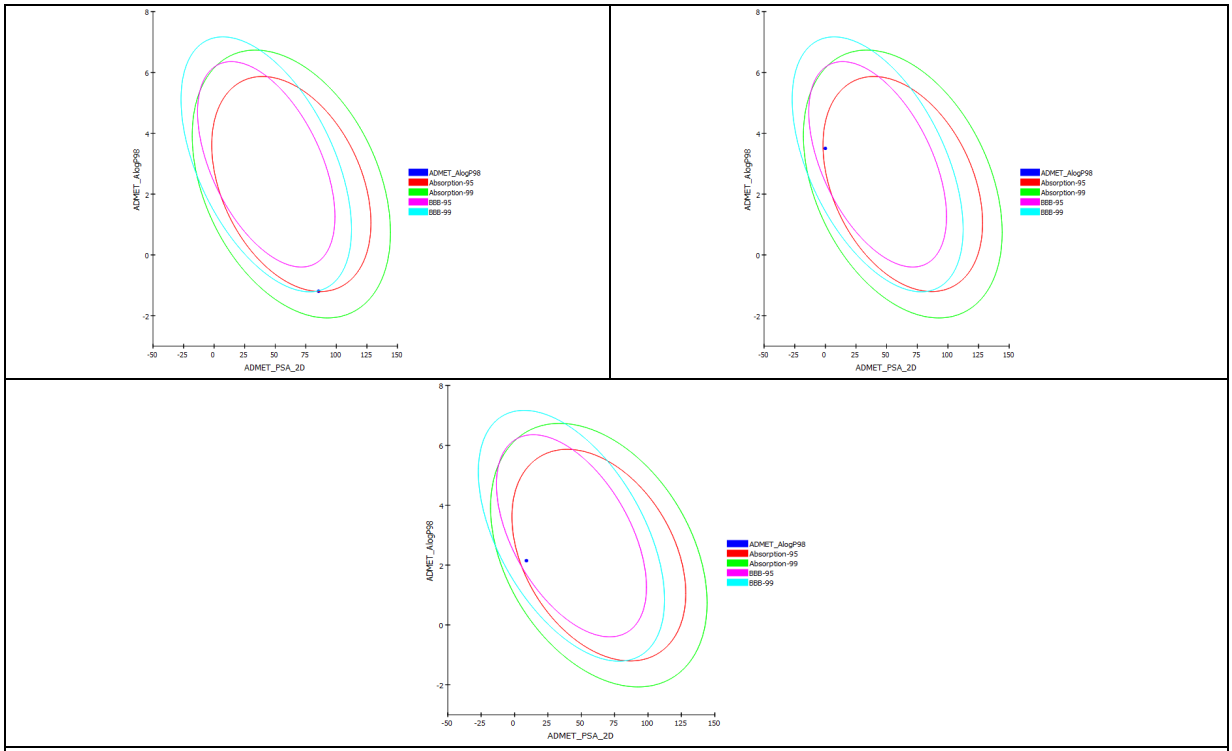

Fig 6: ADMET analysis Plot

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REVIEW ARTICLE

A Review on Antimicrobial and Phytochemical Effects of Amla in Skin Care (Anti-Aging)

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ABSTRACT

Emblica officinalis is prominently called as Indian gooseberry or Amla, is among fundamental home grown plant in Indian customary medication. Various pieces of *Emblica officinalis* gainful for restoring different diseases yet the natural products particularly show enormous pharmacological and therapeutic applications. Phytochemical investigation uncovered significant bioactive substance mixes, for example, tannins, alkaloids, polyphenols, gallic corrosive, ellagic corrosive, emblicanin An and B, phyllembein, quercetin, ascorbic acids, nutrients and minerals Different concentrates of amla have strong antimicrobial exercises to counter unique bacterial pathogens. Amla phytochemicals likewise have cell reinforcement, mitigating, hepatoprotective, cardioprotective, immunomodulatory, hypolipedemic, memory upgrading, hostile to malignancy, against diabetic, energizer, against ulcerogenic, insecticidal, larvicidal, and wound recuperating activities.It can either supplant the ordinary therapeuptic specialists because of its boss adequacy and absence of symptoms or can act an assistant helpful operator in this way improving the all out viability of regular operators. The present audit underlines on the phytochemical constituents, components behind the antimicrobial movement and furthermore quickly sums up other restorative and helpful handiness of the E. offcinalis.For understanding the atomic instrument one can likewise embrace in silico approach where the associations, for example, Protein-protein cooperations, Protein-compound connections, DNA-compound communications, DNA-protein collaborations are normally utilized. Here we concentrated on the destiny of these cooperations for a portion of the mixes of Emblicaofficinalis with

ordinary DNA polymerase β. Viability of these mixes includes configuration/taking from the databases of these atoms that are likely to follow up on the bimolecular objective. DNA polymerase beta protein PDB (1DK3) was utilized to dock with mixes like Quercetin, Myricetin and 3,7,3,4-Tetra Hydroxy Flavone. Every one of these mixes demonstrated best restricting investigations with DNA polymerase beta.

Key words: *Emblica officinalis*, Amla, Antimicrobial effects, Phytochemicals, Pharmacological activity, Therapeutic, Docking, DNA polymerase beta, Myricetin, Quercetin.

INTRODUCTION

The unstoppable force of life has talented humanity with huge restorative plants to make an ailment free and sound life. Plenteous restorative plants are introduced in the Indian conventional frameworks of medication (like Ayurveda, Unani, siddha), for the most part utilized one among them is Indian gooseberry or Amla, otherwise called Phyllanthusemblica Linn. (Syn. *Emblica officinalis* Gaertn.) has a place with the family Euphorbiaceae, which is a significant therapeutic herb in Ayurveda and Unani frameworks of medication. It is tremendously utilized as a tonic to reestablish the lost body's vitality and power (Mahima et al, 2012, Tiwari et al. 2018).

Amla is a little to medium measured deciduous tree, found in all through India, Pakistan, Uzbekistan, Sri Lanka, South East Asia, China and Malaysia. It becomes around 8-18m tallness with dainty light dim bark, leaves are basic, light green, sub-sessile, firmly set along the branchlets appears as though pinnate leaves; blossoms are greenish yellow(Edwards et al, 2012) ; organic products are globose, meaty, light yellow with six darken vertical wrinkles encasing six trigonous seeds in two seeded three crustaceous cocci (Vashist and Jindal 2012). Amla is profoundly nutritious and is perhaps the most extravagant wellspring of nutrient C, amino acids and minerals. It contains a few substance constituents like tannins, alkaloids and phenols (Patel and Goyal, 2012). Among every hydrolysable tannin, Emblicanin An and B; gallic corrosive, ellagic corrosive are accounted for to have natural movement (Dhama et al. 2014). Practically all parts have restorative properties, especially natural product, which has been utilized in Ayurveda as an amazing rasayana and in standard medication in the treatment of looseness of the bowels, jaundice, aggravation and a few different illnesses. Amla organic product is broadly utilized in the Indian arrangement of medication as alone or in mix with different plants and is utilized to treat basic cold and fever (Dhama et al., 2018), as diuretic, purgative, liver tonic, refrigerant, stomachic, remedial, hostile to pyretic, hair tonic; to forestall ulcer and dyspepsia. Pharmacological research investigates amla uncovers its pain relieving, against tussive, hostile to atherogenic, adaptogenic; cardio, gastro, nephro, neuro defensive and anticancer properties. Amla is likewise answered to have chemopreventive, radio, chemo and immunomodulatory (Zameer et.al, 2018), free radical rummaging, cell reinforcement, mitigating, hostile to mutagenic exercises. These properties are effectual in the avoidance and treatment of different maladies like malignant growth, atherosclerosis, diabetes, peptic ulcer, sickliness, liver, heart infections and different other disorders (Mirunalini, and Krishnaveni, 2010).

The principle issue of medication enterprises is in Identification of right genotype of therapeutic plant material. Impediments of morphological and substance approaches for confirmation have made requirement for more up to date strategies in quality control of botanicals. DNA based marker for EO ID were created. Arbitrary Amplified Polymorphic DNA (RAPD) strategy was utilized to recognize a putative marker (1.1 kb) explicit for EO contains mixes, for example, tannins, alkaloids, phenolic mixes, amino acids and sugars. Its natural product juice comprises of the most elevated nutrient C (Patel et al, 2011). The natural product when blended in with different organic products, supported their nourishing quality as far as nutrient C content .Chemoprevention with food phytochemicals is directly considered as one of the most significant systems to control ailments .EO is esteemed for its one of a kind tannins and flavanoids, which show exceptionally amazing cancer prevention agent properties. The hindrance of tumor was finished by natural product concentrate of this plant which has been assessed on two-phase procedure of

skin carcinogenesis in Swiss pale skinned person mice .Chemopreventive capability of EO organic product remove on 7,12-dimethylbenz(a)anthracene (DMBA) actuated skin tumorigenesis in Swiss pale skinned person mice was found as of late The security gave by EO was because of its cancer prevention agent limit and through its modulatory impact on hepatic enactment and detoxifying catalysts Phenolic mixes got from plant show various useful impacts and can conceivably hinder a few phases of carcinogenesis. Viability of EO polyphenol part (EOP) on the acceptance of apoptosis in mouse and human carcinoma cell lines and its modulatory impact on N-nitrosodiethylamine (NDEA) actuated liver tumors in mice was additionally explored (Thilakchand et.al, 2013) .The watery concentrate of the products of *Terminalia chebula*, EO and *Terminalia belerica* and their equiproportional blend known as Triphala were assessed for their invitro cancer prevention agent action (Deep et al 2005; Kaur et al 2005). Gamma-Radiation actuated strand break development in plasmid DNA (pBR322) was viably restrained by Triphala and its constituents (Variya et.al, 2016).

PHARMACOLOGICAL ACTIVITIES AND MECHANISMS

Modification in fundamental homeostatic equalization of the body is the beginning of infection. Awkwardness between star oxidant and against oxidant homeostasis places a significant job in larger part of infirmities. Genius oxidant condition rules either because of expanded age of free radicals or potentially their poor extinguishing/rummaging by the counter oxidants (which secures the body against the malicious impacts of free radicals). Amla is perhaps the most extravagant wellspring of nutrient C and low sub-atomic weight hydrolysable tannins which makes Amla a decent cancer prevention agent. The tannins of amla like emblicanin-A (37%), emblicanin-B (33%), punigluconin and pedunculagin are accounted for to give assurance against oxygen radical included haemolysis of rodent fringe blood erythrocytes. The component behind cell reinforcement action is because of the reusing of sugar moiety and transformation of the polyphenol into medium and high atomic weight tannins (Yadav et.al, 2014). The incredible cancer prevention agent Ellagic corrosive, present in Amla, can repress transformations in qualities and fixes the chromosomal variations from the norm. Amla represses the development and spread of different malignancies like bosom, uterus, pancreas, stomach and liver diseases. Preclinical examinations have indicated that amla has antipyretic, pain relieving, antitussive, antiatherogenic, adaptogenic, cardioprotective, gastroprotective, antianemia, antihypercholesterolemia, wound mending, antidiarrheal, antiatherosclerotic, hepatoprotective, nephroprotective, and neuroprotective properties. Likewise, trial contemplates have demonstrated that amla and a portion of its phytochemicals, for example, gallic corrosive, ellagic corrosive, pyrogallol, some norsesquiterpenoids, corilagin, geraniin, elaeocarpusin, and prodelphinidins B1 and B2 additionally have antineoplastic impacts. Amla is additionally answered to have radiomodulatory, chemomodulatory, chemopreventive impacts, free radical searching, cell reinforcement, mitigating, antimutagenic and immunomodulatory exercises, properties that are viable in the treatment and avoidance of malignant growth (Lanka 2017).

DISCUSSION

Quercetin interaction with DNA polymerase β

The best predicted bounding pose of Quercetin showing interactions with key amino acids of DNA Polymerase β (Figure V). The first hydrogen bond interaction was observed between 3′-hydroxyl group of phenyl and carboxyl group of GLU26 residue (OH---O, 2.097 Å) and 3′-hydroxyl group also forming interaction with hydroxyl group of the TYR39 residue (OH---O, 2.52 Å). The another hydrogen bond interaction was observed between 4′-hydroxyl group of the phenyl and carboxyl group of GLU26 residue (O---OH, 2.19 Å). Chromen-4-one moiety of the Quercetin occupies the hydrophobic cavity created by ALA38, ALA42, ALA43, VAL45, ILE46, ALA47, and LEU69.

CONCLUSION

The key constituents (Quercetin, Myricetin,3,7,3'4' tetrahydroxy flavone) of the Emblicaofficinalis formulation have shown stable interaction with DNA polymerase β enzyme on in silico analysis. Both in vivo and in silico analyses have shown an enhanced DNA polymerase β enzyme activity on administration of test item. The in silico studies have shown that major constituents of amalakirasayana form stable interactions with the DNA Polymerase β enzyme. The results of in silicoanalysis which are in well coordination with those of in vivo studies further emphasize on the ability of amalakirasayana on DNA damage repair and its possible application as an antiaging formulation.

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REVIEW ARTICLE

A Review Paper on Tulsi Plant (*Ocimum sanctum* L.)

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ABSTRACT

Tulsi (*Ocimum sanctum* L.), holly basil, is indigenous to the Indian mainland and profoundly respected for its restorative uses inside the Ayurvedic and Siddha clinical frameworks. Numerous in vitro, creature and human investigations bear witness to tulsi having different restorative activities including adaptogenic, antimicrobial, calming, cardioprotective, and immunomodulatory impacts, yet to date there are no precise surveys of human research on tulsi's clinical adequacy and security. We directed a complete writing audit of human examinations that gave an account of a clinical result after ingestion of tulsi. We scanned for examines distributed in books, theories, meeting procedures, and electronic databases including Cochrane Library, Google Scholar, Embase, Medline, PubMed, Science Direct, and Indian Medical databases. An aggregate of 24 examinations were distinguished that announced restorative consequences for metabolic disarranges, cardiovascular malady, resistance, and neurocognition. All investigations detailed ideal clinical results without any examinations revealing any noteworthy antagonistic occasions. The explored examinations strengthen customary uses and propose tulsi is a viable treatment for way of life related constant maladies including diabetes, metabolic condition, and mental pressure. Further examinations are required to investigate instruments of activity, explain the dose and portion structure, and decide the populaces well on the way to profit by tulsi's helpful impacts.

Key words: Antioxidant, Anti inflammatory, Anti bacterial, Cough and Cold, Tulsi

INTRODUCTION

Tulsi (*Ocimum sanctum* L.) in Hindi or Tulasi in Sanskrit (holy basil in English) is an exceptionally adored culinary and restorative fragrant herb from the family Lamiaceae that is indigenous to the Indian subcontinent and been utilized inside Ayurvedic medication over 3000 years. In the Ayurveda framework tulsi is frequently alluded to as a "Solution of Life" for its mending powers and has been known to treat a wide range of basic wellbeing conditions. In the Indian Materia Medica tulsi leaf separates are portrayed for treatment of bronchitis, ailment and pyrexia.It is viewed as a pervasive plant in India. It is a fragrant plant in the family lamiaceae. It is an erect, much stretched sub bush 30-60cm tall with furry stems and basic inverse green leaves that are unequivocally scented. Tulsi assumes a crucial job in our regular daily existence and is supposed to be the sovereign of natural plants. It is the most well-known family plant in India and it is hallowed in Hindu custom. Numerous Hindu legends clarify the significance, properties and employments of tulsi. Tulsi is an erect pleasant smelling bush which develops upto a stature of 3 - 5 feet. It is ordinarily developed in gardens and in the outskirts of sanctuaries. it has an impactful taste and fragrant smell. It is the main plant that can retain carbon dioxide for a mind-blowing duration. It discharges the oxygen in the early morning which is useful for the individuals in breathing dis-orders.

Tulsi plant has a great deal of essentialness for humankind, because of the complex restorative advantages it gives. Tulsi leaves are broadly utilized in the readiness of Ayurvedic prescriptions. It is known to advance the life span of life.The extricates acquired from the plant are widely brought to use for relieving different illnesses, for example, the basic cold, irritation, intestinal sickness, coronary illness, migraines, stomach issue, kidney stones, heart issue, and some more. The Indian basil Tulsi additionally helps in the decontamination of environment. Tulsi plant fills in as a marvelous repellant in battling against flies, mosquitoes and creepy crawlies (Warrier 1995). It is particularly significant in fighting malarial fever. It is said that at the hour of foundation of Victoria cultivates in Bombay (presently Mumbai), the laborers became survivors of mosquito nibbles and experienced interminable jungle fever. Seeing the pitiable circumstance of the laborers, a portion of the Hindu supervisors suggested the manor of Tulsi plant in the nursery. On following their recommendation, productive outcomes were gotten.

Accordingly, sacred basil Tulsi assisted with subsiding the development of mosquitoes and control intestinal sickness. There are various employments of Tulsi plant. The plant is progressively discovering its way in the Ayurvedic treatment of infections. Tulsi leaves are broadly utilized because of their recuperating power. It is a tonic for the sensory system and in this manner helps a lot in honing the memory. This fragrant plant underpins the evacuation of mucus and catarrhal issue from the bronchial cylinder. It additionally does something amazing in forestalling stomach issue. The herb Tulsi is known to fix the respiratory issue. The decoction arranged by blending nectar, ginger and Tulsi leaves is very useful in fighting bronchitis, flu and asthma. The leaves of Tulsi plant are amazingly valuable during the blustery season, when infections like jungle fever and dengue defraud the nation. Heat up the delicate leaves of Tulsi tea and offer it to the patient. The juice separated from Tulsi leaves fills in as the best solution for cut down fever. Tulsi is a fundamental fixing in the planning of Ayurvedic hack syrups. It is exceptionally valuable in disposing of cold and influenza.

Indeed, for sore throat, the leaves of therapeutic plant Tulsi is of extraordinary worth. Simply heat up the leaves of Tulsi in water and request that the patient swish with this decoction. Tulsi can reinforce the kidneys. For those experiencing the issue of renal kidney stones, the decoction arranged by blending the juice of Tulsi leaves with nectar, whenever taken truly for six successive months can remove these stones through the urinary tract. For keeping up solid heart, Tulsi is of most extreme worth. It helps in bringing down the degree of cholesterol in blood. Consequently, Tulsi plant fills in as the best solution for dispose of cardiovascular maladies (Gordon and David , 2001).

Medicinal Properties

Basil is antispasmodic, appetizer, carminative, galactagogue, and stomachic. It is used for stomach cramps, gastric catarrh, vomiting, intestinal catarrh, constipation, and enteritis. It had been sometimes used for whooping cough as an antispasmodic. Tulsi has antioxidant properties and reduces blood glucose levels. Thus it is useful for diabetics. 2. Tulsi reduces total cholesterol levels. Thus it is useful for heart disease patients.3.Tulsi reduces blood pressure

Health benefits of tulsi in our daily life

The tulsi plant has many medicinal properties. The leaves are a nerve tonic and also sharpen memory. They promote the removal of the catarrhal matter and phlegm from the bronchial tube. The leaves strengthen the stomach and induce copious perspiration. The seed of the plant are mucilaginous. Fever and Common Cold: The leaves of basil are specific for many fevers. During the rainy season, when malaria and dengue fever are widely prevalent, tender leaves, boiled with tea, act as preventive against theses diseases. In case of acute fevers, a decoction of the leaves boiled with powdered cardamom in half a liter of water and mixed with sugar and milk brings down the temperature. The juice of tulsi leaves can be used to bring down fever. Extract of tulsi leaves in fresh water should be given every 2-3hrs (Kothari et.al, 2008) .

Respiratory Disorders

Tulsi is an important constituent of many Ayurvedic cough syrups and expectorants. It helps to mobilize mucus in bronchitis and asthma. Chewing tulsi leaves relieves cold and flu (Staples et.al, 1999). Water boiled with basil leaves can be taken as drink in case of sore throat. This water can be used as a gargle (Kuhn et.al, 2007).The herb is useful in the treatment of respiratory system disorder. A decoction of the leaves, with honey and ginger is an effective remedy for bronchitis, asthma, influenza, cough and cold. A decoction of the leaves, cloves and common salt also gives immediate relief in case of influenza. They should be boiled in half a liter of water till only half the water is left and add then taken (Puri et al, 2002).

Kidney Stone

Basil has strengthening effect on the kidney. In case of renal stone the juice of basil leaves and honey, if taken regularly for 6 months it will expel them via the urinary tract (Biswas and Biswas, 2001).

Heart Disorders

Basil has a beneficial effect in cardiac disease and the weakness resulting from them. It reduces the level of blood cholesterol (Jyoti et.al, 2004).

Children's Ailments

Common pediatric problems like cough cold, fever, diarrhea and vomiting respond favorably to the juice of basil leaves. If pustules of chicken pox delay their appearance, basil leaves taken with saffron will hasten them (Devi et al, 1999).

Stress and Headaches

Basil leaves are regarded as an 'adaptogen' or anti-stress agent. Recent studies have shown that the leaves afford significant protection against stress. Even healthy persons can chew 12 leaves of basil, twice a day, to prevent stress. It purifies blood and helps prevent several common elements. Basil makes a good medicine for headache. A decoction of the leaves can be given for this disorder. Pounded leaves mixed with sandalwood paste can also be applied on the forehead for getting relief from heat, headache, and for providing coolness in general.

Eye Disorders

Basil juice is an effective remedy for sore eyes and night-blindness, which is generally caused by deficiency of vitamin A. Two drops of black basil juice are put into the eyes daily at bedtime.

Mouth Infections

The leaves are quit effective for the ulcer and infections in the mouth. A few leaves chewed will cure these conditions.

Insect Bites

The herb is a prophylactic or preventive and curative for insect stings or bites. A teaspoonful of the juice of the leaves is taken and is repeated after a few hours. Fresh juice must also be applied to the affected parts. A paste of fresh roots is also effective in case of bites of insects and leeches (Sharma et.al. 1998).

Skin Disorders

Applied locally, basil juice is beneficial in the treatment of ringworm and other skin diseases. It has also been tried successfully by some naturopaths in the treatment of leucoderma.

Teeth Disorder

The herb is useful in teeth disorders. Its leaves, dried in the sun and powdered, can be used for brushing teeth. It can also be mixed with mustered oil to make a paste and used as toothpaste. This is very good for maintaining dental health, counteracting bad breath and for massaging the gums. It is also useful in pyorrhea and other teeth disorders

Tulsi used as Traditional Indian Ayurvedic Medicine

According to Organic India, an organization dedicated to organic agriculture and sustainable development, one of the qualities that make the Tulsi plant such a potent medicinal herb is its ability to reduce stress. Tulsi is abundant in essential oils and antioxidants, which are tremendously effective in reducing the effect of stress. on the body. Tulsi has got diverse healing properties. Though traditionally used by Hindus or Indians now others are using it too recognizing its immense therapeutic properties. The Tulsi has the property of acting as an adaptogen. It balances different processes in the body and is of great help in stress management. The extracts of Tulsi have been used in traditional Indian Ayurvedic system of medicine. It is also used in the Unani system of medicine. Ayurvedic remedies for common colds, headaches, stomach disorders, inflammation, infections, heart disease, poisoning, cataracts and malaria make use of the Tulsi. The Tulsi acts on the nervous system and strengthens it. It strengthens the heart. It acts as an appetizer and promotes digestion too. It facilitates the secretion of digestive enzymes and prevents flatulence. Having detoxifying properties the Tulsi purifies blood of any toxins that might be present in it.Tulsi may well provide protection from radiation poisoning. It has also been indicated that Tulsi possesses anti cancerous properties. There has come up a belief that a Tulsi leaf swallowed daily will ensure protection from cancer. Apart from its religious significance it is of great medicinal significance, and is a prime herb in Ayurvedic treatment. Marked by its strong aroma and a stringent taste, tusli is a kind of "the elixir of life" as it promotes longevity. The plant's extracts can be used to prevent and cure many illnesses and common ailments like common cold, headaches, stomach disorders, inflammation, heart disease, various forms of poisoning and malaria. Essential oil extracted from karpoora tulsi is mostly used for medicinal purposes though of late it is used in the manufacture of herbal toiletry. The Plant Cultures project of the Medicines and Healthcare Products Regulatory Agency (MHRA) of the United Kingdom notes that in Ayurvedic medicine the Tulsi plant has been used topically for skin conditions like eczema, ringworm and insect bites. It is also commonly used to reduce fevers, improve lung and digestion issue reduce the effects of colds, eliminate toxins/poisons and as a preventative antibacterial for infections.

Tulsi in Modern Medicine

In modern medicine there has been research indicating Tulsi might potentially be an effective treatment for conditions like ulcers, high cholesterol, Type 2 diabetes, obesity and compromised/suppressed immune systems (from conditions like cancers and AIDS). Plant Cultures says the traditional uses of Tulsi in Ayurveda might be due to some intrinsic properties in many varieties of Tulsi--such as the essential oils containing an anti-inflammatory compound called eugenol, and various acids with antioxidant and anti-inflammatory properties that could support the claims of Tulsi being a treatment for so many conditions, according to Ayurveda.Tulsi in your home: The Tulsi plant, like most herbs, is a delicious way to enhance the flavor of your cooking, or make an excellent tea. This sub-shrub looks quite attractive in a decorative pot, is not harmful to animals and it is fairly easy to grow. Even outside of its medicinal properties, the Tulsi plant can make a great addition to your household either in your spice rack or in your garden.Diabetes--Western medicine: According to diabeteshealth.com, "Researchers have theorized that holy basil (tulsi) leaves may improve pancreatic beta cell function and thus enhance insulin secretion." The website reports that a small research study of patients with type 2 diabetes found blood glucose fasting levels lower in patients who took 2.5 grams of powdered tulsi compared to patients who took a placebo. Diabeteshealth.com reports that drug interactions with tulsi have not been reported; however, some interactions might be possible in "diabetics treated with insulin or insulin secretagogues such as sulfonylurea (glyburide, glipizide, Amaryl), Prandin or Starlix." Because of this, diabetics who might consider using tulsi should check with their physicians first.
Natural Medicinal Uses-: Sidha, Unani and Ayurvedic medicine use tulsi to treat a wide variety of skin conditions, fevers, coughs and internal ailments. Ayurvedic medicine treats bronchitis with a liquid tonic made from tulsi leaves, which Indians mix with cardamom or lemon juice. All three medicinal systems date to ancient times and are based on natural remedies and treatments, primarily based on herbs and plants.

Snake and Insect Bites

According to Plantcultures.org, oil from tulsi is a natural antiseptic and natural anti-inflammatory. According to Botanical.com, tulsi effectively treats snake bites, including those of poisonous snakes, when all parts of the plant are either ingested or mixed with other plants to form a paste that is applied to the bite area. Residents of the Asian subcontinent often put tulsi leaves into bowls of water outside their homes and in their bath water to ward off insects, which do not like the smell.

Nutrition Value

Contains vitamin C and A, and minerals like calcium, zinc and iron, as well as chlorophyll and many other phytonutrients. Also enhances the efficient digestion, absorption and use of nutrients from food and other herbs. Protein: 30 Kcal, 4.2 g; Fat: 0.5 g; Carbohydrate 2.3 g; Calcium: 25 mg; Phosphorus 287 mg; Iron: 15.1 mg and Edible portion 25 mg vitamin C per 100 g.

Phytochemical Constituents

The chemical composition of Tulsi is highly complex, containing many nutrients and other biologically active compounds, the proportions of which may vary considerably between strains and even among plants within the same field. Furthermore, the quantity of many of these constituents is significantly affected by differing growing, harvesting, processing and storage conditions that are not yet well understood.

The nutritional and pharmacological properties of the whole herb in its natural form, as it has been traditionally used, result from synergistic interactions of many different active phytochemicals. Consequently, the overall effects of Tulsi cannot be fully duplicated with isolated compounds or extracts. Because of its inherent botanical and

biochemical complexity, Tulsi standardization has, so far, eluded modern science. The leaf volatile oil contains eugenol (1-hydroxy-2-methoxy-4-allylbenzene), euginal (also called eugenic acid), urosolic acid (2,3,4,5,6,6a,7,8,8a,,10,11,12,13,14b-tetradecahydro-1H-picene-4a-carboxylic acid), carvacrol (5-isopropyl-2-methylphenol), linalool (3,7-dimethylocta-1,6-dien-3-ol), limatrol, caryophyllene (4,11,11-trimethyl-8-methylene-bicyclo[7.2.0]undec-4-ene), methyl carvicol (also called Estragol: 1-allyl-4-methoxybenzene) while the seed volatile oil have fatty acids and sitosterol; in addition, the seed mucilage contains some levels of sugars and the anthocyans are present in green leaves. The sugars are composed of xylose and polysaccharides.Although Tulsi is known as a general vitalizer and increases physical endurance, it contains no caffeine or other stimulants. The stem and leaves of holy basil contain a variety of constituents that may have biological activity, including saponins, flavonoids, triterpenoids, and tannins. In addition, the following phenolic actives have been identified, which also exhibit antioxidant and antiinflammatory activities, Rosmarinic acid ((2R)-2-[[(2E)-3-(3,4-Dihydroxyphenyl)-1-oxo-2-propenyl]]oxy]-3-(3,4-dihydroxyphenyl) propanoic acid), apigenin (5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-on), cirsimaritin (5,4'-dihydroxy-6,7-dimethoxyflavone), isothymusin (6,7-dimethoxy-5,8,4'-trihydroxyflavone) and isothymonin. Two water-soluble flavonoids:Orientin (8-C-beta-glucopyranosyl-3',4',5,7-tetrahydroxyflav-2-en-3-one) and Vicenin (6-C-beta-D-xylopyranosyl-8-C-beta-D-glucopyranosyl apigenin), have shown to provide protection against radiation-induced chromosomal damage in human blood lymphocytes (Claus et al, 2003).

Antioxidant - Polyphenol Rosmarinic acid present in the Tulsi chemical composition acts as the powerful antioxidant. It protects the cells in the body from smash up due to the presence of free radicals. Excess of oxidation in the body also causes the cell damage. This acid prevents the formation of excess oxidation (Simoons and Frederick 1998).

Antibacterial – Carvacrol and terpene are the antibacterial agents present in this remarkable plant. Sesquiterpene B-caryophyllene also severs the same purpose. This constituent is FDA approved food additive which is naturally present in Tulsi. It helps keeping the body safe from bacterium that causes illness
Anti-inflammatory - Rosmarinic acid also is a good source of anti-inflammatory along with being an antioxidant. Pegenin is one more compound available in the composition serving the same function. Apart from these two, the most important anti-inflammatory driving force in Tulsi is 'eugenol'. It is main ingredient responsible for controlling the blood sugar levels in the body. It rigs the beta cell function of the pancreas and as a result augments the insulin secretion.

Adaptogenic – Tulsi is ideal source of adaptogenic properties that controls the frequent mood swings and provide the mental peace and clarity. Eugenol and caryophyllene are the most imperative adaptogen agents present in the chemical formula of Tulsi. These are very effective in lowering the corticosterone levels that are main cause of stress. It also enhances the memory and minimizes the risk of mental problems that occur due to growing age. Ursolic acid and oleanolic acid also perform the same function of adaptogen and are very effectual in dropping the stress levels (Gavin 2001).

Immuno-modulator – It is very vital to have some immuno-modulator in the body that stabilizes, recovers and maintains the proper balanced functioning of the immune system. Tulsi possess excellent immune-enhancing properties that prepare the body against foreign elements like bacteria, viruses, microbes, allergens etc. Thus, it maintains the overall balance in the body (Chatterjee 2001).

CONCLUSION

All these restorative fixings make Tulsi an unquestionable requirement have for more and serene life. This little plant is unquestionably an excellent wellspring of restorative properties. After top to bottom and thorough research it has

been demonstrated and ensured that it is sheltered to devour Tulsi in any structure. All these medicinal properties are all around acknowledged and respected by present day science. Tulsi is the herb that fixes the humankind from all chances normally in the present shallow not very great way of life. It is considered as India's sovereign of herbs.They are to a great extent utilized in ayurvedic meidicines. It has restorative properties just as corrective properties. Tulsi is developed in practically all Indian homes. Water overflowed with tulsi leaves is useful for sore throat. It can likewise be swished. Biting tulsi leaves treats cold and flu.Tulsi leaf when eaten in the first part of the day filters blood. It tends to be utilized as tooth powder by drying its leaves and blended in with water. It helps in securing the whole respiratory tract.Its has numerous corrective properties and utilized in home grown cleanser and furthermore for body scour. It helps in controlling dandruff. Tulsi oil can be utilized for controlling dandruff. It tends to be utilized by blending in with coconut oil.Tulsi leaves squeeze and ginger juice fixes stomach throb, cramps and furthermore gets alleviation from stomach worms.

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REVIEW ARTICLE

Exploring Inhibitory Potential of Ginger against Numerous Targets of Diverse Forms of Cancer A Review

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ABSTRACT

The scientific analysis is carried out all over in India since Vedic times and are present in a group of herbal preparations of the Indian traditional health care system (Ayurveda) proposed for their valuable anticancer and other valuable properties. Numerous forms of cancer accounts for 10% of total death worldwide which requires better therapeutic approaches. Ginger is one of the most commonly used herbal medicines for the treatment of numerous ailments and improvement of body functions. Compounds of ginger (*Zingiber officinale),* shown to exhibit antioxidant, anti-inflammatory and anti-carcinogenic properties. In current study, we intended to analyze inhibitory properties of ginger towards target proteins for several cancers by computer aided virtual screening. Docking study revealed that compounds gingerol, shogaol, zingiberol, zingiberene, zingerone, zingerdiol were found to have strong binding affinity towards selected cancer targets. Hence, these compounds can be further investigated in vitro and in vivo to develop novel chemical scaffold on which further derivatization can be done for further optimization of its anticancer activity.

Key words: Antioxidant, Cancer, Ginger, Targeted drug

INTRODUCTION

Ginger (*Zingiber officinale* Roscoe; family *Zingiberaceae*) is a widely used spice, flavoring agent, herbal medicine and is also employed in the perfume industry. Cultivated ginger is a sterile crop, originated in subtropical areas. The main producers are India, China, Indonesia, and Nigeria. *Zingiber officinale*, commonly referred as ginger ,shows effective Hyperglycemic control properties in diabetes mellitus. It is also used to treat a variety of common ailments such as vomiting, indigestion and cold-induced symptoms. It is also useful as an anti-cancer,anti-inflammatory,anti-oxidant and analgesic agent. It can boost the immune system by boosting the lymphatic system which expedites removal of waste products from the body and to fight potential diseases and maintain health. Its anti-oxidant character protects cells against free radical damage and can prevent some forms of cancer,heart diseases , strokes and viral infections.

The aim of choosing this topic is According to World health organization(WHO) Cancer is the second leading cause of death globally, and was responsible for 8.8 million deaths in 2015. Globally, nearly 1 in 6 deaths is due to cancer.Nowadays various types of cancers are reported every month that spread with various mechanisms. There are over 200 different types of cancers for the reason that there are over 200 different types of body cells.

The most frequently diagnosed cancers in India are in man: oral, lung, colorectal and in female: Breast, cervix and ovarian cancers. There are many known causes of cancers like exposure to chemicals, drinking excess alcohol, excessive exposure to sunlight, and genetic differences, to name a few [2]. Ginger (Zingiber officinale Roscoe) is one of the most commonly consumed dietary condiments in the world [3]. In addition to its flavor, ginger is known to contain a number of potentially bioactive phytochemicals, mainly gingerols and their related dehydrating products, the shogaols as well as volatile oils .The anticancer properties of ginger are accredited to the occurrence of certain pungent vallinoids, viz. [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols, zingerone etc. A number of mechanisms that may be involved in the chemo preventive effects of ginger and its components have been reported from the laboratory research in a wide range of investigational models [7].

Lots of experimental evidences are available that support ginger-derived compounds have inhibitory effects on various cancer cell types like 6-shogaol and 6-gingerol in different types of cancer including pancreatic cancer cells Panc-1, Breast cancer cell lines MCF-7 and MDA-MB231,colon cancer cell SW480, H-1299 human lung cancer cells, CL-13 mouse lung cancer cells, HCT-116 and HT-29 human colon cancer cells,Human LNCaP, DU145, and PC3 and mouse HMVP2 prostate cancer cells and Ovarian cancer cells SKOV3.

MATERIALS AND METHODS

From the literature search the most potent cancer targets of various types have been taken [8,9,10] and their three-dimensional structures were available in their native formin online protein structure repository,Protein Databank (PDB)database. The X-ray crystal structureselected targets in complex with selective potent inhibitor were retrieved in pdb format from PDB database which includes vegf (PDB ID: 1FLT), Bcl-2 (PDB ID:1GJH), Bax (PDB ID:1F16), Cox-2 (PDB ID :1cx2), interleukin-6(PDB ID:1alu), tnf-alpha (PDB ID:3wd5), nf-kb (PDB ID:1nfk), the inhibitor from the crystal structure were removed and prepared for receptor ligand interaction studies. Hydrogen atoms were added to the target proteins and all water molecules were removed. Selection of ligands The ligands used for docking study were selected from literature.

The bioactive compounds that are mainly present in the rhizome of Zingiber officinale were considered for the study. Structures of major compounds present in ginger were retrieved from the PubChem compound database in the SDF file format and followed by conversion in PDB format using the tool Marvin Sketch features an extensive set of functionalities to allow the rapid and precise drawing of chemical compounds, reactions, Markush structures and

query molecules). These structures were used for docking calculation. The reference ligand structure is prepared in prior, using Marvin of ChemAxon by cleaned structure up in two dimension (2D) configurations.

Molecular Docking

Molecular docking is very necessary step performed to study the receptor-ligand interaction to select potential hits in virtual screening which regarded as the basis for structure based drug discovery. Molecular docking was performed in Yet another Scientific Artificial Reality Application (YASARA) an Auto Dock based tool for molecular docking and virtual screening. YASARA was used to gain the docking results of the listed compounds with the indicated target proteins.

The energy minimized compounds were imported and the docking conformations were performed twice using genetic evolutionary algorithm and the fitness of the docked structures were calculated. The hydrogen bond, Residues, Dissociation Constant, binding energy was calculated using YASARA Software. Here, the vdW term is van der Waal energy. H-bond and Elect terms are hydrogen bonding energy and electro statistic energy, respectively. The output of docking run is sorted based on binding energy. Yasara docking gives positive binding energy. So, more the positive energy indicates the higher likeness among the molecules.

Pharmacophore

Pharmacophore is defined as the minimum functionality that a molecule has to contain in order to show activity. Pharmacophore mapping was carried out in the workspace of mole sign module of Vlife MDS 4.3. Dataset of different types of cancer targets inhibitors was first aligned with reference to most active molecule as template. The most active molecule gingerol was selected to set it as the reference. The reference molecule is the molecule on which the other molecules of the align dataset get aligned. The minimum number of pharmacophore features for generated model was taken as 3.All spheres in the snapshot indicate all possible pharmacophoric centers. This pharmacophore model can serve as an effective search filter for virtual screening.

DISCUSSION

Evidences confirm the participation of plants extracts in synthesizing many medicines against already existing and even emerging diseases. In order to examine the binding capacity of bioactive compounds in *Zingiber officinale* on proteins related to cancer in human, we have used Yasara software to dock the ligand data set to the structure of target protein. Since all the natural ligands (inhibitors) were found to be docked in a variety of conformations and with varying binding energy.

From the interaction profile numerous interactions including hydrogen bonding interactions, hydrophobic interaction, Van der Waals interactions, and pi–pi interactions were inspected between selected inhibitors and retrieved Hit molecules with target proteins.

Through this methodology of computer aided drug interaction, we examine complexes formed between ligands and interesting targets (often many), for dissimilar types of a particular disease. Target proteins docked with different ligands are shown in Fig 1. The best dock pose was chosen on the basis of high docking score. Top two ligands were selected with better score. Zerumbone was found to be most active compound showing good binding affinity in terms of Yasara binding energy.

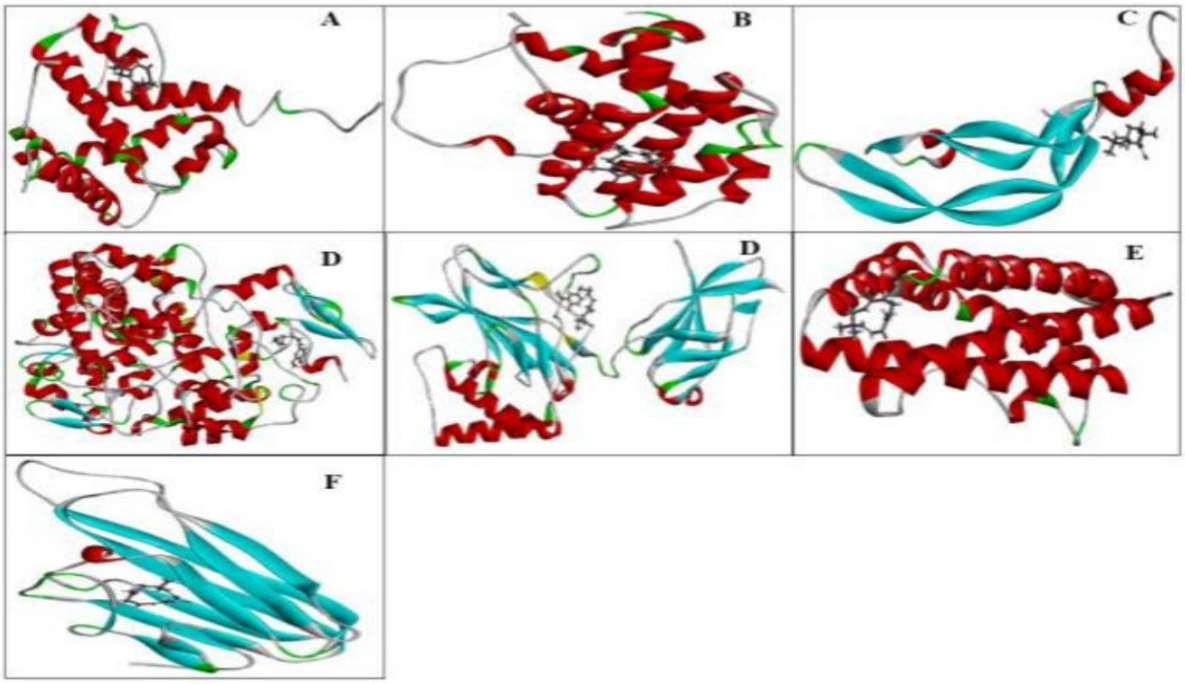

Fig 1.Binding modes and Protein-ligand interaction map of docked complexed ligands with A(Bax), B(Bcl2), C(Vegf), D(Cycloxygenase), E(Nf-kb), F(Interleukin-6)

CONCLUSION

In the recent years, more emphasis has been placed on identifying plant-derived compounds that can be used as an effective treatment for life-threatening diseases such as cancer. All the compounds selected for the study are considered as orally safe compounds. A few compounds showed interaction with the target proteins.Hence, the bioactive compounds that are interacting with the target can be used as potent inhibitor to block the action of target proteins. Thus, the selected compounds can be verified at the clinical-level drug examinations and made into an effective anticancer drug having better inhibitory activity against several types of cancer. Chemo preventive potential of phytochemicals have explored by our in silico findings and further, being natural, they have minimal or null side effects on human body as compared to the synthesized anti-cancer agents and thus could be their promising alternatives. Therefore, this approach is valuable for drug discovery process and anti-cancer therapy. Hence, now there is a requirement to study the pharmacological action of these compounds in in vivo models.

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RESEARCH ARTICLE

Application of Queues to Allocation of Hospital Beds

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ABSTRACT

In this Paper, the idea of Queueing Theory is adopted to model about practical problems like allocating beds in a particular hospital in a certain town. This method can be extended to larger scales and would provide better idea of how to allocate beds for patients which during the pandemic period like COVID – 19 is very essential in saving time, money and energy and most importantly the lives of several humans.

Keywords: Nearest Integer Function, Poisson Distribution, Stochastic Equilibrium, Steady state condition, Mathematical Induction, Geometric Distribution.

INTRODUCTION

Queueing Theory is a branch of mathematics which is very widely used in various real life situations by suitably modeling and applying appropriately. The models in queueing theory depend on the following parameters: number of customers in a queue (queue size), number of queues (channels), servers, number of service channels, queue length, queue discipline, waiting time, service time etc.

For past many years, queueing theory had been developed so much and got applied to address many practical problems. One of such practical problem is discussed in this paper. In particular, we consider a hospital in which we need to decide about the allocation of beds so that the disease is controlled over a period of time. We first consider an example and then develop Queueing models to determine better solutions.

Setting up the Situation

In this example, we develop an queueing model that simulate treatment of patients in a small town hospital The objects in our queueing system are occupied beds, since, only if the beds are free, new patients can be admitted. The

system will be the infrastructure of the hospital which treats the patients. Patients arrive into the queue after he/she acquires the disease and get admitted. Patients exit the queue after he/she gets completely recovered from the disease. Since the treatment given to respective patient depends on the severity of how infected he/she is, we will assume that the workers at hospital follow Service In Random Order (SIRO) queue discipline. Depending on several tests conducted sequentially (see [1]), we can follow the next step procedures for the treatment. In the first and simple model to be presented here, we will assume that there is only one service channel. This can be viewed as the case where the hospital in the small town has only one doctor who can treat the patients.

Developing the Model

We assume first, that our model is deterministic. We assume that the hospital admits 120 patients each day and so it should possess 120 beds for treating them. Notice that this number doesn't consider the count of out-patients, but only those who require rigorous treatment and hospitalization. We therefore can set arrival rate as A = 120 patients per day and service rate as N = 5 beds per hour amounting to 24 × 5 = 120 beds per day. Our queue can be modeled as follows:

Let t represent the time in hours and let $N(t)$ represent the number of occupied beds at time t. We than have

$$(3.1) \qquad N(t) = \max\left(0, A \times \left\lfloor \frac{t}{24} \right\rfloor - B \times t + N_0\right) = \max\left(0, 120\left\lfloor \frac{t}{24} \right\rfloor - 5t + N_0\right)$$

where $\lfloor x \rfloor$ is the nearest integer function. That is, round down $\lfloor x \rfloor$ to the nearest integer. Here, N_0 represent the number of occupied beds at time $t = 0$. Also, observe that $120\left\lfloor \frac{t}{24} \right\rfloor - 5t + N_0 \geq N_0$.

In (3.1), we notice that the maximum is taken with respect to 0 and non-negative quantity $120\left\lfloor \frac{t}{24} \right\rfloor - 5t + N_0$. Hence, $N(t)$ is always non-negative meaning that the number of occupied beds in the hospital will always be non-negative.

Examining this model, it is easy to calculate the equilibrium of the system. Since each day, 120 patients are added to the queue (arrival rate) and due to service offered to the patients, they get discharged at the rate (service rate) of 5 × 24 = 120 per day, the queue will balance itself every day. Thus at the beginning of each day, the queue will be of size N_0+120−5 every twenty four hours and decrease by 5 each hour until it reaches N_0. Thus the equilibrium for this queue is a pattern that cycle every 24 hours.

Of course, this deterministic queueing model is too simple in several aspects. It is unlikely that all the occupied beds would be exactly N_0 every midnight. Second, it is highly unlikely that 5 patients get treated exactly for every hour which makes the occupied beds empty for subsequent use. This doesn't mean that the model is unrealistic, but the model is suitably modified with required data without considering the real nature of the problems that we face. That is, we have ignored the stochastic nature of the problem. In this paper, using stochastic assumptions, I try to present the following probabilistic queueing model.

Generalized Queueing Model

We assume that the arrival rate and service rate are stochastic. In particular, we will set the arrival pattern as a Poisson distribution with a mean of 120 patients per day and the service pattern as a Poisson distribution with a mean of 5 patients per hour. We note that Poisson distribution is an idealized choice for dealing arrival rates for the most queueing models.

Mathematical setup of the Stochastic Queueing Model

Let $P_n(t)$ be the probability that the queue (hospital) contains n occupied beds at time t. The change in probability from t to $t + 1$ can be computed as follows:

$$(5.1) \quad P_n(t+1) - P_n(t) = \mu_1 P_{n-1}(t) + \mu_2 P_{n+1}(t) - \mu_1 P_n(t) - \mu_2 P_n(t)$$

where μ_1 is the arrival rate per day and μ_2 is the service rate per hour respectively. We note that $P_n(t+1) - P_n(t)$ is the change in probability from time t to $t + 1$. This value is viewed as sum of chances that a queue of length $n – 1$ increasing to n and a queue of length $n + 1$ decreasing to n and sum of differences that a queue of length n increasing to $n + 1$ and a queue of length n decreasing to $n – 1$. This explains the logic behind arriving equation (5.1)

If we consider the special case that $n = 0$, from equation (5.1), we get

$$(5.2) \quad P_0(t+1) - P_0(t) = \mu_2 P_1(t) - \mu_1 P_0(t)$$

We note that the first and fourth terms of equation (5.1) would vanish to give equation (5.2)

If we now assume that after a long run of time, the queueing system attains Stochastic Equilibrium, in the sense that the number of occupied beds would be compensated by number of unoccupied beds each day. In this situation, the system will be time independent because it happens for all hours in a day. This time independent state is usually referred as “Steady State Condition”.

The steady state conditions exist not only in queueing systems but they also occur in other practical problems like Wave equations, Heat equations, Propagation of Heat in Membranes and all sorts of physical problems involving partial differential equations.

In the steady state condition, since it is time independent, we have $P_n(t+1) = P_n(t) = P_n$. With this assumption, equations (5.1) and (5.2) can be rewritten respectively as

$$(5.3) \quad P_1 = \frac{\mu_1}{\mu_2} P_0$$

$$(5.4) \quad P_{n+1} = \left(\frac{\mu_1 + \mu_2}{\mu_2} \right) P_n - \frac{\mu_1}{\mu_2} P_{n-1}$$

Solution of Steady State Equations

We now try to solve equation (5.4) using (5.3) and determine the probability of having n occupied beds in the long run (steady state).

First, in equation (5.4), substituting $n = 1$, we get $P_2 = \left(\frac{\mu_1 + \mu_2}{\mu_2}\right) P_1 - \frac{\mu_1}{\mu_2} P_0$

Using equation (5.3), we have $P_2 = \left(\frac{\mu_1 + \mu_2}{\mu_2}\right) \frac{\mu_1}{\mu_2} P_0 - \frac{\mu_1}{\mu_2} P_0 = \left(\frac{\mu_1}{\mu_2}\right)^2 P_0$. We note that this equation exhibits similar property as that of equation (5.3). Continuing this way, we claim that

$$(6.1) \quad P_n = \left(\frac{\mu_1}{\mu_2}\right)^n P_0 \; ; n = 1, 2, 3, 4, \ldots$$

We will prove (6.1) by the method of Mathematical Induction. The result is true for $n = 1, 2$ because of equation (5.3) and expression for P_2 derived above. Hence by induction hypothesis, assume that (6.1) is true for all values of m up to k, and we will prove it for $m = k + 1$.

That is, $P_m = \left(\frac{\mu_1}{\mu_2}\right)^m P_0 \; ; m = 1, 2, 3, 4, \ldots, k-1, k$

For $m = k + 1$, from equation (5.4), we have

$$P_{k+1} = \left(\frac{\mu_1 + \mu_2}{\mu_2}\right) P_k - \frac{\mu_1}{\mu_2} P_{k-1} = \left(\frac{\mu_1 + \mu_2}{\mu_2}\right)\left(\frac{\mu_1}{\mu_2}\right)^k P_0 - \frac{\mu_1}{\mu_2}\left(\frac{\mu_1}{\mu_2}\right)^{k-1} P_0$$

$$= \left(\frac{\mu_1}{\mu_2}\right)^k P_0 \times \left[\frac{\mu_1 + \mu_2}{\mu_2} - 1\right] = \left(\frac{\mu_1}{\mu_2}\right)^{k+1} P_0$$

$$P_{k+1} = \left(\frac{\mu_1}{\mu_2}\right)^{k+1} P_0$$

Therefore, the result is also true for $m = k + 1$ and by principle of mathematical induction, equation (6.1) is true for all natural numbers n.

We further note that for each n, P_n forms a Geometric Progression (G.P.). So the probability function that we have in (6.1) represents a discrete Geometric Distribution. Thus the solution to the steady state equations (5.3) and (5.4) forms a Geometric Probability Distribution.

Since the total probability must be 1, we must have $\sum_{n=0}^{\infty} P_n = 1$

From (6.1), we must have $\sum_{n=0}^{\infty} \left(\frac{\mu_1}{\mu_2}\right)^n P_0 = 1$.

Since $\sum_{n=0}^{\infty} r^n = \frac{1}{1-r}$; $0 < r < 1$, we have $P_0 \times \frac{1}{1-\left(\frac{\mu_1}{\mu_2}\right)} = 1 \Rightarrow P_0 = \frac{\mu_2 - \mu_1}{\mu_2}$. This is valid only if $\frac{\mu_1}{\mu_2} < 1$.

That is the solution of steady state equations of the stochastic queueing model is given by (6.1) where $P_0 = \frac{\mu_2 - \mu_1}{\mu_2}$ and $\frac{\mu_1}{\mu_2} < 1$.

CONCLUSION

The condition for valid solution to the steady state stochastic queueing model we developed is $\frac{\mu_1}{\mu_2} < 1$. That is, $\mu_1 < \mu_2$. That is, the arrival rate must be less than the service rate. If this being so, then the number of occupied beds in the hospital becomes lesser and lesser so that the hospital may accommodate more of number of patients in case of emergency treatment like the present scenario of getting affected by COVID – 19.

So, the model conveys the fact that though it is ideally not possible to balance the affected and recovered patients every day or for a specific period of time, over a long period of run, with regular treatment methodologies we can ensure normalcy once if the occupied beds are less than the unoccupied beds or in other words, if the affected patients are lesser compared to recovered patients. Thus, the queueing model provides a possible solution for maintaining the hospital beds when patients come for treatment. But the only drawback behind this situation is we actually do not know how long will it take to ensure $\mu_1 < \mu_2$. Until then, we have to continue our treatment regularly. This is the precise reason why the Lockdown period is getting extended for so many days. We expect normalcy only if $\mu_1 < \mu_2$.

More sophisticated models can be developed if there are thousands of patients, in which case, one physician would not be sufficient to treat all the patients effectively. In that case, more physicians can be employed. Then the scenario of the model will become multi-server channel from single-server channel which we have discussed here. For such scenario see [2].

In Reliability Theory with suitable probability distributions of arrival and service patterns lot of study had been done. The same models can be suitably modified to medical scenario in deciding about bed allocations, maintenance and other aspects. For more sources of queueing models, see ([3] – [5]).

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RESEARCH ARTICLE

Prediction of Phonon Spectra for Ferromagnetic Nickel using BIOVIA Material Studio

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ABSTRACT

We have used CASTEP module in BIOVIA Material Studio to achieve a linear response calculation procedure in order to analyse phonon dispersion and density of states for nickel. We can get this data from neutron scattering experiments on silicon experimentally. We need these theoretical dispersion curves to validate the abinitio approach. The highest peak obtained around 0.0372 eV indicated largest phonon density of states which is dropping in order of declining energy values (or frequency ranges).

Keywords: CASTEP, BIOVIA, Nickel, Phonon Dispersion.

INTRODUCTION

Phonons are avitalnotion in condensed matter physics, which deliversentree to aextensivevariety of vitalproperties such as specific heat, heat expansion, and heat conduction, electron-phonon interactions etc. Density Functional Theory (DFT) methods are capable to know beforehand such properties.CASTEP module in the BIOVIA Material Studio delivers the essential functionality. Finite displacement method and Density functional perturbation theory (DFPT) are the two foremost methods in lattice dynamics calculations. Currently, DFPTin CASTEP can only be utilized without spin-polarization. So, for aextensiverange of materials phonon calculations can only be supported out by using the finite displacement algorithm.

METHODOLOGY

Here, we have used CASTEP to accomplish a finite displacement method to analyse the phonon dispersion and density of states for a ferromagnetic nickel. First, we have built the primitive cell of ferromagnetic nickel. A large cutoff radius is chosen in this finite displacement calculation. The convergence of the phonon frequencies as a

function of the cutoff radius has been investigated properly.The normal modes of vibration of a crystal is obtained by solving the problem of lattice dynamics of a system. Here, we can be able to calculate the energies of the phonons as a function of their wave vector's *k*. The relationship between E and k is called phonon dispersion. Generally, the quantum-mechanical approach is appropriate for Phonon's dispersion relation. The creation and annihilation operators are being used here as the quantum-mechanical operators for the coordinates for the normal mode phonon vibration.

RESULTS AND DISCUSSION

The Phonon dispersion curve relates with the frequency, ω, and the corresponding wave vector. Individually lattice contains acoustic modes. The dispersion relations of the above three modes at insignificant values (near Γ point) is almost linear, that is predictable from the Fig 1.2. The remaining vibrational modes, 3N - 3, are recognized as optical modes. The points denoted by W, L, G, X, W, K represent points in the reciprocal space where the space waves travel in. Each step corresponds a wave vector., each "step" corresponds to a wavevector. Each point contains the information about (a) the magnitude of the *k* vector and (b) its direction. The direction of the vector *k can be imagined as* connecting the origin of the reciprocal space and the point you are currently present. An alternate method may be used for calculations that necessitate phonon frequencies for huge numbers of q-points, to calculate phonon Density of States properties. This system takes benefit of the comparatively small range of active interactions between ions. The precise DFPT calculations are completed only at a very small number of q-vectors, and then an interpolation procedure is utilized to get frequencies at other q-points. Phonon dispersion curves display the dependence of the energy of the phonons on the q-vector, that is along the directions of high symmetry in the Brillouin zone. We can get this data from neutron scattering experiments on silicon experimentally. We need these theoretical dispersion curves to validate the abinitiomethod. Such experimental informationareobtainable for less number of materials, so theoretical dispersion curves are beneficial both for founding the rationality of a modeling approach. Besides, the electron-phonon interaction function, which is straightlinked to the phonon DOS, can be calculated directly in the tunneling experiments. It is thusvital to be able to estimate phonon DOS from the first principles method.Phonon density of states (or vibrational density of states) is the integral over the Brillouin zone over all 3N phonon bands, where N is the number of atoms in the cell. The large intense peak around 300 Hz corresponds to 0.0372 eV, which indicates that large number of presences of energy states around this energy. Density of Phonon states is decreasing in order of decreasing energy values (or frequency ranges).

CONCLUSION

This manuscript presents a simulation data where we have predicted the phonon dispersion curve and phonon density of states in a ferromagnetic nickel.The highest peak around 0.0372 eV indicated maximum phonon density of states. Density of Phonon states is reducing in order of decreasing energy values (or frequency ranges).

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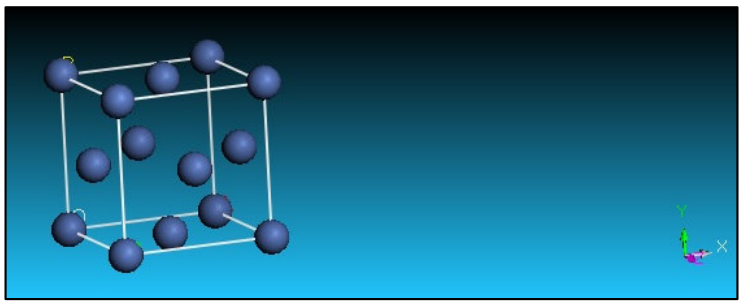

Fig.1.Crystal structure derived from Nickel using BIOVIA

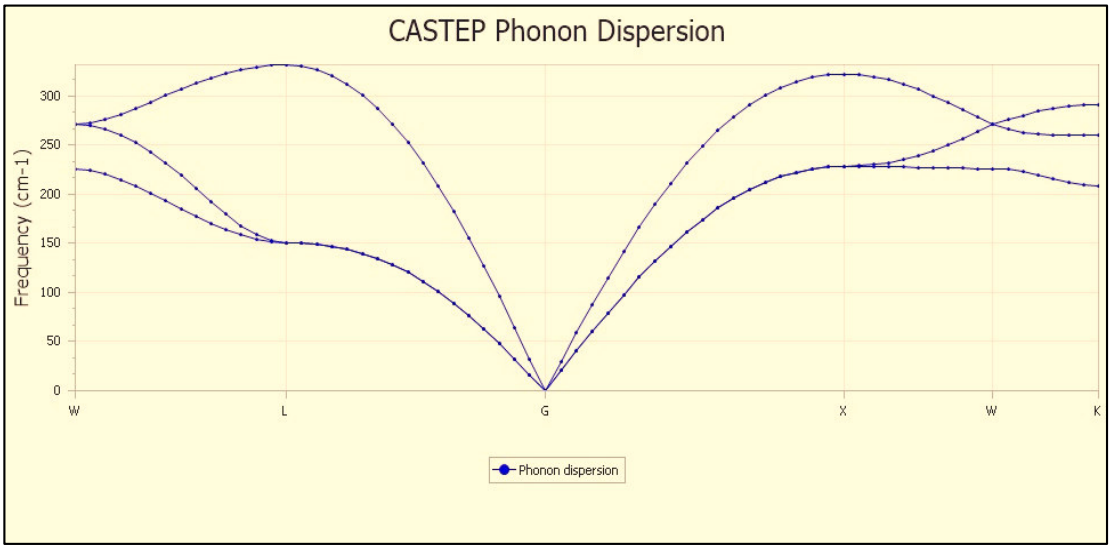

Fig.2.Phonon dispersion curve for Nickel

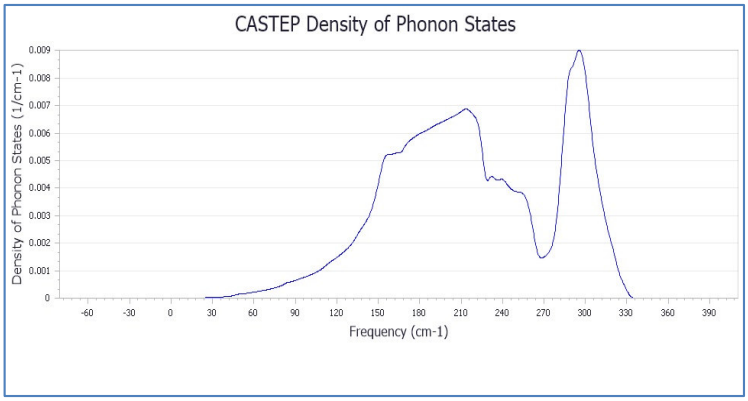

Fig. 3. Phonon density of states for Nickel

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RESEARCH ARTICLE

A Suitable Random Number Generator (RNG) for Computer Simulations

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ABSTRACT

Random numbers are very important in present days, starting from computation to simulation. There are many functions which generated pseudo random number which are continuously using for different purpose. These functions are called random number generators (RNG). A suitable RNG has been identified which can be a potential source for many theorist and experimentalist. A good RNG is very essential, having properties like low repeatability and less time of execution. Many RNG has been studied and comp aired their properties with each other to get suitable one. Finally a proper random number generators (RNG) has been identified and presented. The RNG has been chosen by the evaluation of solid angel of an experimental setup

Keywords: Random number, pseudo random number, solid angles, efficiency.

INTRODUCTION

Computer is very is very essential in present days. People working with computers often speaks about their system's "random number generator" and the "random numbers (RN)" it produces. They are (RN) used as ranging signal in radar system, controlling signal in remote control, encryption codes or keys in digital communication, address codes etc. All this application makes the Random numbers very important and it's generator. These random number generators are applicable in a large number of fields as mentioned above and a wide application to scientific computations like, stochastic experiments [1], cryptography, communications and simulation for many complex experimental set up for basic physics research. In particular, the security of communication and cryptography vitally depends on the quality and quantities of random ciphers (i.e., random bits or numbers). There are two approaches to generate random numbers: software-based and physics-based. All the Computer-generated "random" numbers are

more properly referred to as pseudorandom numbers, They all are software generated. The software based RN produces at high-speed with rates of several Gbit/s utilizing deterministic algorithms, but it is vulnerable when such pseudorandom numbers are used as the keys to encryption systems. the latter (i.e. physics based) can generate physical RNs and ensure the confidentiality of secure communication by means of the inherently random or unpredictable processes in the physical world. Many process like stochastic noise, radioactive decay [2-3] and frequency jitter of electronic oscillator have gotten used for the generation of physical random sequences. Most of the time it is very difficult to keep a separate physical device for random number generation inside a computer. So the generation of a true random number is not an easy task. To overcome this problem a computer based random number generators (RNG) are adopted for many application keeping certain important properties of RNG in mind. Some of the important properties of a pseudo random number generators are having large periodicity, uniformity and speed of generation.

In cases of a simulation of an experimental setup for nuclear physics/ reaction studies, the statistical uncertainties is a very important factor which depends on the periodicity of the RNG. A variety of clever algorithms have been developed which generate sequences of numbers which pass every statistical test used to distinguish random sequences from those containing some pattern or internal order. Most of the time it is very difficult to choose a proper RNG functions for different purposes. In this report we have presented verities of RNG with their important properties and predicted a suitable RNG function for simulation involving experimental physics and theoreticians.

SIMULATION AND RESULT

There are many random number generators are available in literature but out of many we have taken only four random number generator as mentioned RNG1[4], RNG2[5], RNG3[6], &RNG4[7-8].These are some RNG which has been adopted by many groups and also some RNG are available as inbuilt function in many computer programing languages. The mentioned four RNG generates uniformly distributed pseudorandom number between 0 and 1 . We developed a code to use all the four RNG together and made a multi thread parallel program to run them simultaneously to study and compare the different characteristic of the RNG functions. The extracted parameters for four of RNG has been tabulated in Table.1From the Table.1 one can see that two RNG (i.e. RNG2 and RNG4) are suitable choice depending on the speed and periodicity point of view. The average time has been estimated for 10^7 number of random number generation and found very little difference between RNG2 and RNG4. For all the four function the average value are closely ~0.5 which is expected for a good uniformly distributed RN. In order to emphases the choice of RNG functions, experimental simulation has been done by considering the following experimental situation.Fig.1 calculated solid angle for the three experimental situation explained in text. The lines are only to guide the eye. RNG4 has divided by 10 to separately compare the RNG2 & RNG4.

A mono energetic beam of particle has interacted with the target and the scattered particle has been detected using silicon detectors having different opening (0.5mm, 10mm, and 20mm) placed at a distance 30cm from the target. A Monte-carlo simulation has been done using the mentioned RNG2 & RNG4 to predict the solid angle (d⊚) obtained by the detector. The result of the simulation has been plotted in Fig.1. One can see that using RNG2 the uncertainties are less compared to the RNG 4. From Fig.1 one can find that the predicted value for the solid angle for the three experimental situation is nearly same using RNG2 & RNG4. The only difference is the uncertainties associated with them. Using RNG function 2 the uncertainties are very less whereas the uncertainties involved in the RNG function 4 is ~10^2 times more than the RNG 2. This indicates very clearly that for the detector having larger active area (MWPC, Silicon strip) RNG2 is more suitable whereas the RNG 4 is suitable for small opening like SSB detectors.

CONCLUSION

Many varieties of Pseudorandom number generators (RNG) has been considered ad used them in parallel program

to estimate the important properties like periodicity , average time etc. and found that not all RNGs are good/suitable for all situations. It has been shown that RNG2 and RNG4 are very suitable for experimental situations.

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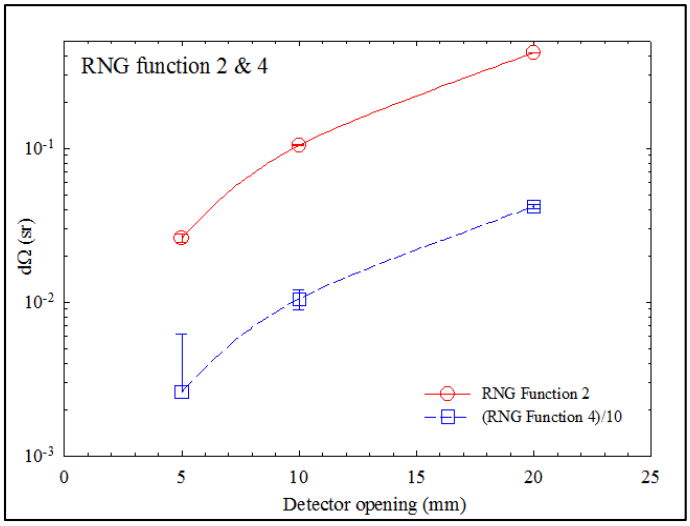

Fig.1.Calculated solid angle for the three experimental situation explained in text. The lines are only to guide the eye. RNG4 has divided by 10 to separately compare the RNG2 & RNG4.

Table.1.Result of the four RNG. The periodicity has been generated upto 12 decimal point and the average time has been extracted for 10^7 RN.

RNGs	Average time (sec)	Average	Periodicity
1	1.880E-01	5.00E-01	1212150120
2	2.600E-01	5.00E-01	132425833947
3	3.360E-01	4.99E-01	48503166576
4	1.480E-01	5.00E-01	315794473

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RESEARCH ARTICLE

Simulation Study of Detection of ions/charge Particles using Gas Detector

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ABSTRACT

A study & simulation has been performed to understand the behavior of energy lose in specific gases which can be the potential candidate for the detection of charge particles. It has been observed that the gas under study has very good response for the heavy charge particle/heavy ion compared to light ion which is a very good situation. Since the use of conventional solid state detectors are goes bad very fast for heavy ion detection, the gas detectors will place a very important role.

Keywords: simulation, specific gases, heavy charge particle/heavy ion, gas detectors.

INTRODUCTION

Starting from the long history people are trying to understand the radiation by detectingthose using different detectors [1-3]. But till now detector design is challenging task. As the interaction of different radiation is different for the material. Therefore verities of detector are used for different radiation. Out of many radiation charges particle detection is one of the interesting fields including others for the case of fission measurement. As the fission is the heart of nuclear reactor which emits lot of charge particles including neutral one. So the detection of heavy charge particles are important.As the detection of charged particle is very important in experimental nuclear physics so in many laboratories in country including abroad people rely on many varieties of detectors for nuclear physics. Out of which one popular and important detector is the solid state detector [4-5]. The most commonly used solid state detector is the silicon semiconductor detector. They are very good for charge particle detections as the efficiency of SSB (silicon surface barrier detector) is 100% for the charge particle but a single detector after using many times for so many experiment reduces the detection performance which lead to a situation to change the detector completely. The situation again worse in case of heavy ion detection (like fission detection). The solid state detectors go bad very fast due to defects and PHD (pulse height defect) which lead to replacement of the detector. This makes it expensive

and far from the reach of normal laboratory. To overcome this situation a new type of detectors can be used and many places people are using it also, the gas detector.

SIMULATION AND RESULT

The gas detectors are very simple and cheap to manufacture. The simplest one is an ion chamber where the gas is enclosed in between a cathode and an Anode. A proper potential will be applied between the electrodes such that the region between them is free from any charge carrier. At that instant if any heavy charge particle (say fission fragment) will enter the gas volume it will interact with the gas molecule and loss energy using Bethe- Block formula. The interaction is random and the generation of electron and ion inside the gas volume also random so it is important to simulate the situation. As soon the ions /electrons will generate they move to the corresponding electrodes and generates a pulse signal using proper electronics. The use of gas is very important at this stage. It must have low threshold for electrongeneration and also the quenching properties should be there. Of course a question will come to mind that whether the same gas detector can be used for light charge particle detection (say proton, lithium etc.) or not.Since the energy loss is depends on same Bethe-Block equation it should same. To understand these effect a monte-carlo simulation has been performed using the code SRIM/TRIM to understand its properties /behavior of energy lose for the ion /recoil in the gaseous medium using differentions varying from heavy to light and shown in Fig.1.

One can see from the Fig.1 that the heavy ion cannot move much distance in the gas volume due to multiple interaction and energy lose. The energy of the ion was 50 MeV which is a typical energy release in fission experiment. The heavy ion has taken as ^{120}Sn. whereas the same energy proton has crossed the gas volume and very small amount of energy loss has happed (the thin red color lines in upper part of Fig.1). This clearly indicated that using gas detector we can measure the full energy of the fission fragments but not the full energy of the light ions. From the lower part of Fg.1 one can see the generation of ion due to heavy and light ion. Once can see that a large distribution of ions for the hevy charge particle case has been found which indicates the production of large number of ions due to the interaction of the heavy ions in the gas volume compared to the light ion which is negligible. The energy loss of the light ion is very high at the end as there is a Brass plate present and the thickness of the plate is so much that the ions will stop there. The plate is grounded so the generation of number of ion and electron in plate will not be considered in the gas volume and only the ion generation will be considered due to heavy ion. The gas used here is a P-10 gas which is commonly used in nuclear experiments. The same thing has also compared with the SSB soild state detector and for the sake of completeness shown in Fig.2 .

The calculation has been performed by shooting by 10000 ^{120}Sn ions having energy 30 MeV. The high mass and the high energy has been chosen as in case of fission experiment the conventional detector goes bad very fast as the mass of the fission fragments are very high and the energy associated also very high ~20-50 MeV. When this high mass and high energy ion will pass the reversed biased junction they will create the defects and those defect sites are occupied by the other ions. It has been shown for the Silicon based detector the defects are occupied by large number of the Al atoms which means that the junction will be not free of defect for longer period and will go bad very fast.Another important investigation has been done, the plasma effect. When the high mass and heavy charge incident ion with high energy will pass the detector it creates the plasma in the track. If the track is narrow the plasma density will be very more as the distribution is not uniform which leads to the more pulse height defect. This is another mode for bad performance of the SSB detector for the heavy ions.

CONCLUSION

A complete analysis has been done to understand the behavior of gas for the detection of ions (heavy and light) using the SRIM/TRIM and found that the Gas detector can be a very good potential for the detection of the heavy charge particle like fission whereas the detection of the light charge particle can be done using solid state detector

(say Silicon detector but not the gas detector). This can be provide enough motivation for the peoples/researcher to produce different gas detector for the charge particle detection

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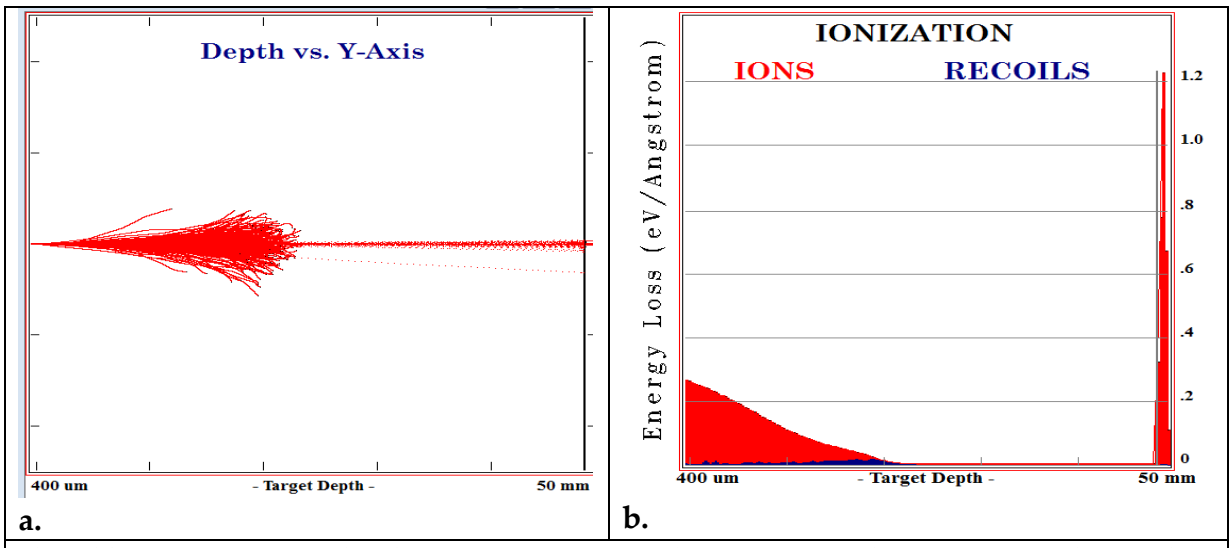

Fig.1. (a) the TRIM calculation for standard P-10 gas using the proton of energy 50 MeV (the straight thin line) and the thick broadening is for 50 MeV ^{120}Sn heavy ion. (b) The ions and recoils distribution within the gas volume for both ions.

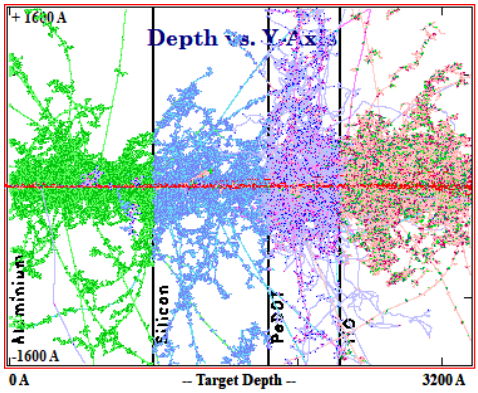

Fig.2.The TRIM calculation for standard Silicon detector which shows the distribution of the energy loss spread. When a charge particle move inside the SSBsemiconductor detector. One can see that the tracks are spread over the full range which is not the case for gas detector.

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RESEARCH ARTICLE

Solar Cell- A Potential Candidate for Charge Particle Detection

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ABSTRACT

A newly designed solar cell has been studied using the Monte Carlo simulation. The detail properties have been explained in order to explore it as radiation detectors. It has found that the newly polymer based semiconductor has a high potential for detector manufacturing.

Keywords: Monte Carlo simulation, semiconductor, radiation detectors

INTRODUCTION

The rapid growing global population, living standard and economic development has triggered mankind to think a new alternative way to find energy sources. The most abundant and efficient alternative energy source is the solar energy [1-3].In addition with the energy generation these tiny wonderful devices can also be used as the nuclear charge particle detection system. As the detection of charged particle is very important in experimental nuclear physics so in many laboratories in country including abroad people rely on many varieties of detectors for nuclear physics. Out of which one popular and important detector is the solid state detector. The most commonly used solid state detector is the silicon semiconductor detector. They are very good for charge particle detections as the efficiency of SSB (silicon surface barrier detector) is 100% for the charge particle but a single detector after using many times for so many experiment reduces the detection performancewhich lead to a situation to change the detector completely. This makes it expensive and far from the reach of normal laboratory.

To overcome this situation a new design of semiconductor has been investigated. The newly proposed detector is using as solar cells. The new solar cell is Indium Tin Oxide (ITO) based solar cell and there is no Silicon inside which is a common material in conventional solarcell. There are many layers but none of the layers have Silicon. It is very important to study the different characteristic and compared with the existing Silicon detector. The present report is based on the simulation studies to understand the characteristics.

SIMULATION AND RESULT

When the junction will be reverse biasedthere will be no any free charge carrier. At that instance if any charge radiation (say proton, alpha, and fission) will fall on the junction it will create electron and hole. The movement of these electron and holes on the opposite direction lead to signal pulse. A monte-carlo simulation has been performed using the code SRIM/TRIM [4-6] to understand its properties like efficiency and the suitability of it innuclear experiments. The same simulation has also performed for existing SSB detector which normally people use in experiments. The comparison has been shown in Fig.2.

One can see from the Fg.1 that the efficiency (i.e. the generation of electron and hole) is nearly same for both the detector. The calculation has been performed by shooting by 10000 ^{120}Sn ions having energy 30 MeV. The high mass and the high energy has been chosen as in case of fission experiment the conventional detector goes bad very fast as the mass of the fission fragments are very high and the energy associated also very high ~20-30 MeV. When this high mass and high energy ions will pass the reversed biased junction they will create the defects and those defect sites are occupied by the other ions. It has been found from the simulation that for the case of Silicon based detector the defects are occupied by large number of the Al atoms which means that the junction will not be free of defect for longer period. Whereasat the same time the newly proposed ITO based semiconductor detector has less defects and the occupancy of the Al atom is also small. This indicates that the longer longevity of the detector for the heavy ion case.

Another important investigation has been done, the plasma effect. When the high mass and heavy charge incident ion with high energy will pass through the detector it creates the plasma in the track. If the track is narrow, the plasma density will be very more as the distribution is not uniform which leads to the more pulse height defect. Whereas from Fig.2 one can see that the plasma distribution for ITO based semiconductor is wide spread i.e. the density is not localized in narrow region which indicates the quick collection of the electron and hole as soon they will create. This is very important as it reduces the pulse height defect which is one of the main drawback of the existing semiconductor detector.

SUMMARY AND CONCLUSION

The details simulation has been performed using SRIM/TRIM software to understand the properties and suitability of newly designed semiconductor for the experimental purpose. The detailed simulation has been compared for both the cases. Electron and hole generation efficiency has found nearly same for both the cases. We have found also the defect generation is less in newly designed ITO based semiconductor compared to silicon based. In addition it has also found that the Pulse height defect is less in ITO based semiconductor compared to silicon based. All these properties indicates the suitability of the newly ITO based semiconductor. More experimental data will required to validate our founding strongly which is our next motivation.

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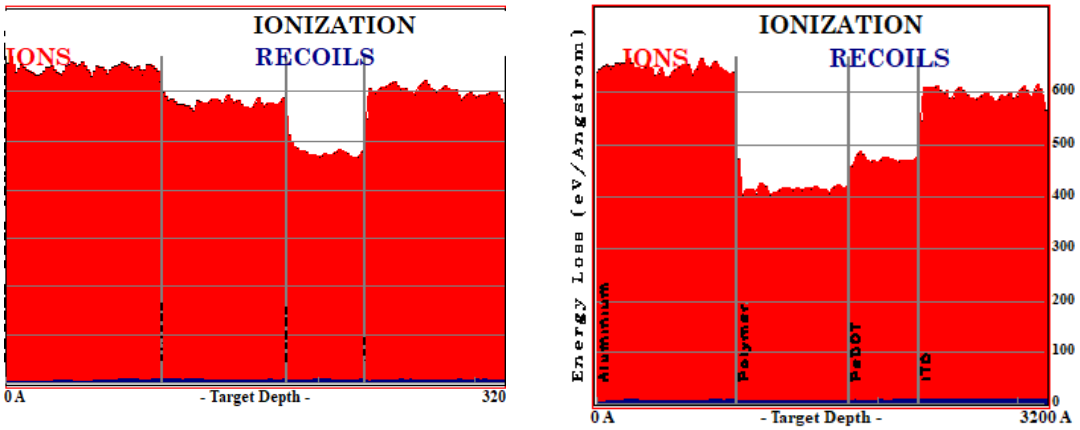

Fig.1.The same TRIM calculation for newly proposed semiconductor. The generation of the electron and hole are nearly same in both. A small increase can be seen in Si based detector which is expected (Left). The proposed ITO based semiconductor. One can see the ionization recoil spectra are almost same for the both the types of detector which indicates the applicability of the ITO based detector (Right).

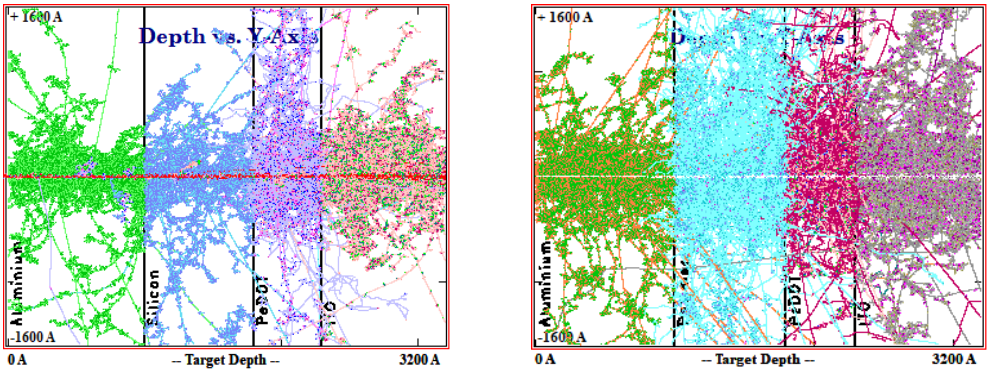

Fig. 2.The TRIM calculation for standard Silicon detector which shows the distribution of the energy loss spread (Left). The same energy loss spread for proposed ITO based semiconductor. One can see that the track is narrow in conventional Silicon whereas wide spread in the proposed ITO (Right).

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REVIEW ARTICLE

A Review on Machine Learning Applications in Transmission Line Fault Analysis

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ABSTRACT

This article is a detailed review of the methods for detecting faults, locating and classifying them on transmission lines. Although all these methods are very interlinked with much correlation, the authors want to clarify the understandings of the concepts separately. Fault detection techniques are discussed based on feature extraction methods such as wavelet transform,support vector machines,support vector regressions,fuzzy logic,neural network,decision trees and fuzzy inference systems are among few key topics under this review. The main purpose to write this paper is to give an idea about different approaches of machine learning with the concern of detection, location and identification of the faults in the transmission lines. For much clarity in the review,the authors have presented and analyzed the results of few articles presented by authors.

Keywords: Transmission line fault, Machine learning, Neural network,Wavelet transform,Fuzzy inference system,Support vector machines,Decision trees.

INTRODUCTION

Transmission lines are a critical part of the electrical power network because they provide the path of transmitting power from generation to distribution and, thus, load centers. They operate at voltage level from 100kV to 1000kV and are ideally interconnected for more reliability. These days with the advanced sensors, communication networks, intelligent automation, etc. have been integrated to enhance its efficiency and reliability. Still, in recent years, the power quality is also the main issue in electrical power system. Faults in transmission lines do occur, however, have a major effect on customers.Since the power system faults are unavoidable, prediction of the faults with great precision and accuracy is also very important. The prime objective of this paper is to address various machine learning frameworks for the treatment of transmission line faults. Particularly applications of machine learning for

transmission line fault classification and location identification has been explored. Our survey is divided into two parts:

1. Fault classification techniques which determine the type of fault.
2. Fault location techniques measures the distance of the fault.

There are various machine learning methods for classification of faults, such as support vector machine, Neural Network, Decision trees, Fuzzy logic, ELM, K-nearest neighbors etc. Apart from Machine learning, there are some other approaches like wavelet-based approach, genetic algorithm, PMU based approach and Multi information measurement etc.

Wavelet based approach and Fourier transform

Wavelet transform is an efficient method for analyzing transient current and voltages. In frequency bands it analyzes the signals. It uses low frequency long windows, and high frequency short windows [1]. This method has lower error estimates but has an extremely high computational burden [2].Synchronized phasor quantities from all the terminals of the transmission line are used in phasor measurement unit (PMU). Genetic algorithm also plays a significant part in classifying and detecting faults. Yet such methods are bit sluggish and complex [3].Most researchers used Discrete Wavelet Transform (DWT) techniques to decompose the original voltage and current signals rather than Continuous Wavelet Transform (CWT or WT).The Fourier transform is used as an important mathematical method for study of signals in the frequency domain. The DFT (Discrete Fourier Transform) is used for time and frequency domain, where the signals are discrete. The authors used half cycle DFT in [29-31] to measure fundamental and harmonic phasors for classification of fault forms. In [32] the author made a very strong comparison of the mother wavelets in a sequence of compensated transmission line for identification and classification of faults.

Other feature extraction methods

Like wavelet transform and Fourier transform, there are some other feature extraction methods that the authors want to discuss here. In reference [33] the author suggested Principal Component Analysis (PCA) which is very useful in reducing the data dimension by mapping the data from the original long-dimensional space to a short-dimensional sub-space in which the data variance can be better considered. The author proposed a new feature extraction method based on Random Dimensionality Reduction Projection (RDRP) in [34]. This method requires very limited memory space as the extraction process takes place with multiplication of matrixes.In references [35-37] the authors mentioned a new fault detection and classification algorithm. Here's used both DWT and BPNN based on Clarke's parallel transmission transformation. The author made a change in Clarke Transformation in [38-39] that is called Clarke Concordia Transformation. The line currents α, β and 0 components resulting from the artificial neural network-based learning algorithm and Clarke Concordia Transformation are used for detecting all forms of fault. The author has used another type of modal transformation known as Karren Bauer Transformation in which the fault classification and faulted-phase selection based on the initial current traveling wave [40].

Machine learning approach

Machine learning is a branch of Artificial Intelligence (AI) where the computer is trained with a collection of data of intelligence knowledge so that it could be able to take decision without human intervention. The performance of machine learning algorithms can be improved with the help of huge number of available intelligent data.The very first stage to improve power quality is to classify the power system faults. There are different prominent machine learning approaches for fault classifications such as:

Support Vector Machines (SVM)

This is a supervised machine learning algorithm that can be used for both classification and regression. It's mainly used in classification issues though. In this algorithm, we plot each data element as a point in n-dimensional space (where n is number of characteristics) with each characteristic being the value of a particular coordinate. Then we perform classification by finding the hyper-plane which very well distinguishes the two classes.These learning models map high dimensional input space into target space [4].The regularization parameter helps in classifying each training samples. Empirical Mode Decomposition (EMD) and SVM are used for fault classification in [5].The voltage of transmission line is decomposed into Intrinsic Mode Function by EMD.

The Principal Component Analysis (PCA) and SVM are used for both fault classification and detection to reduce the dimensionality and locate the signal violation point [6].Mosavi et. al., discussed the fault transient travel time information derived by Discrete Wavelet Transform (DWT)[7]. The fault position scheme is based on superimposed voltage at the tap point, measured from the terminal voltage. Another critical factor in the presence of FACTS is devising the fault position scheme. Least square SVM is used for classification of faults[8].

Hanif et al. proposed a combined approach of DWT with SVM for fault classification [9]. The post fault voltage energies and normalized energies are extracted and used as input to the four SVMs used to predict the fault in each phase. The detection and classification of series compensated faults using SVM are done in [10-12].Most of the fault classification methods are associated with many separate sub algorithms where each functions independently and sequentially.Yet in reference [13] the authors suggested a new integrated and groundbreaking algorithm for machine learning, i.e. Summation-wavelet extreme learning machine (SW-ELM) which incorporates extraction of features into the learning process. SW-ELM extension also i.e. Summation-Gaussian Extreme Learning Machine (SG-ELM) has been proposed and successfully applied for fault diagnosis.

Another new approach on Artificial Intelligence, called Hierarchical Temporary Memory(HTM), is suggested by Dikio et. al.[14]. This is a state-of-the-art online learning technique for neural/machine learning and the tool is based on a suite of biologically plausible algorithms coined as Cortical Learning Algorithms(CLA). Compared with Online Sequential Extreme Learning Machine (OS-ELM) it is found to have superior performance.M.Saini et. al. have proposed a new algorithm combining Discrete Wavelet Transform(DWT) and Back Propagation Neural Network(BPNN) for parallel transmission line detection and classification of faults[15].The thyristor-controlled series compensator line is supported by the use of support vector machines [24]. Three SVMs are trained to provide fault ground detection and line segment identification using the Thyristor Controlled Switched Capacitor (TCSC). Polynomial kernel and the Gaussian kernel with different parameter values are used to train three SVMs. The author introduces two new approaches based on Wavelet Transform Support Vector (WT-SVM) and Wavelet Transform Extreme Learning Machine (WT-ELM) in [25]. SVM based approach is found to be more effective for classification of faults than ELM based approach. Yet the average error with SVM is less than ELM for fault position, and the mean error with SVM is marginally higher than with ELM. The feature is extracted using DWT and then input to SVM as described in references [26-28]. The faulty phases are identified and the position of the fault can be calculated using Radial Basis Function Neural Network (RBFNN) with the least square recursive algorithm.

Fuzzy Logic

It's a lot of valued logic between 0 and 1. It's used to tackle the idea between absolutely right and absolutely false. The thorough knowledge of the structure is not needed since the rules are formulated by humans. Through fuzzification, the inputs are redirected into fuzzy membership functions. All of the fuzzy inference system rules are used for measuring fuzzy output function. Defuzzification converts fuzzy values into crisp (bi-valued) values.

Three phase current data obtained from compact reconfigurable devices are used to the proposed method using fuzzy logic [16].

Artificial Neural Networks

With the use of Artificial Neural Networks (ANN), most non-linear and complex real-time problems can be dealt with better. Artificial Neural Networks can estimate the fault position on the transmission line based on modal information [17]. Prony method is used to derive the modal information from voltage or current signal. Two schemes are presented : (i) with signal voltage and (ii) with signal current.Together with four SVMs the proposed two stage FIR filter is used to detect and classify short circuit faults. One can predict the location of the fault and its distance by using Support Vector Regressions (SVR)[18].

Support Vector Regression (SVR)

It also has the same fault-classification concept as SVM. Ray et.al. [19] suggested SVM for classification of Al.[19] suggested SVM for classification of faults and SVR for location of faults. Through taking published data from other studies, a comparative study was performed.Hosseini et. al.presented method for both fault classification and fault location[20].Discrete Wavelet Transform method is used to decompose post-fault voltage samples that are used in combination with post-fault current samples as SVM input for fault classification. The prediction of each phase fault is done by fourSVMs.Depending on 1st stage fault,the 2nd stage fault location is done by SVR.

Some other techniques

Apart from above methods, earlier there were researches on some other topics like K-NN algorithm, Genetic algorithm and ELM etc. All such types are also found to be effective in this regard. Few of the significant researches have been presented here.As shown in Table 1 below, the proportion of single line to ground fault incidence is around 70%.Its occurrence probability is around 14 times more than L-L-G fault at the voltage level of 300-500kV.Mohammad Farshad et.al.[21] suggested a method for designing the SLG fault locator in regression mode on the basis of k closest neighbor(k-NN). Through this proposed approach, both the classification and the location of faults are determined. Decomposed signals obtained from the Discrete Fourier Transform are fed to the classification of type k-NN as data.In regression mode, identification of the fault location is performed by k-NN. The accuracy of the system is not affected by mild change in fault location, fault inception angle, fault resistance, magnitude and direction of current. The full proposed system procedure is illustrated in Fig.1.

Process overview

The entire process is divided into three sections such as: generation of data, identification of the fault type and identification of the fault position as shown in Fig. 8.It is the most important part in case of machine learning approach. Because machine learning approach learns from data. Hence type of data collected defines the type of machine learning approach to be implemented. Data generation process consists of three major steps like post fault transient phase voltage, Discrete Wavelet Transform (DWT) and Training data set.Simulated post fault transients are created by using Aspen one liner. The DWT prepares the discrete data. Wavelet transform provides time resolution for high frequency components. Wavelet for fault location was proposed [22].All the machine learning algorithms are trained properly with simulated dataset. The algorithm will have optimal decision boundaries which will be used to predict the outcome of real-time fault, once the training is done.

Review of Decision Trees

The non-parametric supervised method of learning used in classification and regression is such. Leo Breiman [23] first published the Classification and Regression trees in 1984.Classification trees are used when the dataset needs to be divided into groups that correspond to response variable. The classes Yes, or No, in many situations. They're just two, and special to each other.Regression trees are used on continuous response variables. In a regression tree, using each of the independent variables, a regression model is fit for the target variable. Before that the data for each independent variable is broken at much stages.The error between the expected values and actual values are squared at each of those points to get "A Total of Squared Errors"(SSE). The SSE is measured through variables and the variable or point that has the lowest SSE is selected as the dividing point. The cycle is continuing recursively.Trees of classification and regression work to generate specific predictions or expected classifications, based on the set of if-else conditions. Typically they have many advantages over regular trees for decision as shown in Fig. 9.There are also few limitations of classification and regression trees as shown in Fig.10.

The CART is among the oldest and most simple algorithms. It is used on the basis of certain predictor variables to predict outcome. They are excellent for data mining tasks, since very little data pre-processing is needed. Decision tree models are easy to understand and incorporate which gives them a major advantage over other analytical models. Top-down approach to decision trees is built by selecting a variable at each stage that best divides the target into homogeneous sets.It follows a greedy search for one feature value that can break the target space "best" at a given node which is a decision value. For the next child node, the cycle repeats. There are various metrics used by different algorithms constructing the decision trees to find the “best” feature.

SUMMARY AND CONCLUSION

The author has clarified and checked very clearly the methods used in transmission lines for detecting faults, classifying faults and locating faults. Because the method of identification of fault is highly dependent on the technique of extraction of features, priority is given to this. Likewise the method of classification of faults is discussed using various essential methods of classification such as SVM and ANN etc. Various approaches to improving the efficiency of the fault classification and location methods have been addressed. Support Vector Machine and Support Vector Regression have been found to be very successful in the process of classifying faults and defining fault locations. Summation-wavelet Extreme Learning Machine (SW-ELM) and Summation-Gaussian Extreme Learning Machine (SG-ELM) are used to combine the process of extraction of features and the process of fault diagnosis. Some authors have used the Discrete Wavelet Transform method.

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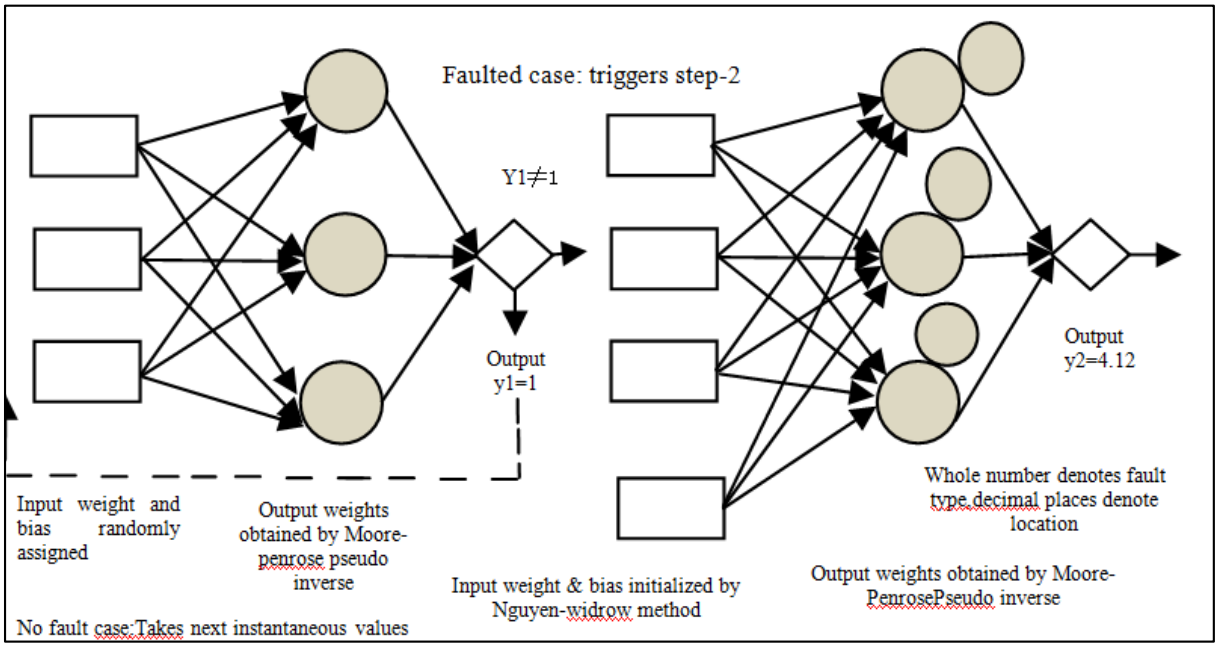

Figure 1.Schematic representation of the proposed fault diagnosis method [13].

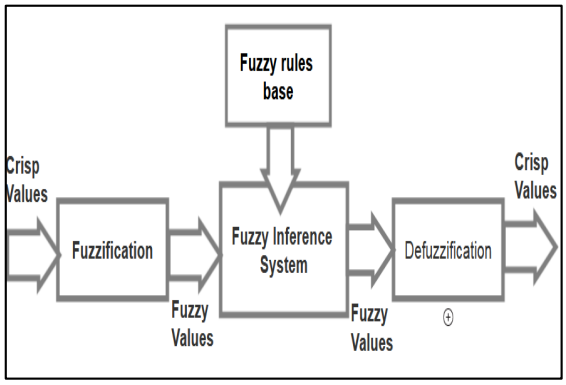

Figure 2. Fuzzy Logic System Architecture.

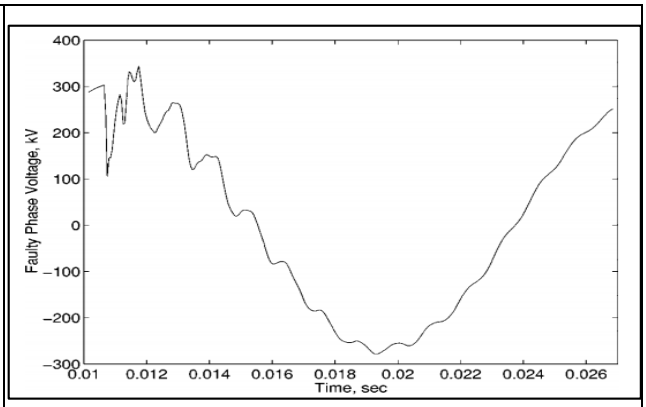

Figure 3.Voltage Waveform of the faulty Phase [17]

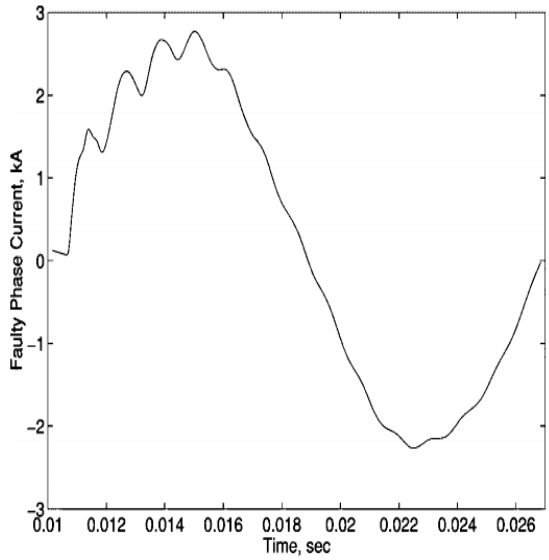

Figure 4.Current Waveform of the Faulty Phase [17].

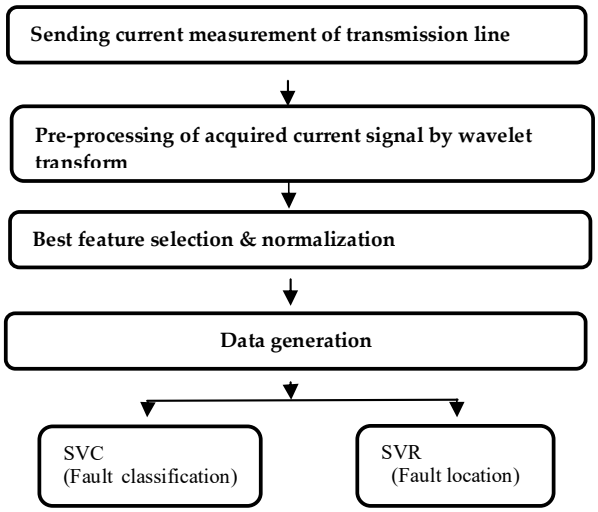

Figure 5.Block diagram of SVM based fault classification and location in a transmission line. [19].

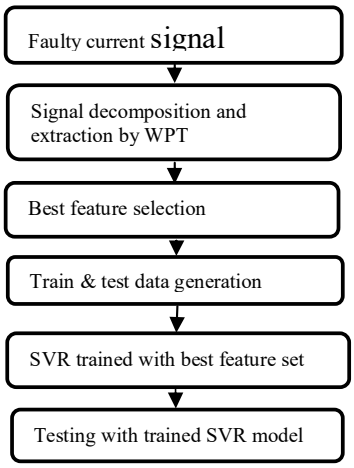

Figure 6: Flowchart of fault location technique [17].

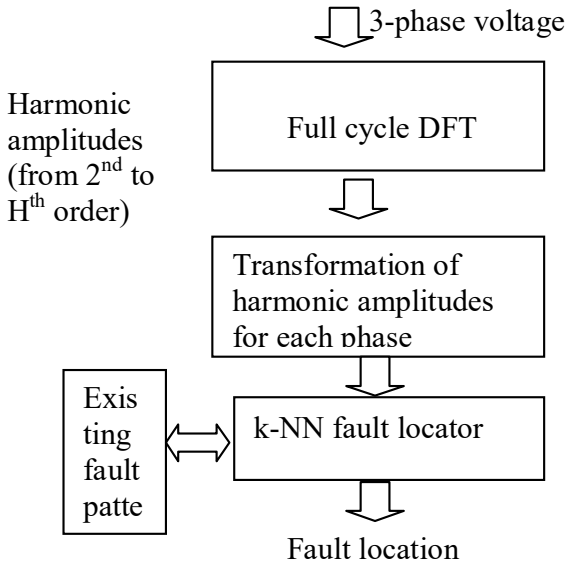

Figure 7: Method of fault location [21].

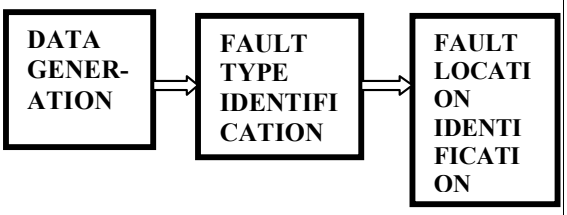

Figure 8: Complete process for fault treatment.

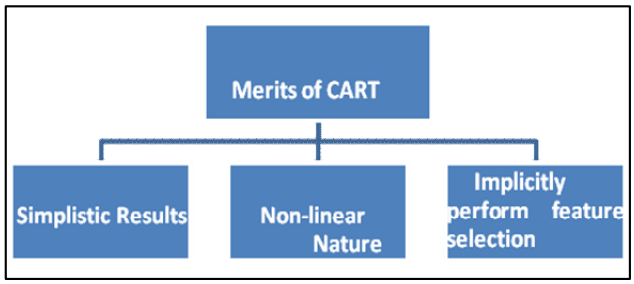

Figure 9: Merits of Classification and Regression Trees (CART).

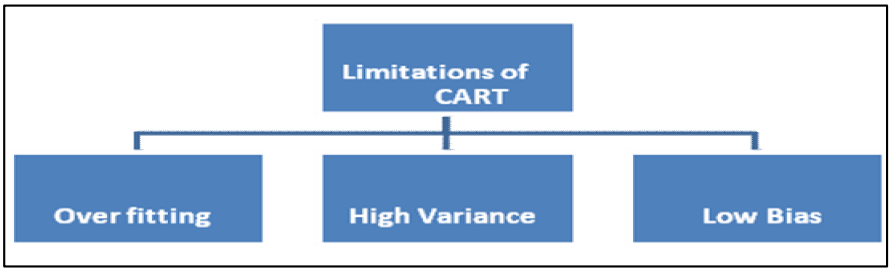

Fig.10. Limitations of Classification and Regression Trees.

Table 1. Relative probability of occurrence of fault in percentage

Type of Fault	L-G	L-L	L-L-G	L-L-L L-L-L-G L-L, L-G	Total
% of occurrence	70	15	10	5	100

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RESEARCH ARTICLE

Simulation of Sodium-ion having Energy 200 keV Induced Effects on Vanadium as Target

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ABSTRACT

We have reported the Monte-carlo simulation of irradiation of alkali ions (sodium) having energy 200 keV on vanadium. We have employed a simulation process namely SRIM which is built on the binary collision approximation technique. The projected average range is 217 nm and the concentration of ions in the vanadium target will be 17416 X 10^{15} atoms/ unit volume at a fluence of 8 X 10^{15} atoms/cm^2. This simulation helps us to gather a rich amount of information regarding ion-induced defects, which is highly essential for experiments on vanadium.

Keywords: Ion Range in 3D, SRIM, Vanadium.

INTRODUCTION

Vanadium is a very effective catalyst for innumerable practical applications. Its oxide VO_2, is utilized in the manufacture of glass coatings to block infrared rays. Vanadium redox batteries are also utilized for grid energy storage. Vanadium is also considered as a suitable significant material for a fusion reactor. The impact of sodium ions on these metal surfaces is vastlysubstantial to see the detailed simulation regarding for each ion, ion incident angle, and incident energy. Here, a Montecarlo simulation viz. SRIM is used here to explore the ion distribution in 3D.

SIMULATION

The TRIM "Ion Distributions" i.e. RANGE.TXT comprises the range distribution i.e. the penetration depth of the incident ions. The range distribution unit is shown in the atoms/(Å-ion). When this value is multiplied by the fluence, the concentration of ions in the target can be realized. The below example of RANGE.TXT is for sodium (200 keV) into vanadium. Fig .1 shows the curve between the variations of sodium ions incident on the vanadium target.

It revealed that almost nearly 8.7 X 10^7 number of vanadium atoms ions i.e. maximum sodium number of atoms i.e. at 2311 Angstrom have reached inside the vanadium target. Fig.2 shows the curve between the variation of recoiled vanadium atoms and penetration depth. Almost 55311 number of ions i.e. maximum sodium number of atoms i.e. at 1680 Angstrom, have reached inside the vanadium target.

ION RANGES 3D

This image in fig.3 shows the plot for ion 3D range of sodium ions having ion range inside vanadium target atoms. The inset image shows the graphical representation in 2D. RANGE_3D.TXT comprises the ending positions of the ions in the target. Here, the sodium ions are charted with their (depth) in X-axis, and Y, Z as (lateral) coordinates. Any ions which are backscattered or transmitted ions are not shown in this graph. This image shows the average ion penetration range is 217nm. The straggle is nearly 82 nm having skewness 0.110.If you multiply ion dose, for example, 8 X 10^{15} atoms/$cm^{2;}$ the concentration of ions in the vanadium target will be 17416 X 10^{15}atoms/ unit volume.Hence, we can obtain the concentration of vanadium atoms in this mechanism

CONCLUSION

We have reported the alkali ion namely sodium having energy 200 keV induce effects on vanadium target. We have found out the average penetration range is 217 nm and at a fluence of 8 X 10^{15} atoms/cm^2, the concentration of ions in the vanadium target is found out to be 17416 X 10^{15} atoms/ unit volume.

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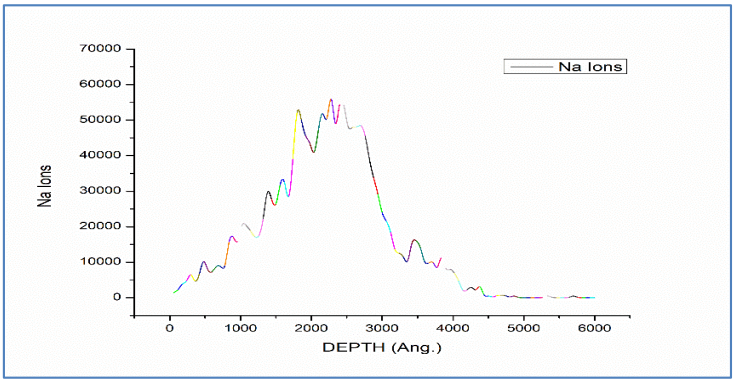

Fig.1.Variation of Sodium ions with penetration depth

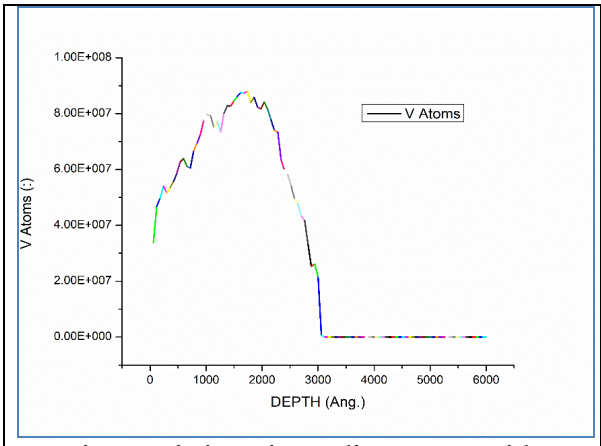

Fig.2.Variation of vanadium atoms with penetration depth

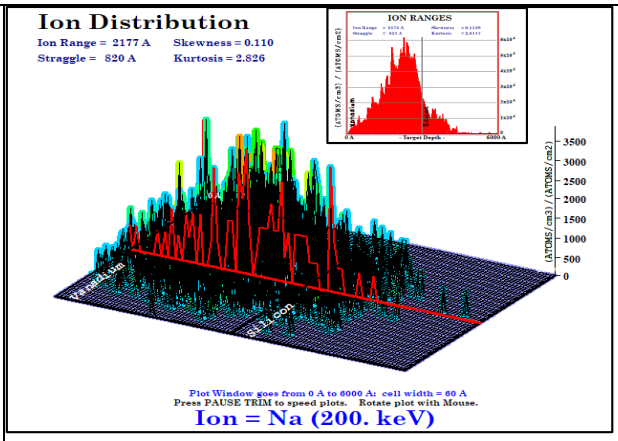

Fig.3.The Plot of Ion-3D range

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RESEARCH ARTICLE

Simulation of 50keV Argon ion on ZnO Nanoparticles using SRIM

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ABSTRACT

The Monte-carlo simulation of irradiation of argon ions having energy of 50 keV on zinc oxide (ZnO) nanoparticles is carried out in order to obtain the distribution of ions, recoil distribution, energy to recoils and ionization data, which will support the experimental dataobtained after irradiation.The SRIM (Stopping and Range of Ions in Matter) software is used to calculate the impact on the structure of ZnO nano particles when irradiated with the Argon ions of potential of 50 keV.

Keywords: Monte-carlo simulation, SRIM, zinc oxide nanoparticles, irradiation of argon ions.

INTRODUCTION

Zinc oxide is a non-toxic inorganic material which is insoluble in water and mostly exist in the powdered form and it has no evidence of any carcinogenicity in human being. Nevertheless, the ZnO powder can be unsafe by inhalation or consumption since it causes zinc fever [1]. The crystalline form of ZnO has a wurtzite structure, where each negative ion is surrounded by four positive ions situated at the four corners of a tetrahedron, giving rise to a noncentrosymmetric structure to the ZnO [2-4]. ZnOis considered as one of the finestengineering material because of its varied applications in different areas [5]. Due to small size of the ZnO nano particles, it has a wide applications in the field of nanomedicines, biosensors and bionanotechnologies [6]. ZnO nano particles have good antibacterial properties because of the high ratio of specific area to volume [7]. Around 50% to 60% of ZnO is utilised in the rubber industry for vulcanisation of rubber process. The mixture of ZnO and Fe_3O_4 is impregnated with the charcoal inside the filter in order to remove the carcinogenic gases like hydrogen cyanide from tobacco smoke. ZnO is extensively used as an additive in various materials including ceramics, rubber such as car tyres, plastics, pigments, ointments, as a nutrient source, fire retardants, sealants, batteries, addhessives, glass and cements [8]. Doped ZnO nanoparticle can act as a multifunctional materials because of its photo catalytic properties in water medium for degradation of severalunusual dyes released into water systems by different industries, producing hydrogen which can resolvethe energy and environmental issues. ZnO nanoparticle doped with different materials can play a vital

role in different fields including medicines, spintronics, photoluminoscent and in the development of various cheap and solar cells [9].

METHODOLOGY

In this study, A simulation based on Monte-Carlo termed as SRIM is used, which can determine the behavior of Zinc oxide when the bombardment with an argon ion. ZnO nanoparticle is synthesized by precipitation method [10]. Here, the simulation is done to interpret the influence of low energy argon ions on ZnO as the target molecule.The experimentation will be carried out after obtaining enough data from the SRIM simulation.

RESULTS AND DISCUSSION

The stopping and range of ions can be calculated by means of TRIM which is a part of SRIM programme. The window for the TRIM set up is shown in the Fig.1.The damage calculated will be based on the thorough calculation with complete damage cascades. The distribution of ion with recoils is being anticipated on the XY plane. The angle of incidence is kept at 0 degree.

The window for TRIM Setup is applied to response the data on the ion, target, and the sort of TRIM calculation. Here, Zinc Oxide (ZnO) is used as the target and Argon(Ar) as the ion data. The energy was taken very low energy 50keV. Fig. 1 (Right) expresses about the TRIM calculation when the energy is 50keV. In this graph Ar ions of 50 keV energies are striking perpendicular to the target atoms such as Zinc and Oxygen. This figure also depicts the ion path for 50 keV energy in the XY plane. The red dots in the Fig. 1 (Right) represent the ion track which predicts that one ion is bombarded with the zinc oxide atoms and consequently vacancies corresponding to that atom are produced. The red dots in the Fig. 1 (Right) represent the ion track which predicts that one ion is bombarded with the zinc oxide atoms and consequently vacancies corresponding to that atom are produced due to displacement of the Zinc Oxide atoms from its lattice site.The red dots in the Fig. 1 (Right) represent the ion track which predicts that one ion is bombarded with the zinc oxide atoms and consequently vacancies corresponding to that atom are produced due to displacement of the Zinc Oxide atoms from its lattice site. The green colored dotsreprsentvacancies produced by recoiling Zinc Oxide (ZnO) molecular atoms. The collections of green dots created due to continuous damage caused by ionsthat is recoiling Zinc Oxide (ZnO) atoms.This phenomena is known as recoil cascade.When the Argon ions strikes a Zinc Oxide molecular atom hard, it causes some amount of energy lost from the system. Each collision between the hard ion and Zinc oxide produces a green cascade and there is a chance that the ions may change their direction.The two dimensional (2D) distribution of Argon ions enhancement in the Zinc Oxide target is shown in the Fig. 2. Here the target depth is set up at 300 A so that the more amount of ions can be easily anticipated in the plot.

In Fig. 2, the X- axis represents target depth while the Y-axis represents the number of atoms per unit volume (concentration) or unit area. For the energy of 50vkeV, the range of ion is 424 A, Straggle is 196 A, Skewness is 0.6641, and Kurtosis is 0.8860. Fig. 2 (Right) shows the 2D plot of Ion/ Recoil distribution for the Zinc Oxide. This plot shows the number of atoms will have recoiled back at the target depth. In the plot, the Oxygen atom recoil distributions are shown by the cyan blue colour and the red coloured curve represents the Zinc recoil distribution. From the plot, one can interpret that all the Zinc Oxide atoms are removed from their lattice sites, generating vacancies by applying 50 keV energy for piercing these atoms. From the plot, one can predict that the number of Zinc atoms will have recoiled back at the average target depth is 8.5 $\times 10^7$ and the number of Oxygen atoms will have recoiled back at the average target depth is 6.2$\times 10^7$.

Fig. 3 shows the 2D plot of Energy to recoil for 50 keV energy. This plot states about the damage of the target by the irradiation of the ions. This plot shows the energies absorbed by atoms when one Argon atom bombards ZnO. Here

the orange color plot represents the energy absorbed by Zinc, the blue color plot represents the energy absorbed by Oxygen. From the plot it is clear that the energy absorbed by Zn and Oxygen atom is 58 eV/Ion and 35eV/Ion respectively. Fig. 3 (Right) represents the 2D plot for collision events. In this graph Green color denotes Replacement Collisions, Blue color represents Target vacancies showing the vacancy is fewer than the target displacement and Red color signifies Target Displacements.

CONCLUSION

In this study, the very low energy argon ions induced effects on Zinc oxide nanoparticles using SRIM. We have calculated the projected average range, ion distribution, recoil distribution, and energy recoils. This work will be tremendously helpful in the experimental procedure of bombardment of Argon ions on these nanoparticles. We have considered 50 keV energy Arions on ZnO nanoparticles.

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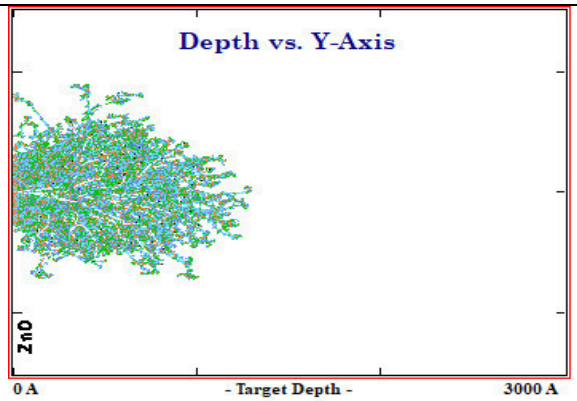


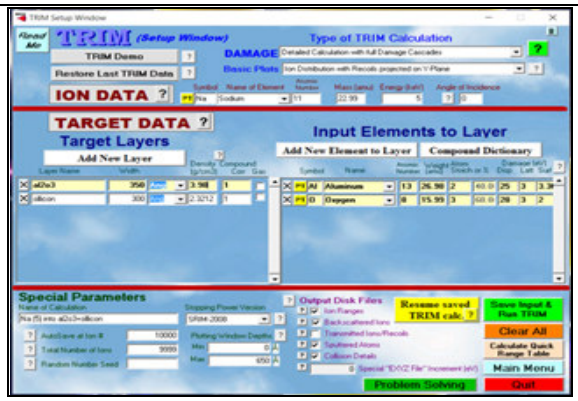
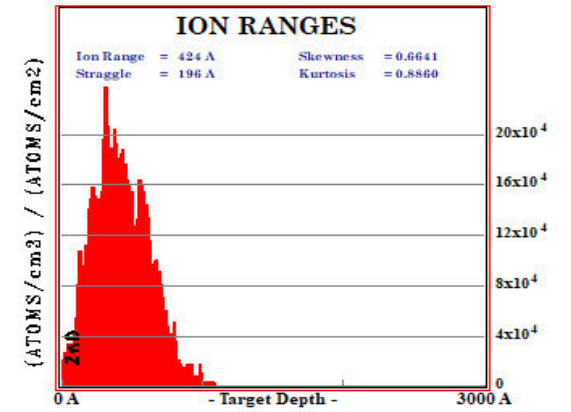


Fig.1.(Left) TRIM Setup Window for 50keV Energy. (Right) 50 keV energy TRIM calculation



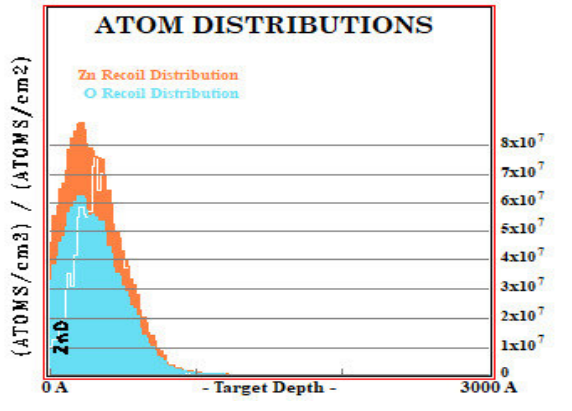
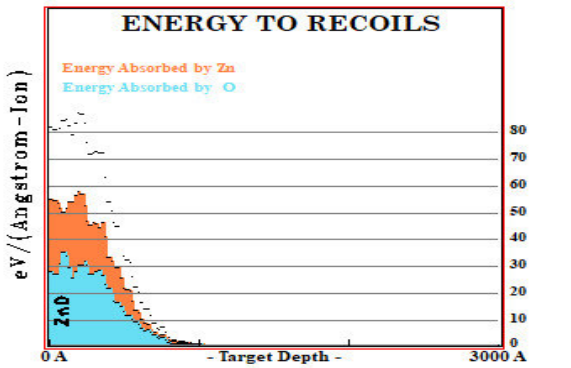


Fig. 2.(Left) 2D plot of Ion Distribution for 50 keV energy. (Right) 2D plot of Ion/Recoil Distribution for 50keV energy



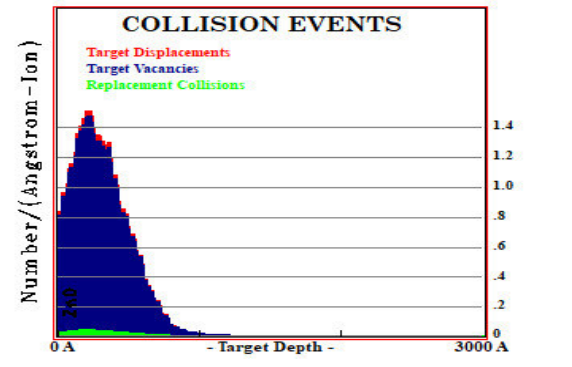


Fig. 3.(Left) 2D plot of Energy to Recoil for 50 keV energy. (Right) 2D plots of Collision Events for 50 keV energy

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RESEARCH ARTICLE

Study of Radiation Damage in Silicon Detector

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ABSTRACT

A radiation interaction has been studied in the Silicon as most of the radiation detector is made of up silicon in the Nuclear and modern physics experiment. A complete montecarlo simulation has been studied and found that the silicon is good for the charge particle detection for light mass and for heavy ion like fission it will be not a good choice to use it. The detail calculation has been presented.

Keywords: radiation, montecarlo simulation, modern physics.

INTRODUCTION

Study of radiation is an interesting subject since decades. As it is not visible to our naked eyes but affect our daily life, researchers have tried to develop different types of radiation detector for investigation of different radiations. Radiation can be classified into charged and uncharged radiations. Their interaction with the matter is also different. The charged ion or charged radiation mostly under goes columbic interaction. Theirinteraction with the matter via columbicinteraction can be understood by the Bethe-block equation. A beautifulexample is the detection of the heavy charged particles(fission) light charged particle (alpha) using the modern silicon based semiconductor[1,2].Detection of the uncharged particles, say neutron and the gamma ray are normally not possible using this silicon detector. So each detector has its own advantage and the fabrication mechanism. At the same time the radiation which interactsthrough the detector also damages the detector with time. In the present work the interaction of the charged particle with matterspecially with Silicon has been studied.

CALCULATION AND RESULT

As discussed above the interaction of the charged particle with matter can be understood by the Bethe block equation and the conventional silicon detector can be used for this purpose. The silicon detector can detect both light and heavy ions as they are charged particles. But there are some limitations from the detector side and some

disadvantage from the radiation side which has been explored here. When light charged particles (i.e. proton, Li or alpha particle) interactwith a detector, they undergo energy loss and pass through the detector. The determination of the charged particle and the separation depends on the thickness of the detector where the energy loss will occur. For the particle identification twosilicon detectors are used one after another most of the time. This is called a telescope, where one of the detectors is thinner than the other. This is because once the radiation (charge radiation) passes through the detector, itloses small amount of energy and pass through it and the remaining energy is lost on the other detector. Experimentally the energy loss in the thin detector vs the total energy are plotted.

On the otherhand when the chargedparticle is a heavy one, it loses huge amount of energy and also most of the time the telescope arrangement does not work for heavy charged particle identification (fission). Detection of the heavy charged particles will also create the plasma defect and creates the vacancies or holes. The plasma whichwill be created by the heavy charge particle during the interaction is not good for the detector and this leads to a situation called the Pulse height defect. It is not advisable to use the silicon detector for the heavy on detection.The example of the particle identification using silicon detector having telescope arrangement has been show in Fig.1. As illustrated inthe Fig.1 particles ^{6}Li, P, alpha, ^{2}H all are very clearly separable whereas with theheavy particles (fission fragment), measurement are not the same .One can see from Fig.1 that there is no particle identification for the fissionfragments as they are heavy whereas for light particle the detection and identification is very clear.

To understand the effect of this radiation (light/heavy) a theoretical calculation has also been done using the code SRIM/TRIM [5]. Particles with the greatest charge will have the largest specific energy loss. Alpha particles, for example, will lose energy at a greater rate than protons of the same velocity but less than that of more highly charged ions.In comparing different materials as absorbers, it has been found that dE/dx depends primarily on the product NZ, which is outside the logarithmic term. This product NZ represents the electron density of the absorber. High atomic number, high-density materials will consequently result in the greatest linear stopping power. Two calculations have been done to understand the energy loss. The ^{6}Li of ~40MeV has interacted with a silicon surface barrier detector (SSB) which is made up of Si and the energy loss has been calculated using the code SRIM which is a montecarlobased program. In one case the detected particle coming out from the reaction is an alpha particle and in another case , one of the fission fragment coming out of the reaction (same reaction) is ^{107}Tc. The calculation has been shown in Fig2.

CONCLUSION

An energy loss has been understood using the projectile of ^{6}Li with 40 MeV energy and also with different target interaction (Si, ^{209}Bi). The results obtained using the code SRIM/TRIM are presented here. It has been understood that for the heavy ion reaction for particle identification the SRIM calculation is very important. On that way it is a significant study to provide information to the experimentalists. Inaddition, the fission spectra has been also simulated and found that the Si surface barrier detector is not a very good choice for fission measurement where as for the light particle measurements itworks the best.

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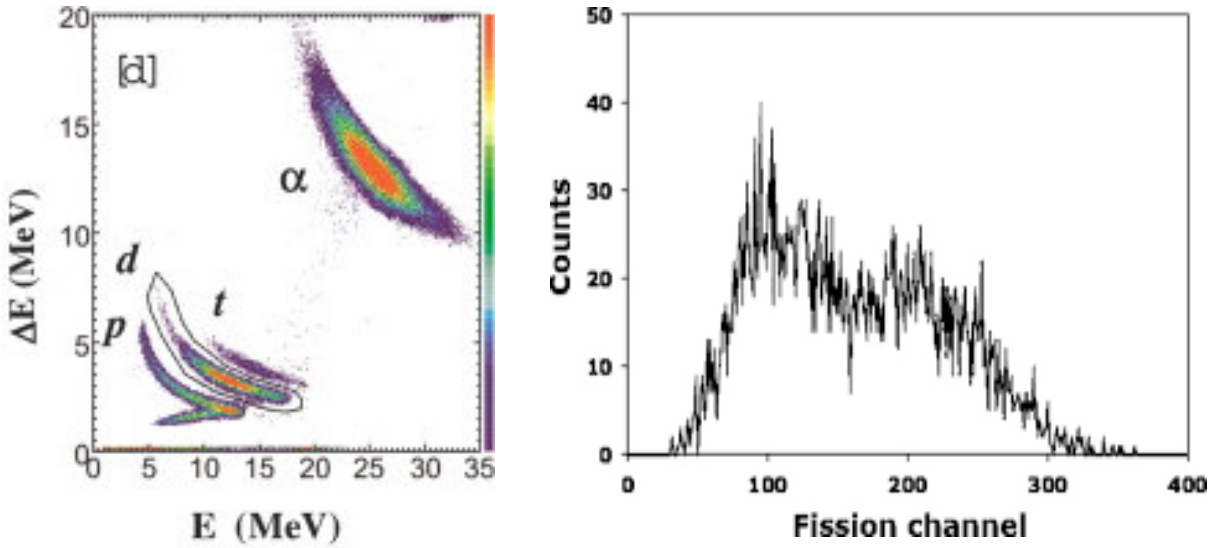

Fig.1. (Left) The identification of the charge radiation using the silicon detector. Each light particle is very clearly seperable. Here the detector looks like in the telescope arrangement (see text for details). (Right) Same detector used for fission, no such particle identification for fission and also the plasma effect makes the detector bad [3,4].

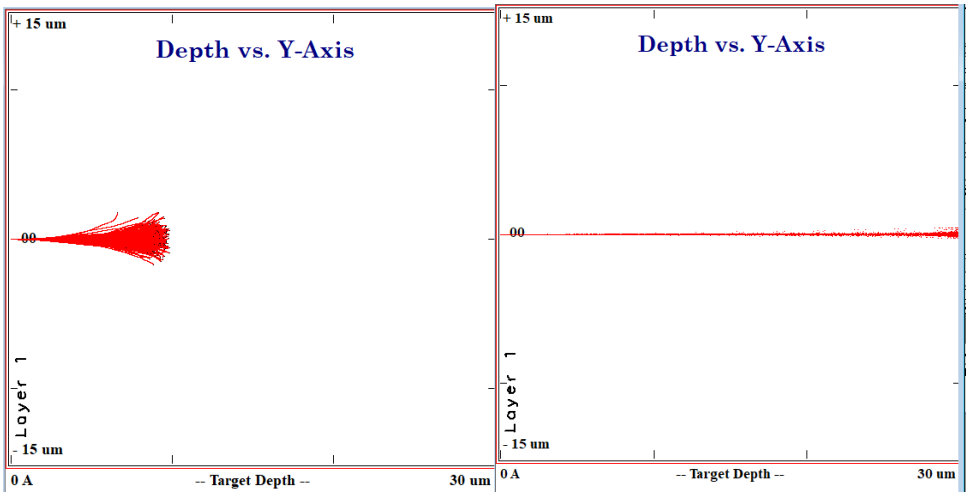

Fig.2. (left) The heavy ion (fission fragement) from the reaction $^{6}Li+^{209}Bi$ at 40 MeV is pasing through the SSB(silicon surface barrier) detector and the range is very less i.e. all the ions will stop there and creat a pulse height defect. (Right) The same expriment but the emitted particle (alpha) is passing through the detctor. In both of the cases the enegy of the particle is same.

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RESEARCH ARTICLE

Facile Alkylation at 9-Position of Fluorne by Varying Different Conditions

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ABSTRACT

Here we describe the synthesis and characterization of alkylation of fluorene. Different conditions have been screened very cautiously to develop a suitable synthetic route for alkylation at 9-position of fluorene. The synthesized monomer was characterized by ^{1}H and ^{13}C spectra.

Keywords: Fluorene, 9-position, alkylation, Potassium tert-Butoxide, Solubility.

INTRODUCTION

Organic π-conjugated materials have become a subject of interest when Shirakawa, MacDiarmid, Heeger and coworkers discovered the significant increase in conducting behavior of polyacetylene by doping with various electron acceptors or electron donors in 1977 [1]. In appreciation of their efforts and contribution to the field they were awarded the Nobel Prize in 2000 in Chemistry. Π-Conjugated molecules are very hopeful materials for electronic device fabrication mainly due to their semiconducting properties [2-6]. Organic semiconducting materials have potential benefits over the use of inorganic semiconducting materials, by virtue of their unique optoelectronic properties including: large scale processibility, flexibility, and low cost of production. Due to this, the science of semiconducting materials has developed rapidly over the last three decades. Various π-conjugated materials such as polyacetylene, polythiophenes, polyfluorene, polypyrrole, polyaniline and poly(phenylene vinylene)s have been developpd for their inherent semiconducting properties [7-10]. Among these fluorene based π-conjugated materials have great importance due to their extraordinary photophysical, thermal, and processing properties.

Fluorene ($C_{13}H_{10}$) is a tricyclic aromatic hydrocarbon. It was first isolated from coal tar in 1867 and its structure was discovered after few years later. The methylene protons at 9-position of fluorene reveal considerable acidity (pK_A = 22.9) [11] since the resulting fluorenyl aromatic anion is well resonance stabilized [12-13]. Consequently, it easily reacts with electrophiles at the 9-position in the presence of base. The solubility of fluorene is enhaced in organic

solvents by incorporating alkyl or aryl group at 9-position of fluorene, which also prevent the oxidation of fluorene [14-17]. Thus the solubility and solution process ability of the fluorene based π-conjugated compounds have been increased by incorporating solubilizing alkyl groups to the 9-position of the fluorene molecule, which also enhanced their chemical and photophysical properties.

RESULTS AND DISCUSSION

All this view keeping in mind our aim is to develop a synthetic route for the synthesis of alkyl substituted fluorene based compounds as alkyl group incorporation is necessary to improve the solubility of fluorene based rigid compounds. For this reason octyl group was incorporated at 9 position of fluorene by varying different conditions. Scheme 1 represents the synthetic approach for preparing 9,9-dioctylfluorene. At first, an attempt was taken to synthesize alkylated fluorene from fluorene using *n*-bromooctane (2.5 eqiv.) and aq. KOH in distilled THF solvent at RT. But in this condition no product was obtained. After that alkylated fluorene was tried to synthesize from fluorene and *n*-bromooctane in a two phase system consisting of toluene and aq. NaOH (50% w/v) using TBAI (Tetra butyl ammonium iodide) as the phase transfer catalyst at 60°C for 12h. But in this case the yield of the reaction was low (27%). After changing the base from NaOH to KOH, we observed almost similar yield (29%). Finally, the alkylated fluorene was synthesized by treating with *n*-bromooctane and strong base ^{t}BuOK (4 eqiv.) with fluorene in distilled THF at refluxing condition in very good yield (82%). In ^{1}H NMR of 9,9-dioctylfluorene, the 8 aromatic protons appeared as multiplet at 7.80-7.69 ppm (m, 2H) and at 7.42-7.28 ppm (m, 6H). The alkyl protons appeared as multiplet at 1.99-1.94 ppm (m, 4H), 1.26-0.93 ppm (m, 20H), 0.85-0.78 ppm (m, 6H) and at 0.61-0.52 ppm (m, 4H). In ^{13}C{^{1}H} NMR the aromatic carbons are appeared at 150.7, 141.1, 126.9, 126.7, 122.8 and at 119.6 ppm. The carbon at 9-position of fluorene appeared at 55.0 ppm. The alkyl carbons appeared at 40.4, 31.8, 30.1, 29.2, 23.7, 22.6 and at 14.1 ppm.

Synthesis of 9,9-dioctylfluorene

Octyl bromide (1.45 g, 7.25 mmol) was added using a syringe to a mixture of fluorene (0.5 g, 3 mmol) and ^{t}BuOK (2.02 g, 18.05 mmol) in THF (25 mL) in 100 mL round bottomed flask at RT. The reaction mixture was refluxed for12 h. The compound was extracted with ethyl acetate and then was washed with brine and water. It was dried over anhydrous Na_2SO_4. The solvent was then evaporated under vacuum to dryness. The compound was purified by silica gel column chromatography using hexane as eluent to obtain 9,9-dioctylfluorene as yellow oil in 82% yield.
^{1}H NMR ($CDCl_3$, 200 MHz) δ (ppm): 7.80-7.69 (m, 2H), 7.42-7.28 (m, 6H), 1.99-1.94 (m, 4H), 1.26-0.93 (m, 20H), 0.85-0.78 (m, 6H), 0.61-0.52 (m, 4H); ^{13}C{^{1}H} NMR ($CDCl_3$, 50 MHz) δ (ppm): 150.7, 141.1, 126.9, 126.7, 122.8, 119.6 , 55.0, 40.4, 31.8, 30.1, 29.2, 23.7, 22.6, 14.1.

CONCLUSION

Alkylation at 9-position of fluorene was carried out by varying different conditions. It was reveled that the better yield was obtained by using ^{t}BuOK (4 eqiv.) in THF. The synthesized compound was characterized by ^{1}H and ^{13}C NMR spectroscopy.

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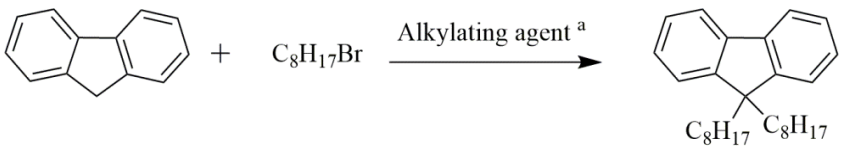

Scheme 1. Synthesis of 9,9-dioctylfluorene (listed in table 1)

Table 1.Reaction condition and yield for preparing 9,9-dioctylfluorene

Reagent	Solvent	Condition	Yield
KOH (10 eqiv.)	THF	RT, 12h	0%
TBAI (10 mol %) Aq. KOH (50% w/v)	Toluene	60°C,12h	27%
TBAI (10 mol %) Aq. NaOH (50% w/v)	Toluene	60°C,12h	29%
^{t}BuOK (4 eqiv.)	THF	Reflux, 12h	82%

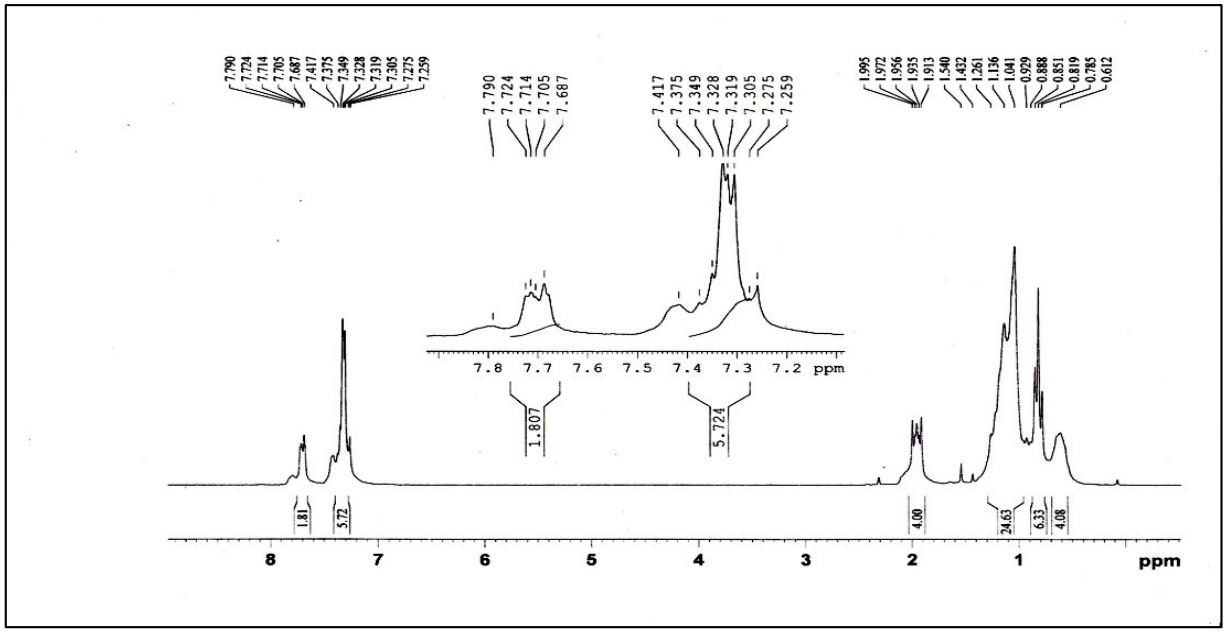

Figure 1. ^{1}H NMR ($CDCl_3$, 200 MHz) of 9,9- dioctylfluorene

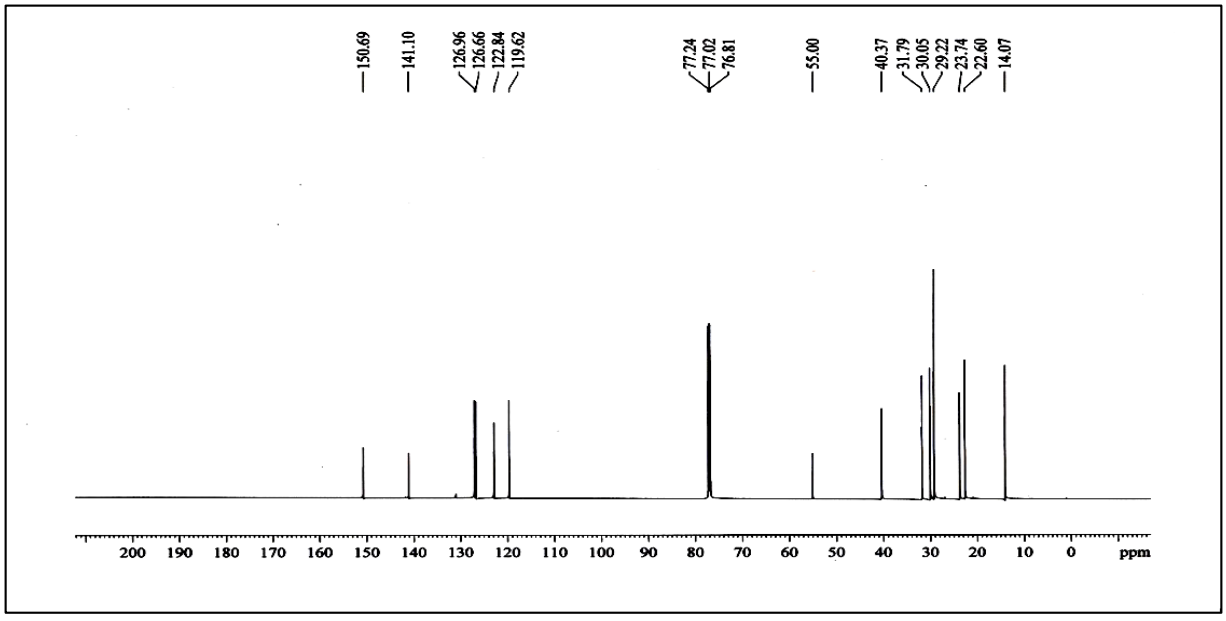

Figure 2.$^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 50 MHz) of 9,9-dioctylfluorene

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REVIEW ARTICLE

Review on Structural and Optical Properties of Rare Earth Modified Barium Tungstate Ceramic

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ABSTRACT

Rare earth doped Barium Tungstate ($BaWO_4$) materials were studied due to high special level structure and luminescence properties, and have been widely used in solid-state lasers, medical diagnosis infrared anti-counterfeiting and optical fiber communication. The selection of rare earth ions and matrix material has great influence on the up-conversion of the luminescence performance. This paper reviewed on the structural and optical properties of RE doped $BaWO_4$ (RE: Dysprosium(Dy), Erbium (Er), Samarium (Sm), Europium(Eu), Holmium(Ho), Praseodymium(Pr), Ytterbium (Yb) and processing method. In this review, the Judd– Ofelt intensity parameters, Ω2 and Ω4 were obtained from the fluorescence emission spectra. The hypersensitive nature of the transition is confirmed from the higher value of the Ω2. The lower symmetry of RE^{3+} coordination environment and the covalent character of RE–O bond are also confirmed from the higher value of Ω2. By using the calculated J O intensity parameters, the various radiative and laser parameters of the excited level are determined.

Keywords: phosphors; photoluminescence (PL), Rare earths, Judd-Ofelt (J-O) parameters.

INTRODUCTION

Alkaline earth tungstates AWO_4 (where A=Ba, Ca, Sr) have significant luminescence properties. These are used widely in preparations of optical fibers, phosphors, scintillators and laser host materials[1], such as $PbWO_4$, $CaWO_4$

and $ZnWO_4$[2]. Materials of this kind are suitable for application as laser materials. These materials have some characteristic properties like high X-ray absorption coefficient, refractive index and chemical stability. Therefore, different techniques have been used to elaborate such films such as traditional solid-state reaction methods, flux method, vacuum evaporation, sputtering, combustion, sol gel method, pulsed laser deposition and spray pyrolysis. Among alkaline earth metal tungstate families, $BaWO_4$ has a capacity to be a Raman crystal [3]. The material is non-hygroscopic, transparent over a large range of wavelength. The Raman gain is high reaching up to 36cm/ GW at 532nm for pump pulses of 10^{-12}s to 10^{-9}s duration[4]. The material is known for its useful properties like phase transformation under high-pressure, spontaneous Raman transition and electro-optics properties[5]. But its capability to act as active medium for laser is not fully explored. The present research paper, a review on scope of rare earth doped Barium tungstate crystal for laser applications is carried out. The barium tungstate a tetragonal lattice with lattice parameters a = b = 5.61Å, c = 12.71Å in the space group I41/a. There are eight nearest-neighbor oxygen ions for the Ba^{2+} site, with two sets of distorted interpenetrating tetrahedral. The trivalent rare earth ions replaces some of Ba^{2+} positions and maintains the tetragonal (s4) site symmetry since the charge compensation takes place from far enough distance from the impurity center [6]. There are numerous reviews on rare-earths (RE) ions due to their potential application in technology and commerce such as flat panel displays [7], solid state lasers[8], planar waveguide[9], high density frequency domain optical data storage [10] and even biological multicolor imaging [11]. The 17 RE chemical elements form a group having singular properties due to their electronic configurations. The elements of this group have their 4f-shell partially filled which allows transitions of electrons giving radiations with characteristic frequencies in the electromagnetic spectrum.The objective of this review is to review on the properties of rare earth which could improve the optical and microwave dielectric properties of $BaWO_4$.

Review on optical and dielectric properties

Dy-doped $BaWO_4$

In 2017, Hridaya et.al [12] studied the structural, optical and morphological properties of dysprosium-doped $BaWO_4$ films synthesized by RF magnetron sputtering technique. They reported that the crystalline quality of the film is enhanced by moderate doping of dysprosium. The crystalline quality is reduced with higher doping. The presence of characteristic bands in the Raman spectra for the Dy^{3+}-doped $BaWO_4$ films may due to the formation of the $BaWO_4$ crystalline phase in all the films. From the surface morphology, it is found that the smaller grains have a tendency to form larger structures with higher dysprosium concentration. They compared the photoluminescence (PL) spectra of pure $BaWO_4$ films and Dy^{3+} doped $BaWO_4$ films. The pure $BaWO_4$ film shows no PL emission and all doped films have a broad emission in the wavelength range 390 nm to 500 nm. The intensity of the PL emission increases with the increase in doping percentage up to 3 wt.% and thereafter decreases due to the usual concentration quenching. Among the doped films, the B5 film has minimum intensity of the PL emission. This may due to quenching of PL emissions caused due to non-radiative processes like cross-relaxation between neighboring Dy^{3+} ions. The Dy^{3+}-doped films have intense bluish PL emission which is due to the transition between the lower must Stark levels of 4F9/2 to different Stark levels of 6H15/2.

In 2018, Patra et.al reported the effect of Dy^{3+}/K^{+} doping/co-doping concentration on the structural and *Photoluminescence* (PL) properties of Dy^{3+} doped and K^{+} co-doped barium tungstate*phosphor* prepared by a solid state reaction method. As a result of Dy^{3+}doping with K^{+} co-doping, the Colour point got improved due tocharge compensation. The reduction in the non-radiative transitions increased the internal quantum efficiency from 56 to 67%, as proven by J-O theory. The $Ba_{1-x-y}Dy_xK_yWO_4$ (x = 0.10; y = 0.05) crystal has a short life time (281.60 μs) and CCT value (5392 K) very close to day light. Hence the *Tungstate* based phosphors are suitable for white light emitting diode applications.

Yb-doped $BaWO_4$

Jingcun et.al [13] studied the optical properties of Er^{3+}, Yb^{3+}: $BaWO_4$, crystal synthesized by Czochralski process. Absorption spectra were analyzed and accordingly energy levels were assigned. The spectrum parameters of Er^{3+} in $BaWO_4$ crystal was calculated using J-O theory and the up conversion properties were studied aswell. In this article, the doping of Yb^{3+} was to sensitize Er^{3+}. On the basis of absorption pumping energy, sensitization mechanism can be divided into direct sensitization up-conversion (DSU) and indirect sensitization up-conversion (ISU). Under 930 nm laser excitation, Yb^{3+}absorbs pumping energy directly and then transfers energy to Er^{3+}. It belongs to direct up-conversion sensitization. Yb^{3+}cannot absorb pumping energy directly under 808nm laser excitation. Er^{3+} absorbs pumping energy, and then transfers energyto Yb^{3+}. Er^{3+} transfers energy to Yb^{3+} at last. Therefore, it belongs to indirect up-conversion sensitization. Lin et. al [14] studied the effect of Yb^{3+} doping on $BaWO_4$. The absorption cross-section of 0.12%Yb: $BaWO_4$ crystal is 1.37×10^{-20} cm^2. This absorption cross section is more than that of Yb:YVO_4 and Yb:YAG crystals. The lattice volume decreases with increase of the Yb^{3+} concentration and the absorption spectra of the Yb^{3+}-doped $BaWO_4$ crystals shifts towards the shorter wavelength. The peak of abortion spectra is at 990 nm, which is suitable for InGaAs laser diode pump. So for laser host material Barium Tungstate is suitable.

Eu, Sm -doped $BaWO_4$

Bouzidi et. al [15] investigated the structural and optical properties of barium tungstate doped with rare-earth powders(RE=Eu, Sm). The J–O parameters Ω2, Ω4 of (Eu, Sm) doped barium tungstate have been calculated from emission spectra. The parameters then used to calculate the total transition probabilities (AT), the stimulated emission cross-sections (σ_e), the fluorescence branching ratio (β_R) and radiative lifetimes (τ_R) of the $^5D_0$ level. The measured lifetimes (τ_{mes}) were compared to the calculated (τ_R) using the J–O method. From the excitation spectra, the energy transfer is obtained. From the results it is found that there is a broadening of the excitation bands for wavelengths 396nm and 465nm for $Sm^{3+}$and Eu^{3+}co-doped barium tungstate in comparison to Eu^{3+} doped barium tungstate.So, co-doping of Sm^{3+} with $Eu^{3+}$to barium tungstate improves the optical properties, the luminescent intensity of $^5D_0\rightarrow{}^7F_2$ transition. The PL life time of the state $^5D_0$ in $Ba_{0.98}Eu_{0.01}Sm_{0.01}WO_4$ (BWOES) are much stronger than that of $Ba_{0.99}Eu_{0.01}WO_4$ (BWOE). It implies that the PL intensity and PL lifetime are enhanced due to further excitation transfer from Sm3þ to Eu3þ. The higher fluorescence branching ratio of the $^5D_0\rightarrow{}^7F_2$ transition and the improvement of the stimulated emission cross-section (σ_e), band-width ($\sigma_e\Delta_{\lambda eff}$) and quantum efficiency (η) in (BWOES) implies that it can be promising material for use in optical devices. Lin et.al [16] studied the effects of multiple irradiations on luminescent materials and energy savings of Eu^{3+} doped $BaWO_4$.

Shi et.al [17] synthesized pure $Ba_{1-x}WO_4$: xSm^{3+} in $LiNO_3$-KNO_3 by low temperature molten salt method. Their crystal structures and PL properties are studied. The XRD analysis and Rietveld refinement suggests scheelite-type structure for all samples. All the samples crystallized into scheelite-type tetragonal structure with space group I41/a. There is a slight distortions in $BaWO_4$ crystal structures due to the doping of Sm^{3+}ions. With increasing concentration of Sm^{3+} ions, the optical band gap increased due to the localized electronic energy level in the band gap. The color shifts gradually from near green-yellow region to orange-yellow region, the CCT values were also varied and turned from cool white (5479 K) to warm white (4308 K). The PL spectra showed that for a doped concentration of 3mol%, the most intense yellow luminescence is produced. The corresponding CIE color coordinate was (0.4589, 0.5133). From the results, it is revealed that Sm^{3+} doped $BaWO_4$ yellow phosphors have an important advantage of near-ultraviolet based white light emitting diodes applications. Hence, barium tungstate is suitable material for preparation of phosphors.

Pr-doped $BaWO_4$

Jinsheng et.al [18] prepared $BaWO_4$:Pr^{3+} microcrystals following a hydrothermal route.The results of X-ray

diffraction, scanning electron microscope reveals that they have scheelite structures with different morphologies of egg-shape rod, olive-like and quasi-sphere with the addition of the surfactants and chelating agents, The photoluminescence excitation and emission spectra of BWO:Pr microcrystals are analyzed. The spectra showed a strong red emission (642 nm) which is attributed to the Pr^{3+} ions of $^3P_0 \rightarrow {}^3F_2$ transition with blue excitation (484.6 nm, $^3H_4 \rightarrow {}^3P_0$).

CONCLUSION

By doping RE into $BaWO_4$, it was proved that it can improve the optical behavior.The selection of dopant is important to improve the optical properties of $BaWO_4$ for laser host material.

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REVIEW ARTICLE

A Survey on Image Processing for Detection & Classification of Rice Crop Diseases using Machine Learning and Other Approaches

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ABSTRACT

Economy highly depends on agricultural productivity. Increasing amount the growth of crops need automatic monitoring disease. Detecting disease from the images of the rice crops is one of the essential research areas. The author in this paper presents a review of various machine-learning techniques used to classify rice plant diseases. These surveys presents different image processing techniques used in detection of rice crops images of different techniques and also discuss the image processing technique applied on rice leaf disease detection and classification. Here we include size of image dataset, no. of diseases, segmentation techniques, pre-processing, accuracy of classifiers etc. We design our work to utilize our survey on detection and classification of rice plant diseases.

Keywords: Rice crop diseases, Image processing, Machine learning,SVM, classification; clustering, disease classification, disease identification

INTRODUCTION

Much of the income for Indians is dependent on agriculture. Rice is the crop that is most grown around the world. The main constraints in rice cultivation are environmental stresses including biotic (bacteria, viruses, and fungi) and abiotic (salinity, heat, heavy metal and high temperatures). Rice plants are continually subjected to various biotic and abiotic stresses; together they not only impact plant growth and development but also reduce their productivity significantly. Overall, about 70 per cent of crop yields are lost due to various biotics and abiotics [31].The crop losses it brings on the agricultural field decrease in the Indian economy, since 70 percent of the Indian population depends on crop production. Rice crops in Asia kill 10 to 15 per cent. Fungus, bacteria, and viruses are responsible for the

plant's disease, for the essential function of effective production is plant disease monitoring. The leaf blast, brown spot, sheath blight, and leaf scald are various diseases that occur on rice plants. This survey focuses on how the image processing is used in rice plant disease detection. The diseases of rice crops (Fig.1)are discussed in more detail.

1. **Leaf Blast Disease:** A region varying from small round, dark spot to oval spots with narrow reddish-brown margins and gray or white centre.
2. **Brown Spots Disease**: Round to oval shape with dark brown lesions. It occurs on leaves of the rice plant.
3. **Bacterial Blight Disease**: Lesions consist of elongated lesions near the leaf tip. Turn white to yellow and then gray due to saprophytic fungi.
4. **Sheath Blight Disease**: Lesions consist of alternating wide band of white, reddish-brown or brown. Fungal survival structure may from on the leaf surface.
5. **Sheath Rot Disease:** General reddish-brown or brown. It affected on the leaf surface.
6. **Node Blast Disease**: Clum mode turns black and grey as plants approach maturity; nodes turn dark to blue-grey.

Contribution by Various Researchers

Here we describe different works that already done by researchers in different fields like leaf disease classification, classification and segmentation of rice leaf. So aim of the survey is to present all these control methods for a good harvesting rice plantation.Different type data mining application building a model for classification. Here, for attribute selection they proposed discrete particle swarm optimization algorithm. It deals with discrete variables and different size of particles. For the comparison the criteria used: i) Maximizing predictive accuracy and ii) Finding the smallest subset of attributes. The overall performance is showed that DPSO algorithm is better than binary PSO algorithm. DPSO algorithm found smallest subsets of attributes [24].Texture analysis of rice leaf and leaf blast disease identification of the rice plants are done by the researchers. Multilayer preceptors used like classifiers by the pattern recognition method rice leaf images are analysed. Results showed that 89% images identified accurately [26].

In [1] the input is digital a colour image of paddy disease leaf. For segmentation of images they used method of morphology. Erosion method has been used to removes small-scale details from binary images but simultaneously reduces the size of regions of interest. In morphology dilation is the basic operations. The operation of dilation always uses a mesh of expanding the shapes contained in the input.In [2] the researcher proposed an automated system that can detect two different kinds of diseases present in a rice leaf using colour image analysis. In the system, the outlier region is first obtained from a rice leaf image which is tested utilize histogram intersection between the healthy and tested rice leaf images. The K means technique is applied to cluster the pixels into a number of similar and dissimilar groups. Lastly, these groups of pixels are compared with the system library to determine the suspected diseases of the rice leaf.

Methodology to classify & identify the different diseases of the damaged plants is discussed [32].The author makes use of the feature extraction of the Colour Co-occurrence method. Neural Networks are used for automatic detection of leaf diseases. The advantages of the proposed method can significantly support an accurate detection of leaf.In [4], the image processing technique is used for achieving appropriate quantity & concentration of pesticide by estimating disease severity. For segmentation of the leaf area and lesion region, they used simple threshold and triangle threshold. The main purpose is the accurate and fast detection of leaf disease. They test programs such as paddy blast, brown spot paddy spot, and normal paddy. The proposed approach is based on image processing. They use a set of paddy leaf images as a dataset. Due to this experiment, the paddy disease can be identified at the initial stage. This eliminates the subjectivity of human induced errors.

Enhancing the quality of image is proposed in [6]. The main focus of this paper is detecting the banana disease. Here, the author also used neural network technique to classify banana disease. Image acquisition, segmentation is

required classification of the disease.In [7], proposed methodology was used for accurately plant diseases detection using Artificial neural network (ANN). The approach is based on ANN classifier for classification & Gabor filter for feature. 91% accuracy is the experimentalresult showed. ANN based classifier can classify different plant diseases.A method was proposed to classify the leaf brown spot and leaf blast diseases based on the morphological changes caused by diseases. Here the researcher used SVM classifier. SVM and Bayes' was applied best approximates of the region. Colour distortion of leafs occurred in mess classification. Bayes' classifier was used in time complexity.

In [8], the author presents a segmentation technique of GA that is used for automatic detection and classification of leaf diseases. An advantage of this method are very less computational efforts and shows the efficiency and classification of leaf diseases and also it can identify diseases at early stage or initial stage.In [9], the author proposed a method classifying diseases of the rice plant. Their approach the limitation of selecting proper threshold value they used fermi energy based extraction method. To identify shape used genetic algorithm for best the structure. Their used rough set theory forminimize loss of information. The advantage of this method is lesser computational complexity.

In [10], the author proposed a method to identify leaf diseases by classifying the different diseases. Then these features are the author proposed different techniques for plant leaf disease detection. Development of hybrid algorithms & neural network is done in order to increase the recognition rate of final classification process [12].In [14], the author proposed Scale Invariant Feature Transform (SIFT) is used to get features from the disease affected images. Then these features are taken to recognize the image using Support Vector Machine (SVM) and K-Nearest Neighbours. This work mainly concentrates on three main diseases of paddy plant namely brown spot, leaf blast and bacterial blight. It is useful to farmers. Experimental result showed that SVM and K-NN is capable of predicting disease accuracy of 91.10% in SVM and 93.33% in K-NN.

Manoj Mukherjee, et al, used histogram to avoid large scale effect of these diseases [15]. Detect the disease at a primary stage and take necessary steps to minimize the loss of production is the prime job here. Three paddy leaf diseases; blast leaf, bacterial leaf blight, and rice tungro disease have been considered. The result of the test showed 92% in bacterial leaf blight using image processing.The author in [19] proposed the method to analyse leaf diseases using different Image Processing technique. First, it uses k-Means clustering to easily detect the disease. Second, it uses GLCM for feature extraction which is more efficient to extract the features.It also uses SVM as classification tool. Result from the SVM is able to predict the images accurately.

An approach to detect leaf diseases using Support Vector Machine (SVM) is presented in [21]. For the segmentation of the affected region of the rice leaf, they used k-means clustering algorithm. Finally, the result showed that 82% accuracy of the classified diseases.India is an agricultural based economy. For preventing diseases in fauna, farmers face lot of problems. There are several diseases seen on the plants [22]. Here, the authorshowed the use of image processing for detecting leaf diseases. Goal of this paper is to detect the symptoms of the diseases. This system reduces the losses and increases the economic advantages. Image processing, feature extraction and classification are the steps of this paper. The result showed that the proposed method is effective with accuracy level of 92.94%.

In [23], proposed method is an improved RFC approach for classification problem by different disease. Improved RFC approach is learning algorithm method by the combination of an attribute evaluator method and an instance filter method. Improve RFC approach performs is better than random forest algorithm which accuracy is 97.80%. Therefore, improved RFC approach method is good multi-classification problems.In [25], the author introduced modern technique to find out leaf diseases. Here, they used digital image processing and k-means clustering to estimate the leaf blast diseases. Digital image processing is used to find out fast and accurate disease detection. For, accuracy of leaf disease and classification using MATLAB image processing. K-mean and SVM algorithm provide high accuracy and less time for entire processing.

Nikita et al. in [33] discussed various method and techniques; images cropping, compression, Otsu method; to detect the diseases in the heterogeneous plant. They make use of neural networks classifiers such as BPNN, RBF, GRNN and PNNs to diagnose wheat diseases. Canny filters and feature extraction is applied to recognize the diseases on cotton and rice leaf.

Review on the current segmentation, which is used for automatic detection and classification of disease plant leaves [34] are presented here. It is done by genetic algorithm. This work mainly concentrates on plant leaf diseases like banana, beans, and mango. Experimental result showed that the model is capable of predicting the disease with an accuracy of 97.6% using Genetic algorithm.

CONCLUSION

The literature survey done provides a new insight in detection of the diseases of plant. The scope in doing research in this field is to design such system that automatically estimates the severity of the detected disease. Rice plant diseases will cause enormous losses in agriculture if there is not enough care. An automated system can be designed using computer and communication technology which can provide early disease warning. This paper analyzed and outlined the image recognition and machine learning approaches that were used to classify diseases.

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Table 1.Various Segmentation Techniques.

Sl. No.	Technique name	Segmentation Type	Segmentation Effect	Threshold Type	Complexity	Demerit	Merit
1	Fermi energy Based	Thresholding	Better compared to Otsu and k-means	Global	Low	Only works when non-uniform illumi-nation is present	Overcomes the limitation of selecting proper threshold value
2	Fuzzy c-means	Clustering	Better compared to Otsu and k-means	Local	High	Sensitive to initia-lization condition of cluster number and cluster center	Uses partial membership; therefore, more useful for real problems.
3	K-Means	Clustering	Accurately distinguish infected & uninfected regions of plants	Local	Low	Difficult to predict k with fixed number of clusters.	Minimizes sum of square distance between object and centroid
4	Otsu's method	Threshold	Good/stable	Global	Very High	Takes more time in processing	Regardless of uniformity & shape measures, it works on real world images
5	Grey-level thres-holding	Threshold	More accurate compared to Otsu's method	Global	Normal	Every time needs to select proper threshold value for getting better result in segmen-tation.	grey level transformation(2G-R-B) provides contrast for disease region and background

Fig.1. Diseases of Rice Crops

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RESEARCH ARTICLE

Structural and Electrical Properties of La doped BFO-STO based Solid Solutions

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ABSTRACT

The polycrystalline sample of (1-x)[$Bi_{(1-y)}La_yFeO_3$]- x[$SrTiO_3$] (x=0.5, y=0.5) was prepared by using the conventional solid-state reaction technique and sintered at high temperature(1170^{0}C).Structural analysis of the materialwith room temperature X-ray diffraction data confirmed the formation of compound in the rhombohedral crystal system. The surface morphology recorded by scanning electron microscopy (SEM) reveals a polycrystalline nature of sample with uniform distribution of grains. The homogeneous mixing of the components was confirmed by energy dispersive spectroscopy of X-ray (EDAX). Dielectric and complex impedance spectroscopic studies were carried out in a wide frequency (i.e.10^2–10^6 Hz) and temperature (30–450^{0}C) range. Dielectric studies indicate a ferroelectric–paraelectric phase transition at 325^{0}C in the material.Complex impedance spectra confirm the significant contribution of grain to electrical response of the material. With rise of temperature, the bulk resistance of the compound decreases like thatof a semiconductor, which shows a negative temperature coefficient of resistance (NTCR) behavior.The nature of frequency dependence of ac conductivity of the sample follows the Jonscher'spower law, and calculated dc conductivity follows Arrhenius behavior.

Keywords: Multiferroics; perovskite, Jonscher's universal power law, ferroelectric-paraelectric phase.

INTRODUCTION

Multiferroics are materials which simultaneously show more than one ferroic orders i.e. ferromagnetism (or antiferromagnetism), ferroelectricity (or antiferroelectricity) and ferroelasticity. Magnetization can be controlled in these materials with the suitable application of electric field and vice versa. These materials possess interesting ferroelectric and magnetic properties along with existence of coupling between the ferroics orders which imparts a great significance to these materials for device applications such as actuators, data storage, high-sensitivity ac field sensors, transducers, memory devices, spintronic and electrically tunable microwave devices as filters, oscillators, and phase shifters [1-6]. $BiFeO_3$(BFO) is a unique material which exhibits rhombohedrally distorted perovskite (ABO_3) crystal structure with R3c space group, where A represents a divalent or trivalent cation, and B is typically a tetravalent or trivalent cation. It exhibits G-type antiferromagnetism due to the local spin ordering of Fe^{3+} which forms a cycloidal spiral spin structure having spin periodicity of 62 nm[7]. Due to the existence of Fe^{2+} and oxygen vacancies, BFO suffers from large leakage current, which limits the applications of BFO. In order to reduce the current leakage, improve the ferroelectric behavior which hinders its practical applications, doping with rare-earth elements or transition metal is done [8]. Researchers worldwideare trying to improve the magnetic properties, without modifying the ferroelectric properties of the original BFO materials system. Doping of BFO with rare earth elements is done to improve multiferroic properties and also by making solid solutions of BFO with other perovskite materials.Several research groups have reported that the superior ferroelectric property can be obtained through reduction of leakage current due to suppression oxygen vacancies with single doping or co-doping. Strontium and calcium titanates are not ferroelectrics, but STO-and CTO-doped BFO have indeed been explored [9-13]. Rare earth (RE) elements possess large magnetic moments, large magnetocrystalline anisotropy and very large magnetostriction at low temperatures due to the localized nature of 4f electrons. So we have synthesized the Solid solution of $(1-x)Bi_{(1-y)}La_yFeO_3$-$xSrTiO_3$ (x=0.5, y=0.5) was prepared by solid state ceramic route and systematically studied its structural and electrical properties.

MATERIALS AND METHODS

Solid solution of $(1-x)Bi_{(1-y)}La_yFeO_3$-$xSrTiO_3$ (x=0.5, y=0.5) was prepared by solid state ceramic route using high purity ingredients Bi_2O_3, Fe_2O_3, $SrCO_3$, TiO_2, and La_2O_3. Stoichiometric amounts of these ingredients were taken and ground thoroughly in dry and wet (acetone) medium for 1h each in agate mortar. The powder was calcined at 1150°C for 5h in an alumina crucible. The quality and formation of the compound were checked using x-ray diffractometer (RigakuUltima IV, Japan) with CuK_αradiation (λ = 1.5405Å) over a wide range of Bragg angles $2\theta(20^\circ \leq 2\theta \leq 80$. The powder was then mixed with polyvinyl alcohol (PVA) as a binder for granulation. The ground mixture was then pelletized under the uniaxial pressure of 3.5 ton. La doped BFST pellets were sintered at 1170°C for 5h. The surface morphology of the sintered pellet was studied at room temperature using a scanning electron microscope (HITACHI SU3500). Energy Dispersive Spectroscopy (EDS) was carried out by OXFORD INCAX analyzer attached with SEM to study the elemental composition of the compound. The sintered pellets were polished and electroded with silver paste and then dried at 150 °C for 1 h. The dielectric and impedance parameters of the pellet were recorded as a function of frequency (1 kHz to 1 MHz) using a computer-controlled HIOKI 3532 LCR Hitester over a wide range of temperature..

RESULTS AND DISCUSSION

Structural study

Figure 1 shows the powder X-ray diffraction pattern of La doped BFST at room temperature. The diffraction pattern consists of sharp and single diffraction peaks, which are different from those of the ingredients of the prepared

compound. This exhibits better homogeneity and crystallization, and thus confirms the formation of a new compound with single-phase [14]. Most of the observed peaks were assigned to different crystal systems with different unit cell configurations by using a standard computer program package''POWD'' [15]. On the basis of minimum error between observed and calculated inter planar spacing (d) rhombohedral crystal system was selected. The refined lattice parameters of the material are found to be very much consistent with those of reported compound of similar structure [16]. Further, the particle size (P) of the compound was calculated using the broadening of some widely spread (over Bragg angles) strong and medium reflections in the Scherer's equation: $P_{hkl} = \frac{k\lambda}{\beta_{1/2}\cos\theta}$[17], where k (constant) = 0.89, k = 1.5405 Å and β_1 = full widthat half maximum (in radians). The average value of P_h is foundto be 22nm. The least-squares refined unit cell parameters are: a = 8.4567 Å, c = 11.7396 Å and volume V= 727.08 Å^3 in unit cell parameters. Figure 2shows the scanning electron micrographs of La doped 0.5BiFeO$_3$-0.5SrTiO$_3$ in different ranges i.e. 20, 10 and 5 μm recorded on the bulk pellet sample. The nature of the micrographs indicates that the ceramic has compact and highly dense microstructure due to uniform distribution of grains without any foreign particle. In spite of sintering at high temperature some small voids of irregular shape and dimension are seen which may be due to background effect. The elemental analysis by EDS (Figure 3) gives the information of the quantification of the component elements.

Dielectric study

The temperature dependence of relative dielectric constant (ε'_r) and tangent loss (tanδ)at different frequencies is shown in Figure 4.The value ofε'_r increases with the increase in temperature up to transition temperature (Tc) and then decreases. Above Tc the decrease in ε'_r indicates the paraelectric behavior of the sample. However, above 350^{0}C the increase in ε'_rcan be ascribed to the thermally activated transport of space charges. For space charge creation, oxygen vacancies (OVs) are inevitable due to high-temperature sintering.The presence of OVs will lead to the valance fluctuation of (Ti^{+4}-Ti^{+3} ions) [18]. In addition to the contributions of OVs, the increase inε'_r can also be attributed to the energetic hopping of electrons along the direction of applied field between Ti^{+4}-Ti^{+3}octahedral sites [19, 20]. The higher values of dielectric constant at lower frequency (1 kHz) are also due to the charge accumulation at grain boundaries. The observed higher values of dielectric constant at lower frequency (1 kHz) are due to the charge accumulation at grain boundaries [21]. The compound has the same Tc at all the above-mentioned frequencies indicating that the compound does not show relaxer behavior [22].It is clear that in the low-temperature region, tanδ is almost constant up to a certain temperature and then increases faster up to a highest temperature. The dielectric loss has been interpreted in terms of the polarization of mobile charge carriers, most probably oxygen vacancies which are activated at high temperatures. As the polarization is induced by oxygen vacancies, it increaseswith the increase of temperature and the decrease of frequency because of the inertia of oxygen vacancies [23]. Therefore, significant dielectric loss at the reduced frequency and at high temperature may be attributed to the enhanced space charge relaxation due to the increase of oxygen-vacancy concentration in the system.

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Impedance and Modulus Spectroscopy

Aunique and powerful nondestructive technique to characterize some electrical properties of ferroelectrics and ionic materials over a wide range of frequency and temperature is Complex impedance spectroscopy (CIS). This technique separates the contributions of (i) bulk, (ii) grain boundary and (iii) electrode polarization in complex impedance and other related electrical parameters with different equivalent circuits. In this technique, an AC signal is applied across the sample in the form of a pellet, and the response of output is recorded. From the complex impedance parameters of the materials, the resistive component can be obtained from the real part and reactive component from the imaginary part.

The following are the basic equations of impedance which are normally used in this technique: complex impedance, $Z(\omega) = Z' - jZ'' = R_s - \frac{j}{\omega C_s}$, complex admittance $Y^* = Y' + jY'' = j\omega C_0 \varepsilon^* = (R_p)^{-1} + j\omega C_p$ and complex permittivity $\varepsilon^* = \varepsilon' - j\varepsilon''$, where $\omega = 2\pi f$is the angular frequency; C_0 is the geometrical capacitance, j = $\sqrt{-1}$. The subscripts p stands for the equivalent parallel circuit and the subscript s stands for equivalent series circuit components. The relaxation frequency (ω_{max}) of the bulk material cab be evaluated from the peak of the high frequency semicircular arc in the complex impedance spectra from the relation

$$\omega_{max}\tau = \omega_{max} R_b C_b = 1 \Rightarrow 2\pi f_{max} R_b C_b$$

Impedance Analysis

The variation of Z'with frequency at different measuring temperatures is given in figure 5. The value of Z' decreases with an increase of both frequency and temperature which indicates that conduction is temperature and frequency dependent and increases with rise in temperature and frequency. The coincidence of Z' values at higher frequencies at all temperature indicate a possible release of space charge from the grain boundary. As, Z'decreases with increase in temperature in low frequency region, the negative temperature coefficient of resistance (NTCR) behavior in the sample is implied.The curves show that the Z" values reach a maxima peak (Z"max) above 225°C. The value of Z"max shifts to higher frequencies on increasing temperature. A typical peak broadening, which is slightly asymmetrical in nature, can beobserved with the rise in temperature. The broadening of peaks (explicit plots of Z") suggests that, there is a spread of relaxation time (i.e. the existence of a temperature dependent electrical relaxation phenomenon in the material [24]. The merging of Z" values below Tc (i.e. ≤ 325°C) in the high frequency region may possiblybe an indication of the accumulation of space charge in the material. Above Tc, the curves merge in the lower frequency region. The peaks shift toward high frequency region with rise in temperature. For the temperatures below 225°C, the peaks were beyond the range of frequency measurement.

AC Conductivity

The frequency dependence of electrical properties of the material can be studied from ac conductivity measurement. The frequency dependence of ac conductivity also provides information regarding the nature of charge carriers. The ac electrical conductivity (σ_{ac}) was calculated using the dielectric data and an empirical relation, $\sigma_{ac} = \omega \varepsilon_r \varepsilon_0 \tan\delta$, where $\varepsilon_0$is permittivity in free space and ω is angular frequency. Conduction mechanism in the material is followed from Jonscher's universal power law [25]: $\sigma_{ac} = \sigma_{dc} + A\omega^n$, where σ_{dc} is the dc conductivity, A is the temperature dependent frequency pre-exponential factor and n is the power law exponent in the range of 0≤ n≤1. The amount of interaction between mobile ions with the lattice is represented by exponent n. The pre exponential factor A determines the strength of polarizability. The conductivity spectrum in figure.6shows the variation of ac conductivity of the material as a function of frequency and temperature. The material obeys the universal power law, and is confirmed by a typical fit of the above equation to the experimental data at various temperatures. At low temperature (below 100^0C, not shown here),the conductivity increases with increase in frequency with a characteristicω^n of dependence. At higher temperatures (above 100^0C), a low frequency independent plateau have been observed, whereas at higher frequencies, ω^n dependence (i.e., frequency dispersion) of conductivity is still retained. The conductivity is found to be increasing with increase in frequency and temperature. There is more dispersion in the low temperature than in the high temperature. As suggested, this may be due to electrode polarization. Again the conductivity is less at low frequencies because, at these frequencies, the mobility of charge carriers is less due to less concentration of oxygen vacancies. At high frequencies there is a tendency of merger of conductivity curves and hence dispersion becomes temperature and frequency independent. With increase in temperature, the conductivity response become more and more flattened in low frequency and high

temperature region which may be due to transition from long range hoping to short range ionic motion, and thus conductivity relaxation phenomena occurs [26].

DC Conductivity

Figure 7 shows the temperature dependence of the dc conductivity as obtained from ac conductivityfitting. The dc conductivity increases with rise in temperature confirming the negative temperature co-efficient of resistance (NTCR) behavior. This plot follows the Arrhenius relation: $\sigma_{dc} = \sigma_0 e^{-\frac{E_a}{K_B T}}$.

CONCLUSION

Finally, it is concluded that the synthesized (1-x)$Bi_{(1-y)}La_yFeO_3$-x$SrTiO_3$ (x=0.5, y=0.5) sample has an rhombohedral crystal structure at room temperature. Studies of the dielectric properties showed that, the compound undergoes a ferroelectric-Para electric phase transition at Tc 325^{o}Cwell above the room temperature. The compound exhibits negative temperature coefficient of resistance (NTCR), which indicates the intrinsic semiconductor property of the material in the high-temperature range. The compound shows the grain and grain boundary effects.

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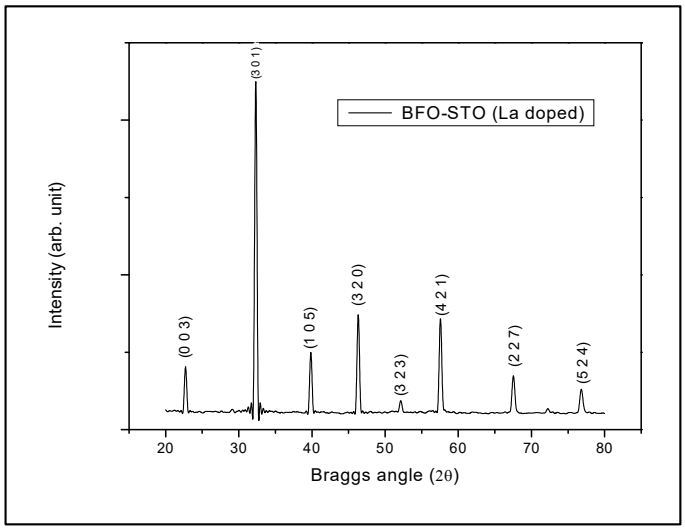

Figure 1. Indexed XRD pattern of La doped BFST

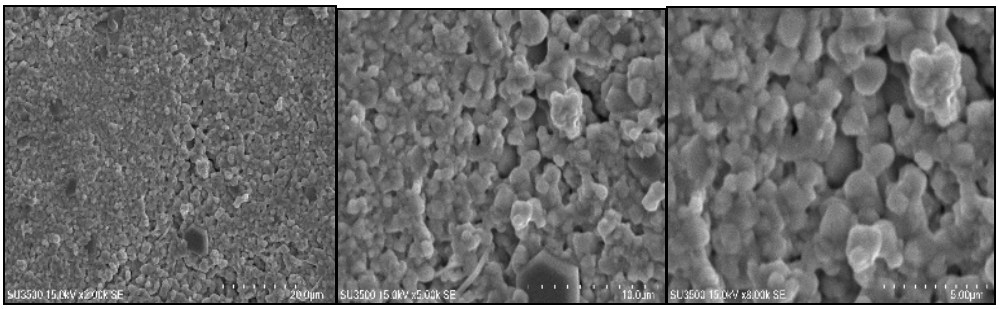

Figure 2.SEM micrograph of La doped BFST

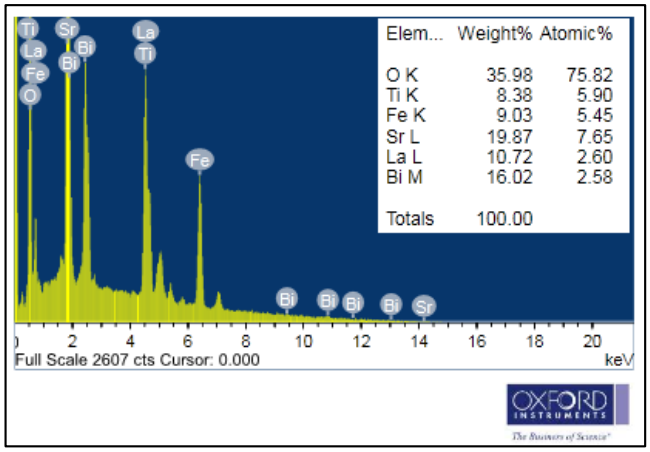

Figure 3. EDX spectrum measured for La doped BFST

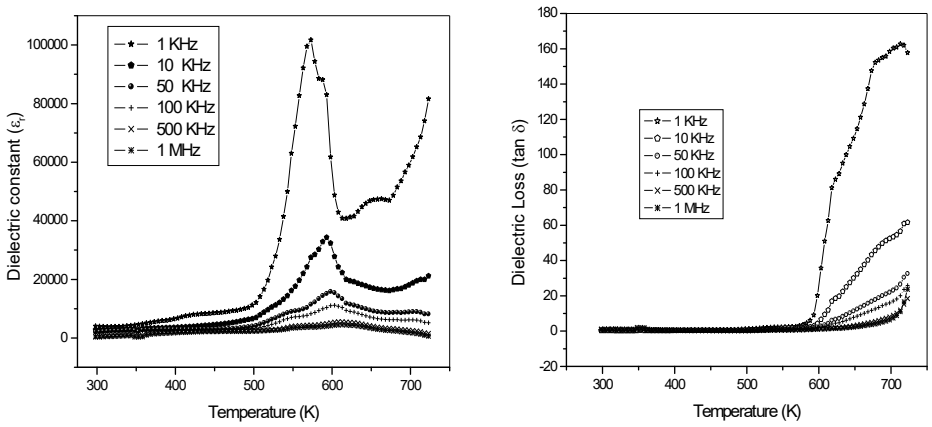

Figure 4. Variation of relative dielectric constant & tangent loss with temperature of La doped BFST

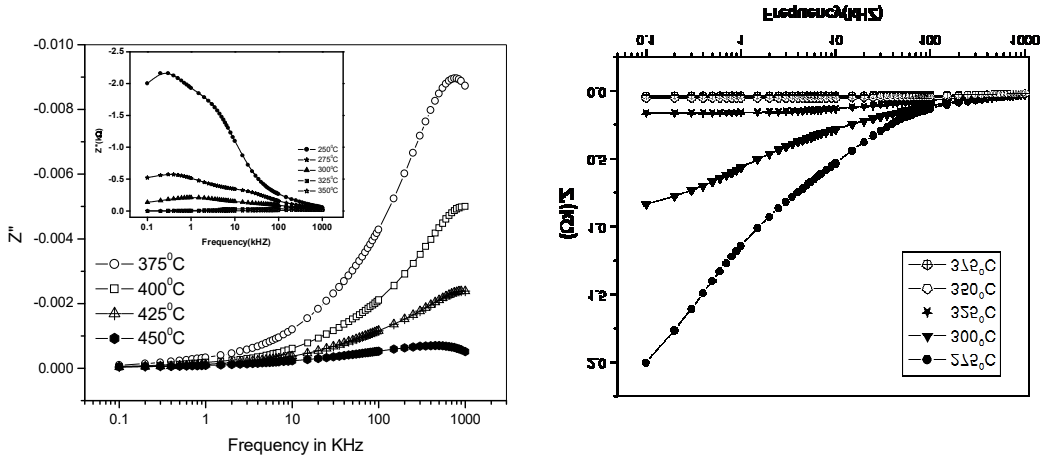

Figure 5.Variation of Z' and Z'' with frequency of La doped BFST

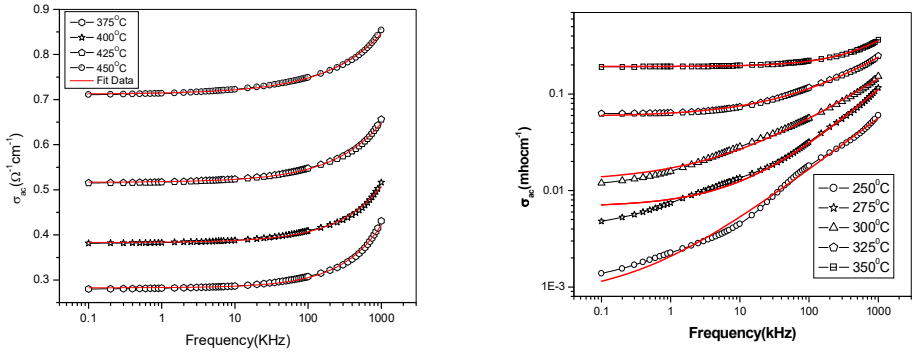

Figure 6.Variation ofac conductivity as a function of frequency at different temperatures.

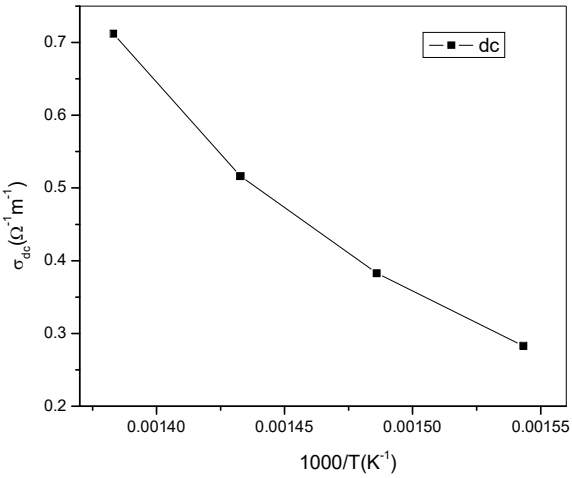

Figure 7. Variation of dc conductivity with temperature of La doped BFST

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RESEARCH ARTICLE

Ease Synthesis of 2,7-Dinitrofluorne

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ABSTRACT

Here we illustrate the synthesis and characterization of nitration of fluorene. In general nitration of fluorene has been carried out by using fuming nitric acid. Here, we have developed an easy synthetic route to carry out nitration of fluorene by using commercially available concentrated nitric acid. By varying different conditions, it has been observed that use of 2:1 HNO_3 and CH_3COOH at 100 °C is the best suitable conditions to obtain 2,7-dinitrofluorene. The synthesized monomer was characterized by various spectroscopic tools.

Keywords: Fluorene, 2 & 7 positions, Nitration, Nitric acid, Acetic acid

INTRODUCTION

From the first demonstration of polymer light-emitting diodes (PLED) in the nineteenth century, the work on π-conjugated materials has been widely explored for their various potential applications [1-5]. Conjugated compounds have attracted great interest of many researchers because they contain the mechanical, physical as well as electrical characteristics. In 1977, the first synthetic conducting polymer was reported by Shirakawa `and co-workers is polyacetylene (Nobel prize in 2000) [6]. Though polyacetylene still serve as an excellent descriptive example as well as the basic model-compound for conjugated polymers, its improcessability and instability towards photo-oxidation initiated the synthesis of more elaborate materials with improved characteristics. In this regard various π-conjugated polymers such as polypyrroles, polythiophene, polyanilines, poly(p-phenylenevinylene)s, and polyfluorenes have been developed [7-10].

Among the aforesaid aromatic core structure containing conjugated polymers, fluorene derivatives exhibit unique chemical and physical properties. It contain a rigid planar biphenyl unit, and substitution at 9-position increase its solubility and processability without increasing the steric interactions [11-14]. Polymerization of fluorene was carried out by incorporating functional group at 2 and 7 positions of fluorene [15]. Thus it is important to develop new synthetic route for incorporation of functional groups at 2 and 7 positions of fluorene.

RESULTS AND DISCUSSION

In this regard our aim is to develop a synthetic strategy to incorporate $–NO_2$ group in fluorene. According to literature reported, fuming HNO_3 has been used to incorporate $–NO_2$ group in the fluorene backbone [16]. But here, we have carried out the nitration fluorene bu using commercially available concentrated HNO_3. By varying the concentration, we can obtained both mono and di- substituted fluorene monomers. Scheme 1 represents the synthetic route for preparing 2-nitro-9,9-dioctylfluorene (1) & 2,7-dinitro-9,9-dioctylfluorene (2).

Attempts were taken to incorporate nitro group in fluorene in two ways. In the first case concentration of HNO_3 and H_2SO_4 were varied at RT. But after varying several conditions, we are able to obtain very low amount of nitro derivative (shown in table 1). In the second case, amount of HNO_3 and CH_3COOH were varied at different reaction condition. The reaction did not proceed when HNO_3 (5mL/10mL) and glacial acetic acid (5 mL) were used at RT. But when HNO_3 (5mL) and glacial acetic acid (5 mL) (i.e in 1:1 ratio) were used at reflux condition, 2-nitro 9,9-dioctylfluorene (1) was obtained. Finally the yellow oily compound **2** was synthesized through the treatment of alkylated fluorene with HNO_3 (10 mL) and CH_3COOH (5 mL) at reflux condition for 12h. The synthesized monomers were characterized spectroscopically.. In ^1H NMR (Figure 1) the protons at 1 & 8 position appear as singlet at 8.28 ppm, whereas other aromatic protons appear as multiplet 8.36-8.34 and 7.95-7.94 ppm. In $^{13}C\{^1H\}$ NMR (Figure 2) the aromatic carbons are appeared in between 153.5 and 118.5 ppm. In FTIR (Figure 3) the $\bar{\upsilon}_{NO}$ (of NO_2^-) appears at 1523 cm^{-1} (for asymmetric stretching) & 1339 cm^{-1} (for symmetric stretching).

CONCLUSION

Nitration of fluorene at 2 & 7-positions was carried out by varying different conditions. Instead of fuming HNO_3, to carry out the nitration we have used commercially obtain concentrated HNO_3. It was reveled that the use of 1:2 CH_3COOH and HNO_3 at 100 °C is the best preferable way to obtain 2,7-dinitrofluorene. The synthesized compound was characterized by ^1H and $^{13}C\{^1H\}$ NMR spectroscopy and FTIR.

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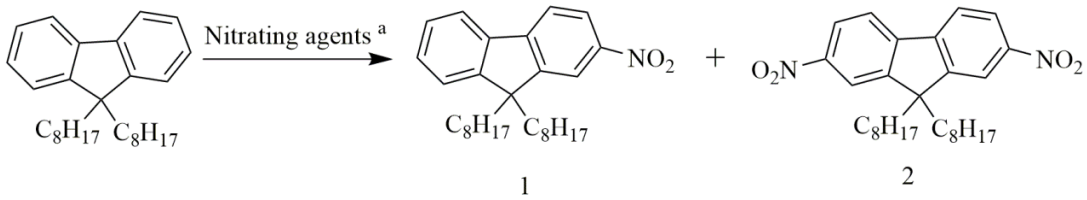

Scheme 1.Incorporation of nitro group to fluorene backbone (listed in table 1)

Table 1.Incorporation of nitro group at 2 & 7 position of 9,9-dioctylfluorene (* refers that the yield was calculated after purification through column chromatography)

Reagent	Condition	Yield
HNO_3 (10 mL) H_2SO_4 (5 mL)	RT, 12h	12%*
HNO_3 (1 mL) H_2SO_4 (4 mL)	RT, 12h	14%*
HNO_3 (0.5 mL) H_2SO_4 (3 mL)	RT, 12h	17%*
HNO_3 (5 mL) CH_3COOH (5 mL)	RT, 12h	No reaction
HNO_3 (10 mL) CH_3COOH (5 mL)	RT, 12h	No reaction
HNO_3 (5 mL) CH_3COOH (5 mL)	100°C,12h	52%* (1)
HNO_3 (10 mL) CH_3COOH (5 mL)	100°C,12h	48%* (2)

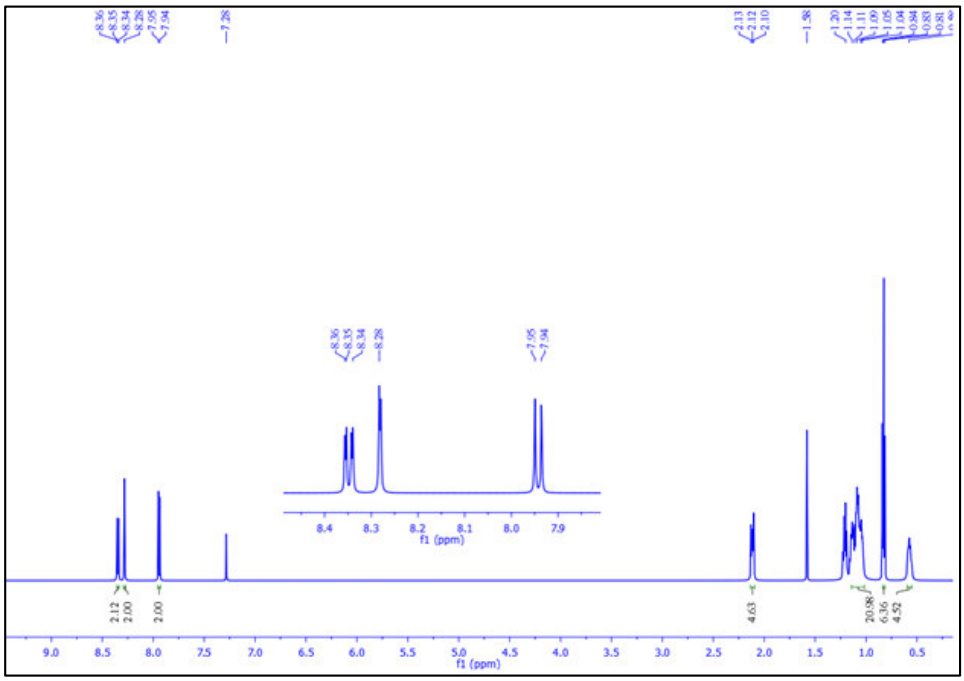

Figure 1. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of 2,7-dinitro-9,9-dioctylfluorene

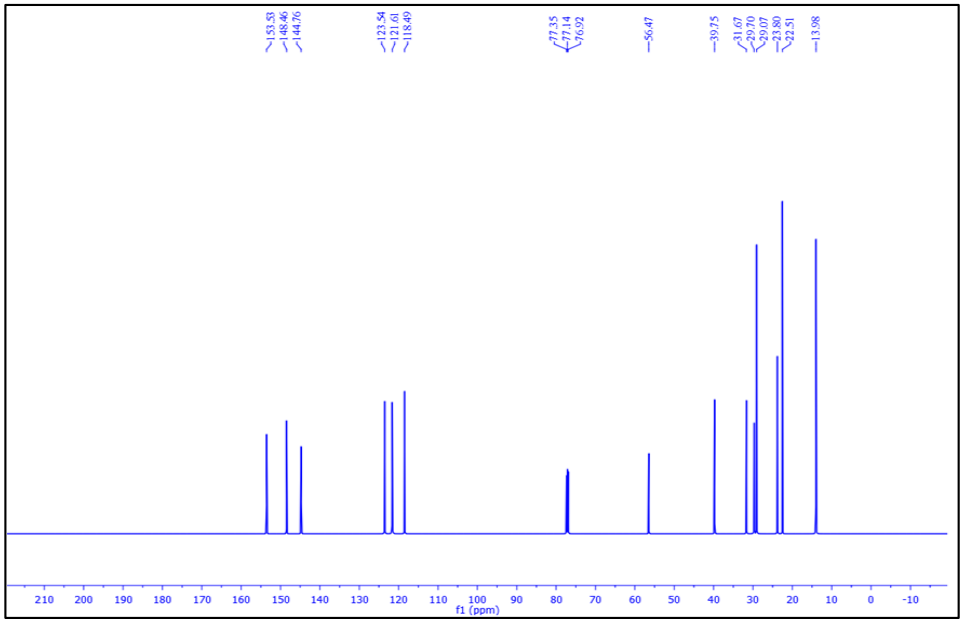

Figure 2. $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz) spectrum of 2,7-dinitro-9,9-dioctylfluorene

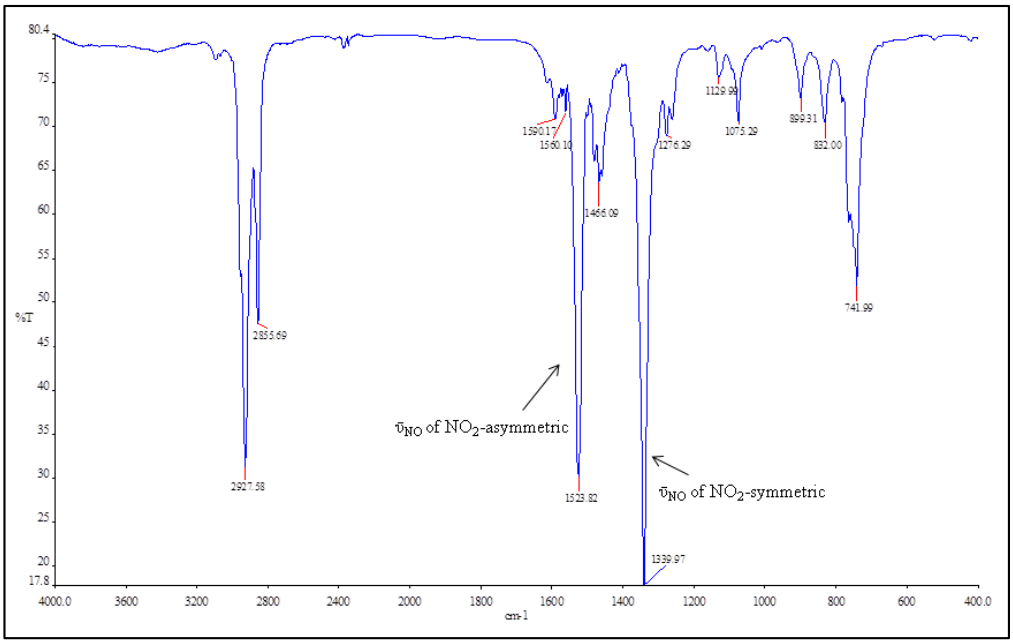

Figure 3.FTIR spectrum of 2,7-dinitro-9,9-dioctylfluorene

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RESEARCH ARTICLE

SRIM Simulation on Perovskite Solar Cell Device (A Potential Candidate for Space Science)

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ABSTRACT

The study of radiation is very important and special the radiation detectors. In space the radiaction condition is much different the lab condition. So it is very difficult to test anything in space and the correct again and again. One of the important components is the solar cell. A perovskite based solar cell has been studied and found that it is a suitable candidate for the space mission.

Keywords: Perovskite, SRIM, Monte Carlo Simulation, Solar Cell, Low cost.

INTRODUCTION

Due to gradual increase in consumption of global energy and limit of fossil fuels, significant research interest has been observed on renewable and sustainable energy resources [1-5]. The most efficient and effective source energy is sunlight [6]. The most talented technology to accomplish the increasing energy demands in future is the production of electricity from sunlight, having no negative effect on the world climate. The photon energy can be converted directly into electricity in an ecofriendly way by utilizing solar cell tools. In this connection, various research groups have developed different types of photovoltaic cell, crystalline silicon-based (first generation), thin film of CIGS and CdTe (second generation) and organic and hybrid materials (third generation) worldwide over the past two decades [7-10]. So far developed photovoltaic cells have several drawbacks such as heavy weight, high manufacturing expense, and lack of elasticity, which restricts their extensive applications. Nowadays scientists are much more interested in developing high efficiency, low cost, and large-scale fabrication based photovoltaic devices but unfortunately did not succeed yet. However, effective materials and efficient device structure will require establishing the solar cell technology as well as to reduce the cost and increase in power conversion efficiency.At present the research community has great interest in perovskite (organic-inorganic halide) solar cells (PSCs) due to inconceivable device efficiency [11-12]. Perovskite was first discovered by Gustav Rose in 1839 and was named by

Lev Perovski. It is composed of mainly calcium titanate crystal structure. To replace the silicon photovoltaic (PV) devices, perovskite based solar cells gained much attention.

MATERIALS AND METHODS

The device structure of PSCs was designed from the device structure of dye-sensitized solar cells (DSSCs) [11]. The main characteristic of perovskite material is that it has large tunable band gaps (e.g., $CH_3NH_3PbX_3$ has a band gap, ranges from 1.5 eV to 2.3 eV). It also has high light absorption coefficient (greater than 10^4 cm^{-1}), similar to thin film solar cell materials [13-16]. It has advantages over silicon-based solar cell devices, due to its low-cost and suitable fabrication techniques. Thus, we can say that Si will be replaced by perovskite due to its exceptional structural, electrical and optical properties.

RESULTS AND DISCUSSION

A perovskite based solar cell has been studied under radiation conditions. Here the radiation has been assumed as the low energy ions /charge particle (200 KeV) [17]. It is also very important as the secondary radiation at space is the low energy charge radiation or the gamma rays [18]. In our earlier work we did the simulation with the normal Si based solar cell and found that the TiO_2 based cell has a potential candidate for the heavy ion detection. But here we studied the perovskite based solar cell. The results have been shown in Fig.1. One can see from Fig.1 that the energy loss at different layers of the perovskite based solar cell. Infact towards the end of the path which is in the layer of perovskite the loss is more so the ion will maximum . The ion will completely stop on the material indicating no signal loss i.e a full energy information can be received if the signal will be detected which will be generated by the electron and hole in the reverse bias condition. In the same Fig.1 one can also see the ion range which is mostly the gaussian distribution. The width will be the representation of the straggling.

The recoil spectra and also the collision details have been shown in Fig.2. One can see from Fig.2 that the recoil of the ions and the atoms inside the different layers. As the recoils are not spread more so the recombination will occur and they form the stable configuration. The displacement of the atoms and creation of the vacancies has also shown in the same Fig.2 and one can see that the vacancy is not so high which is a good situation for recombination i.e. the longevity of the detector will be more.

CONCLUSION

A Monte Carlo based simulation has been done for perovskite based solar cells. Different spectra have been generated and compared with each other. It has been seen very clearly that the ion will stop inside the cell indicating the complete energy absorption or the energy information. The recoil and the vacancy has also studied and found that they are not very high. This leads to a situation where the perovskite based solar cell may be a good potential candidate for the space mission. The more experimental data will require validating our finding.

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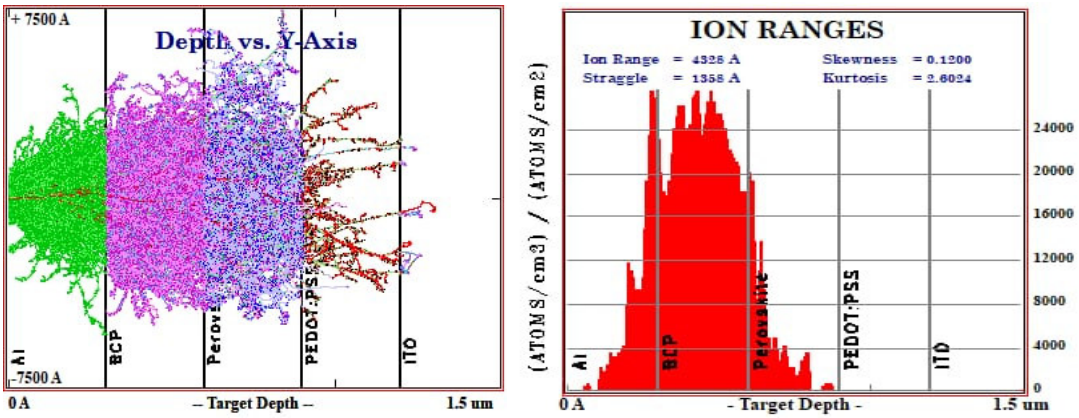

Fig.1.(Left) The passage of ion inside the perovskite based solar cell. Different colors indicate the passage of radiation at different layers. One can see that the ion will completely stop in the cell. (Right) the 1D histogram of the range of the ion which is nearly a gaussian distribution and the spread will tell the straggling.

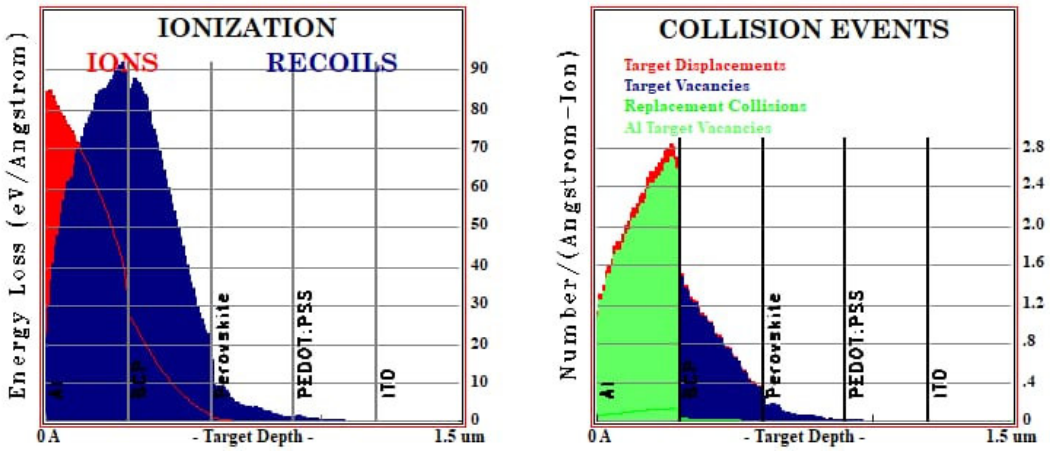

Fig.2.(Left) The ion and the recoil spectra. Once can see that the recoils are present but not very huge spread. (Right) the spectra of the target displacements and the vacancies created. One can see that less vacancy is there which leads to the long time operation.

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RESEARCH ARTICLE

Simulation of 50 keV Argon ion on SrO_2 Nanoparticles using SRIM

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ABSTRACT

In this work, the Monte-carlo based simulation of irradiation of inert gas (Argon) ions with energy 50 keV on Strontium peroxide nanoparticles has been reported. SRIM, a process of simulation has been used to study the impact of collision of the ions on the target, Strontium peroxide (SrO_2). The average ion range is 992 A and the concentration of ions in the target SrO_2 is found to be 7936×10^{15} atoms/cm^3 when the fluenceis 8×10^{15} atoms/cm^2. The advantages of the simulation process is that, it aids to collect a very good quantity of information about ion induced effects, that is extremely necessary for the experiments on the irradiation of ions on the surface of SrO_2 nanoparticles.

Keywords: Monte-carlo, SRIM, Strontium peroxide nanoparticles, irradiation, argon ions.

INTRODUCTION

Strontium Peroxide (SrO_2), an alkaline earth metal peroxide is well known for its excellent reactivity and oxidant property [1]. Strontium peroxide compounds can be used in various fields comprising of energy storage, medicines, different material science and energy storage devices [2-4].SrO_2has been commonly used as an oxidizing agent for the purpose of bleaching. [5-6]Strontium Oxide can be manufactured in the purest form among all kind of peroxides of alkaline earth metals. [7]SrO_2 acts as an important constituent in different industrial products including clay and ceramic products [8].

METHODOLOGY

In this present work, SRIM based on Montecarlo simulation is used to observe the distribution of ions in 3D.

RESULTS AND DISCUSSION

The ion distributions in the TRIM (RANGE.TXT) include the depth of penetration of the incident ions. The unit of the range distribution is denoted as atoms/ (Å-ion). The ion concentration in the SrO_2 target could be obtained by multiplying the fluence values with the ion range values.

Ion Path 2D

Fig. 1 shows the distribution of recoil atoms, ion path and the vacancy produced when the target is irradiated with the argon ions. The red dots represent the recoiled atoms, sky blue dots represent the vacancies produced due to the displacement of the atoms from its lattice site and the blue line represents the path followed by the ions after collision. The RANGE.TXT for the Argon ions of energy 50 keV into $SrO_2$is illustrated as below.

Variation of ions and recoil atoms with penetration depth

Fig. 2 demonstrates the graph between the variations of argon ions fall on the SrO_2 target. It is manifested, almost nearly 87645 number of argon ions with penetration depth of 849Å have reached the strontium oxide target.Fig. 3 represents the plotamong the variation of recoiled target atoms (i.e. Sr and O atoms) and the penetration depth. Nearly 1.7×10^7 number of oxygen atoms and 2.84×10^7 number of Sr atoms are distributed with the penetration depth of 462 Å.

3D- Ion Ranges

The 3D ion ranges of argon an ion inside the SrO2target is shown in the fig. 4. The 3D-RANGE.TXT consists of the termination sites of the ions inside the target. In this figure, the argon ions are plotted with depth along the X-axis, Y and Z axis are the side coordinates. The ions which are transmitted or backscattered are not presented in the plot.The ion range displayed in the plot is 992 A and the staggele is 345 A with the skewness of 0.001.The number of ions per unit cubic centimetre (volume) in the target SrO_2 will be 7936×10^{15} atoms/ cm^3 when the ion range value is multiplied with the ion dose i.e. $8 \text{ X } 10^{15}$ atoms/cm^2. In this way the target atoms'concentration can be determined through this mechanism.

CONCLUSION

We have stated the ions of inert gas such as argon with energy 50 keV induce some effects on SrO_2 target. We have concluded that the averagerange distribution is found to be 992A and the concentration of argon ions in the target SrO_2 is ascertained to be7936×10^{15} atoms/ cm^3at anion dose of $8 \text{ X } 10^{15}$ atoms/cm^2.

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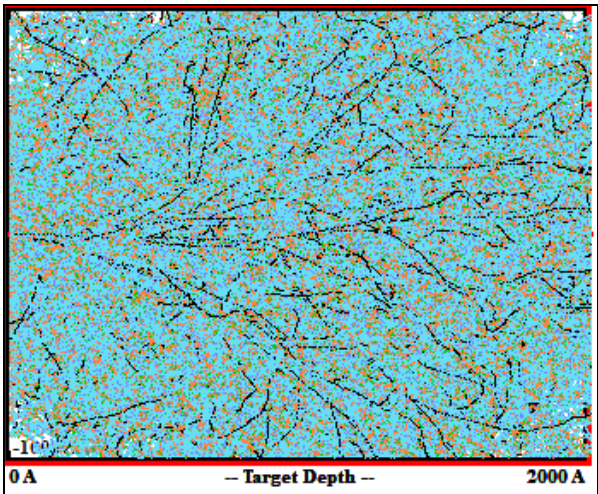

Fig.1.50 keV energy Ion path

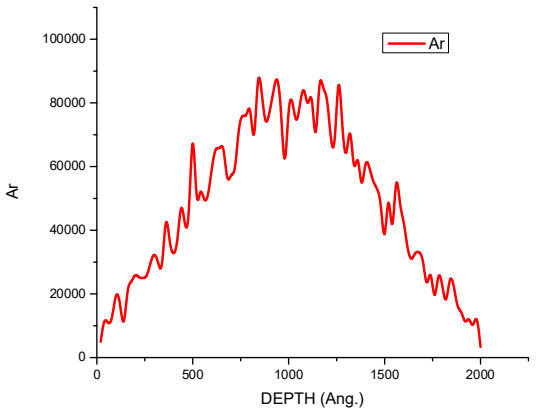

Fig.2.Variation of Argon ions with penetration depth

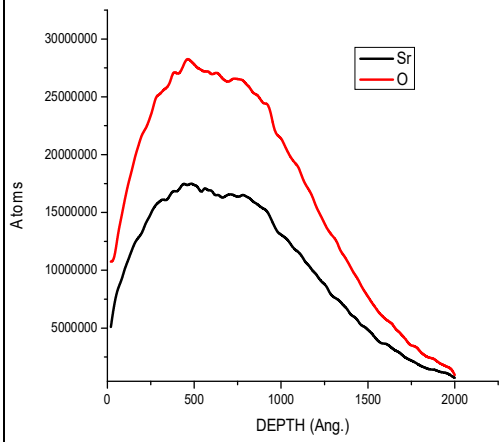

Fig. 3 .Variation of Sr and O atoms with penetration depth

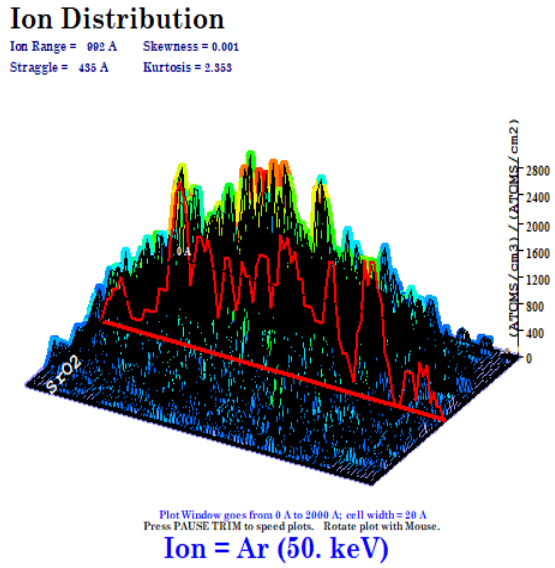

Fig. 4. 3D ion ranges of argon ions inside the SrO_2target

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RESEARCH ARTICLE

Study of NaI and CsI Scintillator for Radiation Detection

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ABSTRACT

The radiation detection is very important and from decades, people are trying to synthesize many varieties of detectors. Out of which scintillators are very important. A montecarlo based study has been done using inorganic scintillator and found that these are very good response to radiation dose and also for different charge particle. The details have been presented.

Keywords: radiation detection, detectors, montecarlo, inorganic scintillator

INTRODUCTION

Scintillators are one of the most interesting detection materials for the varieties of radiation. Sometime these scintillators are used for gamma detector as well as for particle detection. The most important application comes when they are used for the neutron detection. There are two groups of scintillators such as organic and inorganic scintillators. The organics scintillators are made up of organic molecules and they are mostly used for the neutron detection. The Inorganic scintillators aretypically the crystals of alkali halides with small activator impurity.NaI, CsIare the most common Scintillation mechanism in characteristic of the electronic band structure found in crystals. When an Incident particle strikes these materials, it ionizesthe crystal, eject electrons from valence to conducting band, creating free electrons and free holes. It creates an exciton by exciting electron to a band located just below the conducting band. Hole-electron remains bound together as a pair, but are free to move.

If there are impurity atoms, then electronic levels in the forbidden energy gap are created. The free hole or electron can ionize the impurity atom. If the transition is radiation less, the impurity center is a trap and the Energy is lost in other processes time response is bigger than for plastics ~500 ns. inorganic crystals are hygroscopic, must be housed

very tight to avoid contact with humid air in addition they have major advantage as the inorganic scintillators is due to their higher Z and density, they have greater stopping power. They also have the highest light output, which results in better energy resolution. This makes them very suited for detection of X and gamma ray and high energy electron and positrons in addition with the charge particle. In the present paper we have used a monte-carlo based simulation to understand the behavior of these two scintillator.

SIMULATION AND RESULTS

A beam of proton having 6 MeV incident energy with a beam current of 1 microampere has incident on the CsI and NaI. The range and the recoil distribution has been studied and presented in the below figures. Cesium iodide (CsI) is a robust material that doesn't cleave or crack under stress. It is minimally hygroscopic and a relatively bright scintillator. The emission of CsI itself is located above 500 nm where it is very effectively read out by silicon photodiodes or silicon photomultipliers (SiPM). CsI crystals are frequently used in arrays or matrices in particle physics research. Fig.1 shows the results for the NaI. One can see from Fig.1 that the complete projectile will stop inside the material and loss all of its energy, which follows the Braggs curve. The recoil distribution has also shown in the same figure and found that the distribution is not only Gaussian towards the end but also a long left side trailing. This indicates the statistical nature of radiation and also the pulse each time it will provide is not unique. Therefore the linear behavior is not always achieved.

This is the reason the scintillators are used as the first timing device not for the energy measurement as the resolution is not so good compared to Silicon surface barrier detector. The same situation is with CsIalso. The results for the CsI have been shown in Fig.2.

CONCLUSION

A montecarlo based simulation has been done for NaI and CsIinorder to understand their effect on the same incident radiation (proton here) it has found that both are behaving similar way. So any one can be adopted for the experiment. But one thing has to kept in mind that NaI is hygroscopic in nature whereasCsI is not so. One ccan use CsI for particle detectorwhereas the NaI mostly use for the gamma detection as they are inside a vacuumed seal container.

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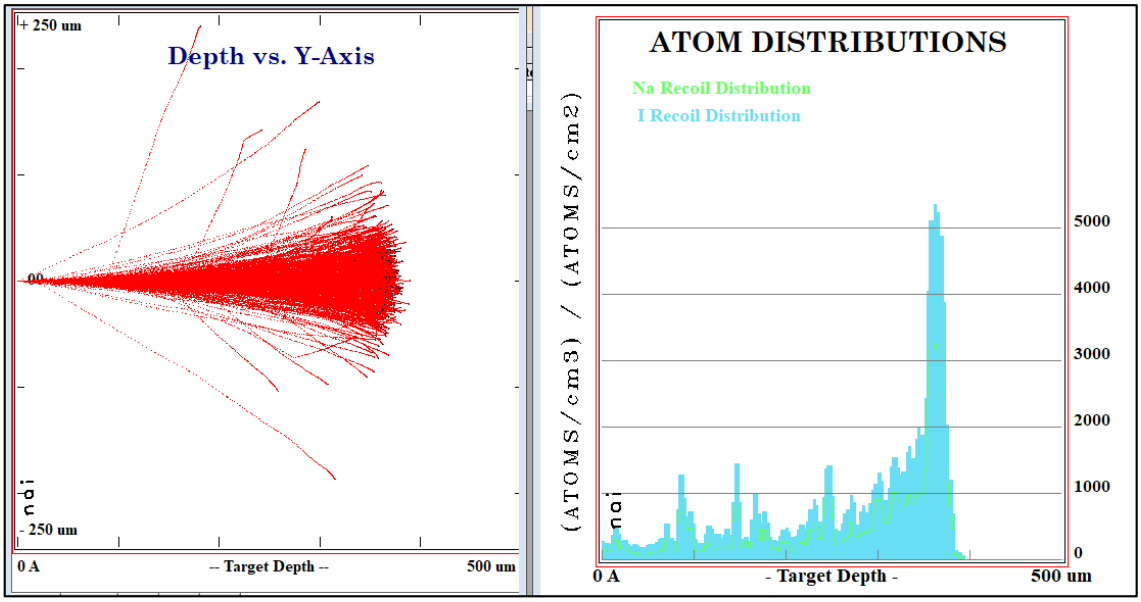

Fig.1. (Left) The range and the tracks of the Proton ion having 6 MeV incident energy inside NaIdetector. (Right) same incident ion but the recoil distribution.

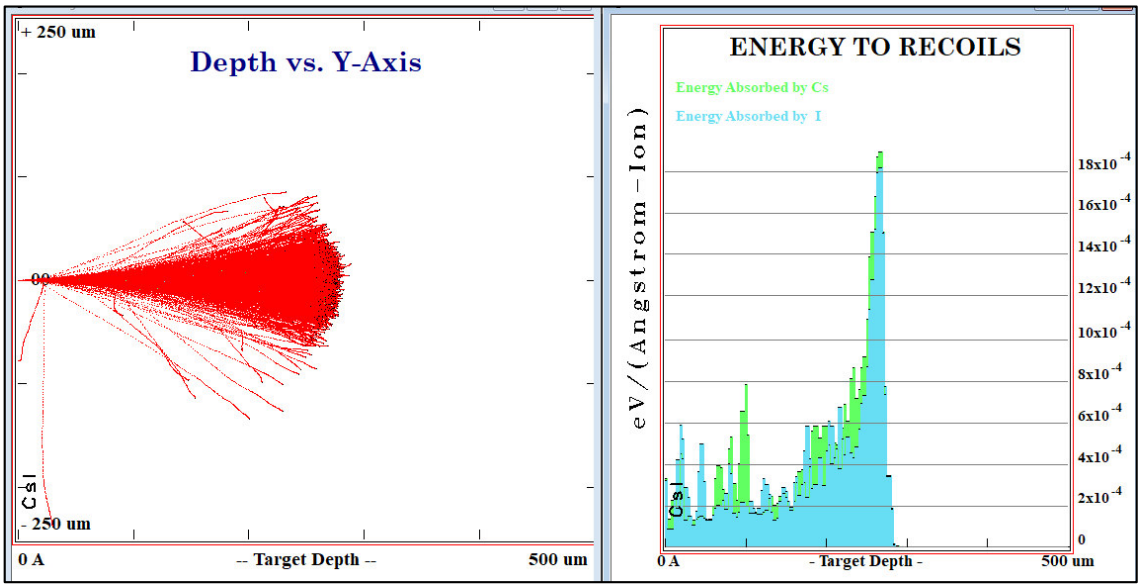

Fig.2.(Left) The range and the tracks of the Proton ion having 6 MeV incident energy inside CsIdetector. (Right) same incident ion but the recoil distribution (here one can see both Cs and I atom independently)

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RESEARCH ARTICLE

Study of Organic Scintillator Stilbene for Radiation Detection

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ABSTRACT

Detection of radiation is very important and many types of radiation detectors are being developed progressively by researchers. Scintillation detector is one of the most robust detectors which have found wide use. In this present work, we have studied the properties of stilbene, an organic scintillator for the radiation detector and the result has been reported. Interesting Pulse shape discrimination method has also been explained.

Keywords: radiation detection, detectors, stilbene, organic scintillator.

INTRODUCTION

For nuclear reactors and particle accelerator facilities, precise measurement of fast neutrons is most vital. Elastic scattering of neutrons is the widely used on which detection the dectection of fast neutrons including thermal one is very important..The fast neutrons are passed through a scintillator to produce recoil protons. Energy of the neutron is then measured from the highest energy of a recoil proton[1]. The materials showing scintillating properties can be organic or inorganic including gaseous scintillator. The design and study of scintillators is an interesting topic since decades. Each scintillator has its own properties; for example, the inorganic/organic scintillator detectors are very fast response time and the identification of some types of radiations can be done using the pulse shape discrimination technique which is an important method to separate neutron and gamma ray. On the other hand, stilbene, which exists as two geometrical isomers, *(E) or trans-stilbene* and (*Z*) or *cis-stilbene*(Fig. 1) has been long considered as an important organic scintillator to detect fast neutron.

It is a daunting task to detect different radiations as the radiations are invisible but the effect is not ignorable. Certain materials, when struck by radiation, emit a small flash of light, a scintillation. When this small light is coupled to an amplifying device such as a photomultiplier tube, this light is transformed into electrical pulses, which can be

analyzed and provide us with precise information about the time of passage of that particle. Pulse shape discrimination technique is an important method to separate neutron and gamma rays,both are neutral radiations.It is very difficult to separate neutron and gamma directly from the signal (online) as the detector is sensitive to both the radiations. So it is important to distinguish them using some method and one of the important method is the pulse shape discrimination method [2] which is an important property of the organic scintillators.

Scintillation signal provide sensitivity to energy of the particle striking the scintillator. Most scintillators have linear response to energy deposited light output proportional to exciting energy. If photomultiplier is also operated linearly, then scintillator detector can be used as energy spectrometer. The response and recovery time is short w.r.t other detectors. Time between two events can be determined very precisely (~100 ps) and they can also accept very fast counting rates.In the present study we have used an organic scintillator (stilbene) to study the response of it towards a high energy charged particle.

CALCULATION AND RESULT

A beam of proton having 6MeV energy and intensity of 10micro Ampere was incident on scintillator (Stilbene). The response of the detector through the recoil energy of the atoms has been calculated using the code [3,4]SRIM/TRIM as shown in Figure 2. It can be seen from Figure 2 that the range of the particle inside the detector is not so high due to energy lose and the behavior follows the Bragg's mechanism. The interesting recoil distribution has been shown in Figure 2 (Right) for the motion of the incident radiation inside the detector. One can see from both the figures that therecoil of hydrogen is very sharp and follows a sharp Gaussian distribution with left long small trailing which indicates the complete head on collision leading to maximum energy loss and more emission of fluorescence light. The recoil is very less spread as it is heavy compared to the incident ion. From the figure 2 we can say that the maximum energy loss can be possible using head on collision leading to maximum scintillation and strong signal output. The rangeis very small which ensures the completetransfer of energy to the detector.

CONCLUSION

The SRIM calculation has been studied for organic scintillator stilbene. Very interesting result shows that the energy loss for the chargedparticle followsBragg's law. The pulse shape analysis has been shown with very clear distinction between gamma and neutron.

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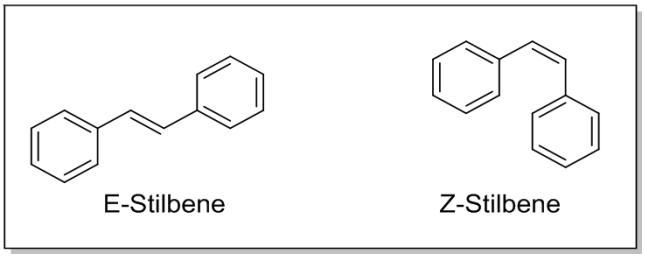

Figure 1.Structures of (E)-stilbene and (Z) -stilbene

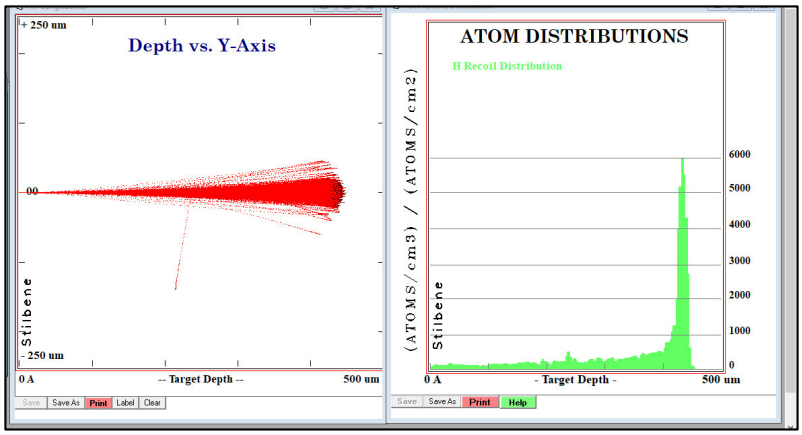

Figure 2:The passage of radiation (proton) inside the scintillator the stilbene. One can see that they will stop in 500um. (right) the recoil distribution inside the stilbene and it is a perfectly sharp distribution towards the end indicates the full energy loss.

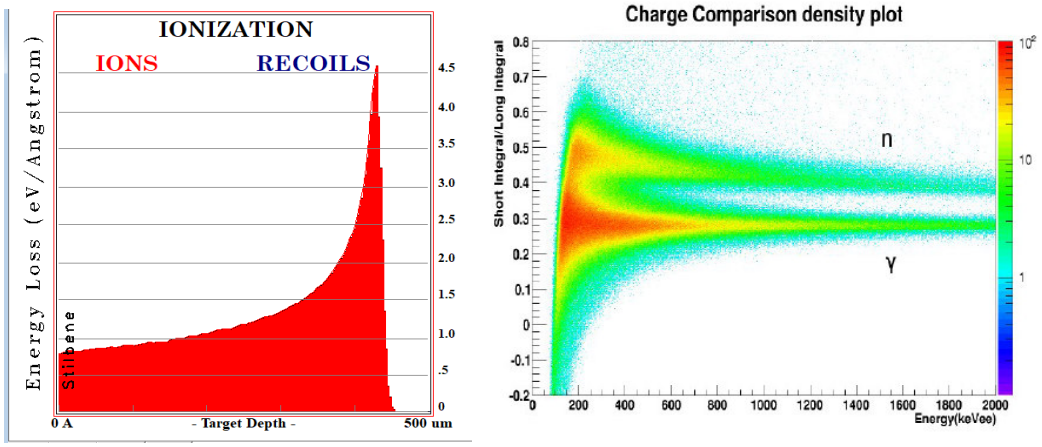

Figure 3. (left) Bragg's curve and the full energy loss (right) the [4]pulse shape analysis and the identification of the gamma and neutron.

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REVIEW ARTICLE

Sustainable Energy Irrigation Model for Enhancing Livelihood in South Odisha

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ABSTRACT

India has about 21 million irrigation pumps, of which more then 9 million pumps runs on diesel and another 12 million runs on electricity. Electricity consumption by irrigation pumps alone, consumes about 15 percent of the India's total electricity consumption. These irrigation pumps are less efficient as well. Undertaking a grid connected system will also be too expensive as the rural households are located in a far away distance. Even if the fuel is available, it is difficult to transport to remote rural areas, other than poor physical infrastructure. The use of solar operated water pumping system or solar pumps is an attractive option here. It requires low maintenance, low labour, no fuel cost, transportation is easy and pumps water when needed. Solar operated water pumping system will provide a better sustainable alternative option to fulfil irrigation requirement for agriculture purpose. The objective of this paper is to provide a snapshot on the diffusion of cycle mounted solar operated irrigation system in the region of South of Odisha. A case study analysis has been adopted to understand the diffusion process of cycle mounted solar operated irrigation system. Factors were found out which helped in diffusion of the irrigation system in South Odisha. The case is related to Kundra and Jeypur block of Koraput district of South Odisha. The study was undertaken by a cooperative, Pataneswari Agricultural Cooperative Society and Centurion University based at the city of Jeypore and Bhubaneswar in the state of Odisha and an action research approach was adopted.

Keywords: Sustainable Energy, Irrigation Model, Cycle Mounted Solar Irrigation System, Income, South Odisha

INTRODUCTION

South Odisha is basically a hard rock, hilly area, with scanty and uneven rainfall. There is absence of irrigation facility and farmers in the those area face difficulty in harvesting a good yield in the Khariff season and there is hardly any scope for raising crops in Rabi season (Activity Report, 2017-18, Dept. Agriculture, Government of Odisha). In the view of providing solutions to the people, a cooperative named "Pataneswari Agriculture Cooperative Society (PACS)" along with Tata Trust and Centurion University took the initiative to design and develop a cycle mounted solar operated irrigation system. Odisha government lunched Soura Jalanidhi Scheme to provide around 5000 solar pumpsto the farmers with 90% subsidy (1, 2). The detail of the diffusion study is described in the subsequent sections.

About the Study

This study was undertaken in Jeypur and Kundra blocks of Koraput district. It consists of 22 and 12 gram panchayats, with 125 and 85 villages respectively. Whole of the population of these two blocks resides in rural areas. With about 98 percent of the people of Jeypur and Kundra blocks depending on agriculture, were facing the problem of water crises for irrigating their fields (1-3). In order to provide solution to it, a cycle mounted solar operated irrigation system was designed and developed to help the farmers and bringing in livelihood security in the region. This system used a PENTAIR DC operated submersible pump of 0.25 HP, with maximum head of 70 m head, with a discharge of 310 LPH. The system uses 2 solar panels of 175 W producing about 4.1 amp current. The system was used in a open dug well, with a overhead tank to store water. The solar panels were mounted on the carrier of the bicycle for easy movement from one farmer's field to another. This system is basically used for irrigating small patch of land used for cultivation of vegetables (4).

Member farmer of cooperative used this system. It was provided at Rs 25000 and was bought by the farmers from Heruguda village of Kundura block of Koraput district initially. Through this initiative, defunct bore wells (due to unavailability of electricity) was revived for irrigation and the member farmer went for year-round vegetable production, thus enhancing his income as well. Here the cooperative took loan of Rs 2 lac from State Bank of India (SBI) to facilitate the promotion of cycle mounted solar operated irrigation system to other member farmers. The system was provided to other member farmers on instalment basis. Farmers took the system and rented the system to other farmers as well which helped them in improving of their income. The Community Service Providers (CSP) were trained on technical and managerial aspects provided by Centurion University. Further the CSPs went on in giving training to other members farmers on installation, repair and maintenance of the system. Use of the system was considered as a ray of hope for the rural farmers having limited resources. Farmers, who had closely seen their crops dying due to scarcity of water, unavailability of electricity started using the system to ensure at least two-season crops in their field. Focused group discussion was carried out with the member farmers of the cooperative for understanding the impact of use of cycle mounted solar operated irrigation system (5-6). It has been discussed later in later part of this paper. Below is the small case study described of a tribal farmer from Heruguda village of Kundura block of Koraput district of South Odisha.

Krushna, of Heruguda village got benefited by using cycle mounted solar operated irrigation system. He was a tribal farmer who owned a tiny piece of land measuring 0.25 acre. In the past, he depended on rain-fed agriculture and could grow vegetables only during the rainy season. After paying for seeds, seedlings, fertilizer and pesticides, his net annual income from agriculture was Rs 6600. After getting a demonstration of the system by CSP, he agreed to take a loan and adopted it for growing vegetables in his field. To start with, he invested further in this system and spent money on purchasing trellis, vegetable seeds, fertilizer and pesticides. The total investment amounted to Rs 60000. Since water was available on a regular basis, he was able to raise a nursery in his field (7). At the end of the first season, he was able to increase the production significantly and earned Rs 13700. He could further go for the

second and third crops within the year. After deducting for the money spent on seeds and fertilizer, he was able to earn Rs 33350 after the second season and Rs 31000 from the third season. After paying off the capital borrowed for the system, he was left with a net earning of Rs 18600, which was about 3 times higher than what he earned in the past. In the next year he invested Rs 12000 for wire-mesh fencing around his plot on remembering the loss due to cattle grazing in previous years. Further he rented his system on an hourly basis to other farmers who would seen their crops dying due to scarcity of water and electricity, helping him in earning more and securing his livelihood (8). In relation with the application of the framework a process flow has been given in figure 1.From the process flow, the bank, SBI provided loan to Pataneswari Agriculture Cooperative Society (PACS) and Tata Trusts provided the pump and the system was designed and developed in Centurion University. The major role was played by the implementing agency (PACS) in implementation aspect and Centurion University in designing aspect. Factors such as cost of the product, payment through EMI, portability of the product, renting the product, easy to operate, repair and maintenance by CSP and asset creation for the member farmer were some of the important factors which helped for the diffusion to take place. There was a need for a strong technical service partner to last mile connectivity which was fulfilled by the presence of a godown or a warehouse with the availability of spares parts of the DC pump, provision of training to CSPs on service, repair and maintenance and a designated toll free number for quick and better service was also put in place. Involvement of all these actors and factors helped in the diffusion to take place.

METHODOLOGY

The major role was played by the implementing agency, PACS, facilitating institution, Harsha Trust and technical partner, Centurion University. For successful diffusion and implementation, interaction was held with the CSPs of the cooperative.With farmers facing the problem of water, and unable to irrigate their fields, they saw their crops dying. Member farmers approached the CSPs in a motive to get the solution. As a result, CSPs discussed this problem of member farmers with the officials of the cooperative. In the view of solving the problem, PACS approached the bank and applied for the loan for designing and development of a cycle mounted solar operated irrigation system. The reason for using a cycle mounted design was mainly because of its portability and ease of use from one field to field. Further the loan was availed by the bank with a payable interest to PACS. Several meetings were held between the CSPs and the PACS officials. Design for cycle mounted solar operated irrigation system was done by the researcher at Centurion University with the support from Tata Trust by providing the DC pump. After successful design and experiment it was provided to PACS. PACS provided the system to the member farmer, to be used in the fields for irrigation.

Training was provided by the researcher from Centurion University and Harsha Trust, in the local language to the CSPs on the advantages of using a cycle mounted solar operated irrigation system. After completion of the training program, the CSPs trained the member farmer on how to manage and operate the product. An incentive mechanism was placed by PACS. Incentive was only given when the entire instalment for the product was recovered and paid to the cooperative.For purchasing the system it was difficult for the member farmer to access the capital at the initial stage. For solving the problem, members were provided with easy financing options by payment on EMI basis, where the member farmer purchased the system with a minimum amount and rest amount was to be paid in instalment basis. Some member farmers used this system as rent to other farmers who were facing the problem of irrigating their fields. Renting the system helped the farmers in paying their instalment in a easy way.

The major hurdle was, ensuring quality after-sale at minimum effort and with less time. For achieving the same, technical training was provided to CSPs on how to carry out repair and maintenance of the cycle mounted solar operated irrigation system. They provided after-sales service for the product in quick time. A designated toll free number was in place for helping the member farmer for quick and service delivery. The drip irrigation system model is given in the figure 2, to enhance the skill knowledge of the farmers and traines.

With quick service, availability of system on EMI options, portability and renting the system, cycle mounted solar operated irrigation system was used by member farmers of the cooperative. Initially only one member farmer used the system but later, 40 cycle mounted solar operated irrigation systems were bought by other member farmers as well. Apart from the above figures, till date about 730 number of cycle mounted solar operated irrigation system are being used by farmers at different locations of South Odisha (9), given in the figure 3.The cycle mounted solar powered irrigation system consists of Solar modules (40 W each), Charge controller (12 V, 4 A), Water pump (0.5 HP), Cycle, Mechanical structure and Electrical appliances (5).

Impact of Use of Cycle Mounted Solar Operated Irrigation System

This section focuses on the impact of use of cycle mounted solar operated irrigation system on the members of the cooperative. To know the impact of use of cycle mounted solar operated irrigation system, focused group discussions was held with the member farmers of the cooperative with the involvement of CSPs and CEO of PACS office based at Jeypore, a small town based in South Odisha.

Initially only one member, who was also a CSP of the cooperative from Heruguda village of Kundura block purchased the cycle mounted solar operated irrigation system. He used the system in his field and gave it as rent to other member farmers. Gradually the member farmers showed interest in buying the system and approached PACS. Focused group discussion was held with the member farmers who were using the system and they shared their experience of using the system.Focused group discussion was held with the member farmers from Boipariguda village of Boipariguda tehsil in the PACS office. They had to walk to near by water source to fetch water in buckets from the dam site to irrigate their fields to grow different vegetables such as cabbage, brinjal, tomatoes etc. It was taking almost 5 hours starting from fetching of water to irrigation, leaving less time for other essential work such as hoeing, weeding and tending in addition to household chores.

With much difficulty they arranged a diesel pump for pumping water from near by pond but later they could not afford the rising fuel cost, along with the problem in transporting. Eventually the pump broke down and they did not use it further. Later, after discussion with the CSPs and getting a demonstration of the system, and knowing that the system can be purchased through EMI options, they all agreed to purchase the system. Presently they now use the system and fill the tanks each day at mid-day to water their fields in less time. The system was easy to operate, portable and was quick in functioning. They informed that, with the use of the system they are now able to irrigate their fields and grow different vegetables (10).Focused group discussion was held with the member farmers from Kaliagam village of Jeypur tehsil. They told that the system was very easy to operate, and does not require any complex technical knowledge. Further, as the system was cycle mounted it was easy for transport from one field to another, leading to reduction in drudgery.

Another focused group discussion was held with the member farmers from Bhusangaguda village of Kundura tehsil. They started using the system for irrigation in their fields and grew different vegetables. Earlier they were growing only one variety of vegetable, but later they started growing different vegetables and spices through inter-cropping and attaching drip pipes to the system. It resulted in water savings, improved seed germination and high yield. With high yield, now they sell the spices and vegetables in local market. This has led to availability of spices and vegetables when ever they required. They now even sell these items in local haat which has helped them in increase of their income. Focused group discussion was also held with all the members of the cooperative who were using both solar operated lights and cycle mounted solar operated irrigation system. From the discussion it was found that the impact of using the products was same which has been discussed earlier. The community level interactions substantiate that the use of solar operated lights and cycle mounted solar operated irrigation system used by all the 105 members of the cooperative has helped in enhancing their quality of life, given in the figure

Power Interest Matrix of Sustainable Energy Irrigation Model for Enhancing Livelihood

From the case study and implementation process, discussed we have recognised various actors. These actors are Pataneswari agriculture cooperative society (PACS), Bank (SBI), Tata Trust, Centurion University, Clean energy entrepreneurs and member farmers. Here the actors are the stakeholders. Here stakeholders are both the people and organisations (11). From the table 1, it is found that member farmers of the cooperative were the consumers of solar operated irrigation system. They were facing the problem of irrigating their fields. Being the consumers, they were highly interested in adopting this product in order to save their crops. The member farmers have high power in influencing the diffusion process, as they were the key decision makers in adopting the product.

PACS had high power in influencing the decision making process as the members were part of PACS itself and was interested in opening a clean energy vertical through the use of clean energy products where they could provide clean energy solutions to their member farmers. Bank on the other hand had low power as they were only interested in providing loan to PACS in payable interest. Tata Trusts had low power in influencing the diffusion process, but were highly interested in focusing on rural development through sustainable manner. They also provided the pump for the system as well. Centurion University had also low power in influencing the diffusion process, but was highly interested in uplifting the quality of life of the rural people. They designed the system and conducted many experiments before providing the system to PACS. They provided training to the CSPs on the advantages of using a cycle mounted solar operated irrigation system, other technical and managerial aspects. Apart from it, they also designed the monitoring mechanism for easy payment of the system. Community Service Providers had high power and high interest in the diffusion process. They act as a leader in influencing and motivating the member farmers to adopt clean energy products and drove the diffusion process forward (12). With the incentive mechanism in place, they were highly interested in venturing into solar business and and thus became Clean Energy Entrepreneurs (CEEs).

CONCLUSION

From the study some factors were found out which are necessary for diffusion of cycle mounted solar operated irrigation system in the rural areas. Use of local resource, involvement of cooperative was very much essential for the diffusion to take place.Finally all the stakeholders coordinated, cooperate and collaborated with each other so as to achieve diffusion of solar lights in the areas of Kundra and Jeypur tehsil of South Odisha. This not only led to the diffusion of cycle mounted solar operated irrigation system but also was accompanied with service delivery as well. It also helped in enhancement of quality of life of rural people.

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Table 1. Power Interest Table for Actors of Sustainable Energy Irrigation Model for Enhancing Livelihood

Actors	Power-Interest Category
Member Farmers	High power- High interest
PACS	High power-High interest
Bank	Low power-High interest
Tata Trust	Low power-High interest
Centurion University	Low power-High interest
CSPs	High power- High interest

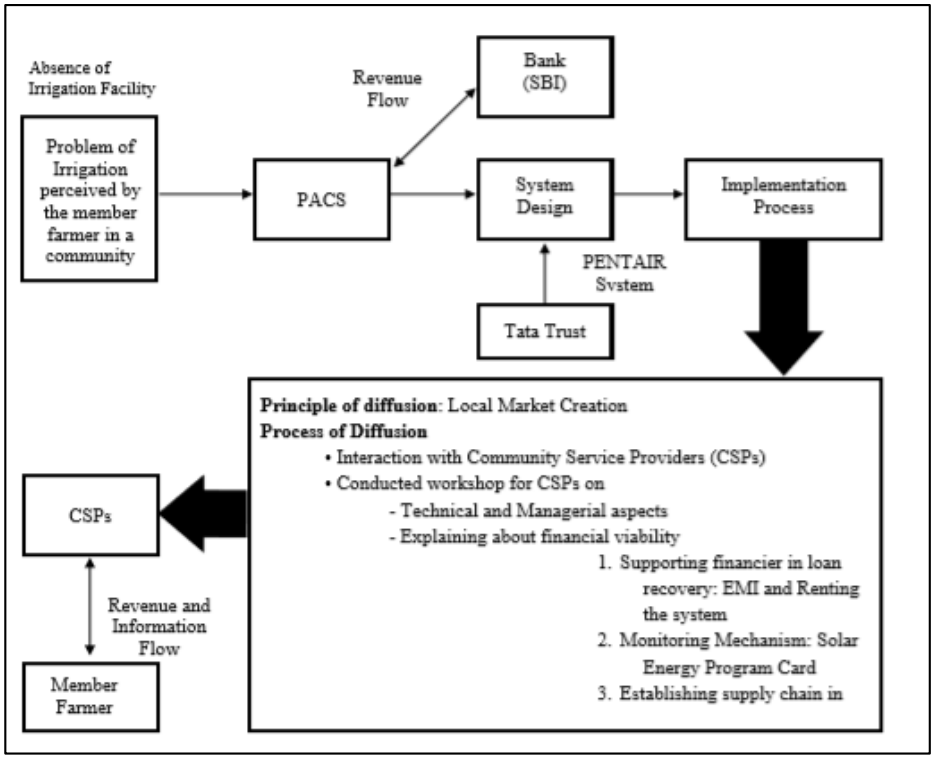

Figure 1. Process Flow for Sustainable Energy Irrigation

Figure 2. Basic solar drip irrigation system model

Figure 3. Cycle mounted solar powered irrigation system

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RESEARCH ARTICLE

Study of Fission Fragment Mass Distribution of ^{252}Cf

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ABSTRACT

Study of fission is very interesting and it has always its own place in the science. When a compound nucleus under goes decay by fission the two heavy fragment called as the fission fragment moves in the opposite direction in the center of mass. A study has been done for the mass distribution of the ^{252}Cf source and found that the mass distribution can be symmetric or asymmetric depend on the excitation energy.

Keywords: fission, symmetric, fission fragment

INTRODUCTION

Starting from long time back people are trying to understand the radiation by detectingthem using different detectors [1-3]. Out of many radiation say charge and uncharged, charge radiation detection is an important and interesting study. The charge particle can be light or it can be heavy. If it is light say alpha, proton one can call it as a light charge particle but if the mass is heavy one can called heavy fragment. In fission mechanism most of the time the heavy mass is one of the output product. Therefore it is very important to study the fission mechanism and the fission mass distribution. It is also important because in many reactors people are using Uranium as the fuel rod and at the end of the process as a waste product many nuclei (radioactive) will be generated and many ofthem are under fission decay. So in order to understand that process one need to study fission and the fission mass and charge distribution including mechanism. It is always difficult to extract the fission mass from the reactor used material as it is not always possible to go inside a reactor or it is not easy to work on the waste product which are highly radioactive. Therefore to study the fission mechanism one need to create the compoundnucleus which will undergo fission decay artificially. One of the way is the heavy ion reaction. Besides the study of fission mass and charge it is important to study it because that also used for the calibration source. Most of the places fission source from the nuclear reaction are not available for experiments and for detector calibration.so people use the fission sources as the

standard to calibrate their detector. One of the mostly used fission source for calibration is the ^{252}Cf.It is a neutron source also but inaddition it is a fission source also.In the present report we have understood the fission fragment mass distribution of ^{252}Cf which normally people use in the laboratory.

CALCULATION AND RESULT

The ^{252}Cf source [4] is a renowned source of fission but also a source of neutron. When one say source of fission means it emits fission fragmentsand in the center of massframe the fragments are move back to back.It is important to study their mass distributionwhether theyare symmetric or asymmetric. It has been understood clearly that the behavior of the mass distribution depend on many input parameters. One of the input parameter is the excitation energy which can be controlled by the incident energy.The compound nuclear excitation energy will be available for the fission fragment. If the excitation energy Ex is very less them most probably the fission mass distribution is asymmetric and as the Ex increase all the shell effect washed out and the fission mass distribution is symmetric. A calculation has been done using a Monte Carlo based code using the Nuclear reaction video (NRV) project.

The excitation energy dependent mass distribution has been shown in Fig.1, Fig.2. One can see from Fig.1 that the Ex is small then the mass distribution is asymmetric which can be understood very clearly. In order to understand the Ex effect on the behavior of fission mass distribution it has found that the distribution changes to symmetric from asymmetric as the Ex changes. Fig.2 show the distribution at excitation energy ~30 MeV. From Fig.2 one can see the distribution is purely symmetric mass distribution.

CONCLUSION

A complete simulation has been calculated using the NRV project and it has found a strong Ex energy depend on the behavior of the mass distribution. It has also clear thatin the same compound nucleus if one want a desired (symmetric/asymmetric) mass distribution i.e the fission fragments of different mass it can be obtained by controlling the Ex. There is effect of angular momentum also but herethe focus has given on Ex. Our next study is the effect of angularmomentum on fission effect.

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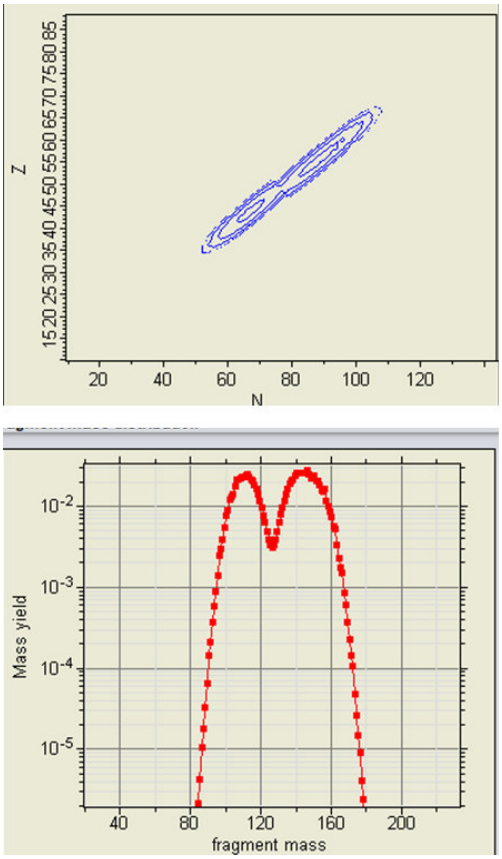

Fig.1.The predicted mass distribution of the ^{252}Cf at low excitation energy ~5MeV

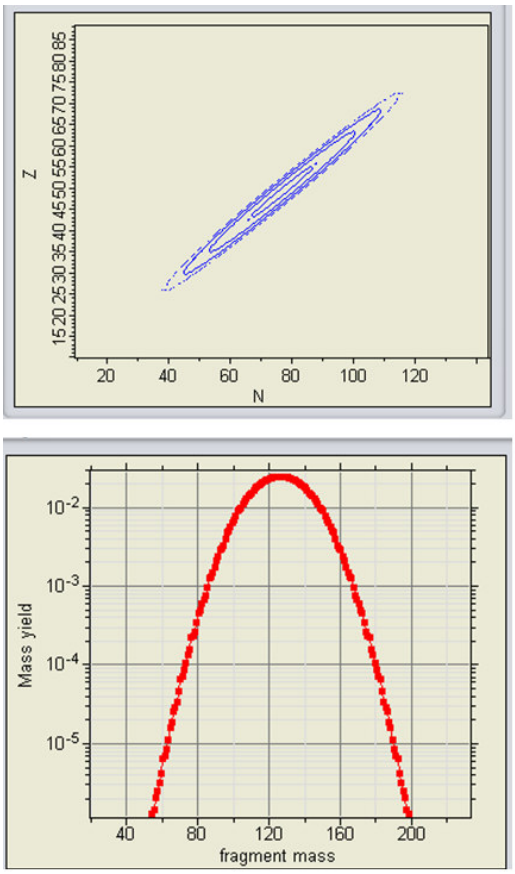

Fig.2.The predicted mass distribution of the ^{252}Cf at high excitation energy ~35MeV

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RESEARCH ARTICLE

SRIM Simulation of Sputtering of Lead by Incident 50 keV & 200 keV Xenon Ions

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ABSTRACT

Lead is well-thought-outto be a vastly substantial material for countless industrial products, especially widely used in bullets. They are sometimes very useful in construction industries. Energetic ions have an elusiveinfluence on innumerable target materials. Montecarlo simulation is extremelyimportant to identify the corresponding defects produced. Here, we reporteda sputtering simulation from SRIM. We have accomplished the simulation for thebombardment of 50 kilo electron volt and 200 keV xenon ions inside thelead atoms. We achieved the sputtering yield is closely12 atoms and 9 atoms per single xenon ion per electron-volt respectively, is almost 3/4th for higher energy which is 4 times higher than 50 keV.

Keywords: Sputtering, Lead , SRIM, Xenon Ion

INTRODUCTION

Lead is a very effective material owing toits application mainly in construction industries. Often, Lead is generally used in batteries apart from its toxicity. Molten lead is also being utilized as a coolant for lead-cooled reactors. Lead is one of three metals used in detecting organic acids, aldehydes in materials in the museum. The influence of xenon gas ions on lead is exceedinglynoteworthy to see the thorough simulation concerning the sputtering for each xenonion and its corresponding energy. We have used SRIM, to explore the sputtering of lead by xenon ions. Cylindrical symmetry is assumed in the final ion distributions in these kinds of simulations.

SIMULATION DETAILS

SRIM is an assembly of programs that compute the ion range and stopping crosssection calculations for ions from eV to the Giga-electron volt range. They employ quantum mechanical calculation of ion-atom impacts. During impacts, the charged atom and staic atom suffer a screened coulomb impact. It also includes exchange interactions between

the overlapped electron shells. The ions may produce electronic excitations and plasmons due to the long-range interactions with targets. These are pronouncedtogether with an explanation of the lead's electronic structure at the beginning of the calculation. The notion of effective charge is being utilized to illustrate the charge-state of the incident xenonion inside the lead. It comprises a charge state which is velocity-dependent &long-range screening because of the electron assemblage of that of the lead atoms.

Full damage cascades option trails every recoil until the energy drips lower than the bottom displacement energy of the lead atom. The lead atom is input as the target having thickness around 300 nm. This simulation is accomplished for 10^6normally incident ions. We have analyzed all collisional damage to the lead atoms.

RESULTS AND DISCUSSION

Fig.1 shows the ion distribution in three dimensions for the energy of each 200 keVxenon ion successively which influences the lead surface.These 3-Dimensional (3-D) distributions help analyze the semiconductor technology of how implanted ions will blowout under a mask. The plot displays the ending spreading of the ions and recoils in the target. The plots display the final position of all vanadium atoms which are evacuated from their native places by the incident xenon ion. This plot is particularly suitable to learn the recoil of target atoms across the vanadium boundaries. We have obtained the projected average ion range as about 30 nm. The accurate data is shown below in a tabular form (Table 1). The data is also being plotted in a 2D graph (Fig.2).

These graphs are only estimated data that illustrate the mechanism by which the sputtering may alter with the surface binding energy (SBE). Actually the surface binding energy is tough to evaluate, it sometimes becomes a barrier to provide accurate sputtering results. These plots simply display approximate data which shows the effect of slight changes will alter the ultimate sputtering yield. The target surface is presumed to be smooth. Sputtering creates the roughness in the target surfaces and this lessens the energy required by adjacent atoms to be sputtered out. Lead, if crystalline in its structure may convert into amorphous because of the surface damage. Preferential sputtering is not considered here because we have only targeted on a single target lead. Sometimes, the sublimation energy of lead is also considered as an agent to approximate estimates concerning the roughening of the lead surface due to the incidence of xenon ions.

Fig.3 revealed each recoiling xenon atom energy which influences the Lead surface. The Y-axis has units of atoms per single xenon ion, so each xenon ion will yield about the lead atoms which touch the surface. The vertical line (2eV) signified the mean SBE for the lead. At 2 eV, the quantity of atoms thatgot to the surface having greater than 2 eV is around 12 for 50 keV and 9 for 200 keV.

CONCLUSION

In this work, we have completed the simulation process for the (200 keV & 50 keV) energy xenon ion stempted effects on lead atoms ofa width of 30 nm. We have predicted the sputtering of retreatedlead atoms after touching the target surface is approximately 12 per singe xenon ion for 50 keV and 9 for 200 keV respectively. Furthermore, the yield for 200 keV becomes 3/4th of that of the data for 50 keV owing to the surface roughness tempted by ion intrusion. This variance in the lead atoms is significantlysmallbecause of the modification of the energy.

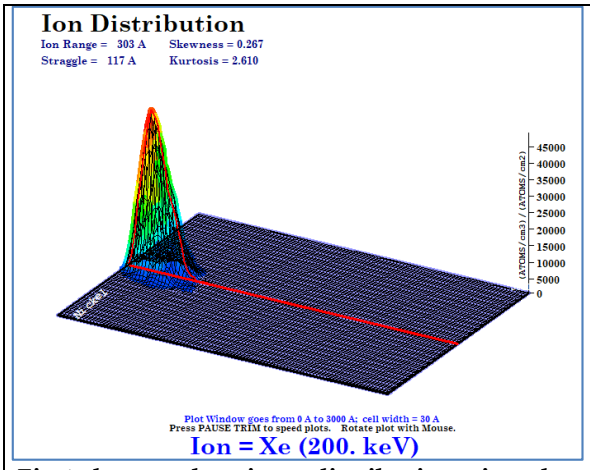

Fig.1.shows the ion distribution in three dimensions for the energy of each 200 keV xenon ion.

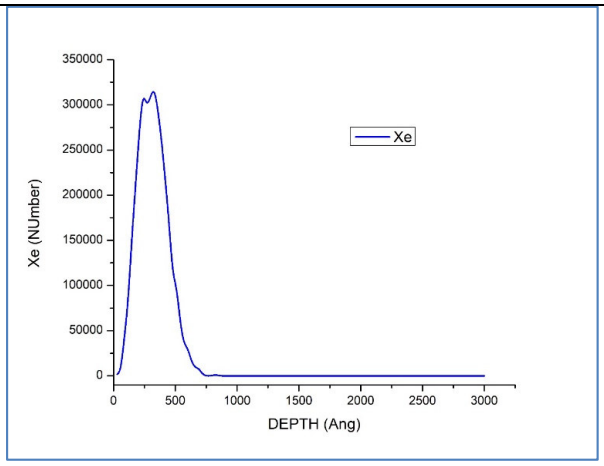

Fig .2. The 2D Plot from the distribution data obtained in table 1.

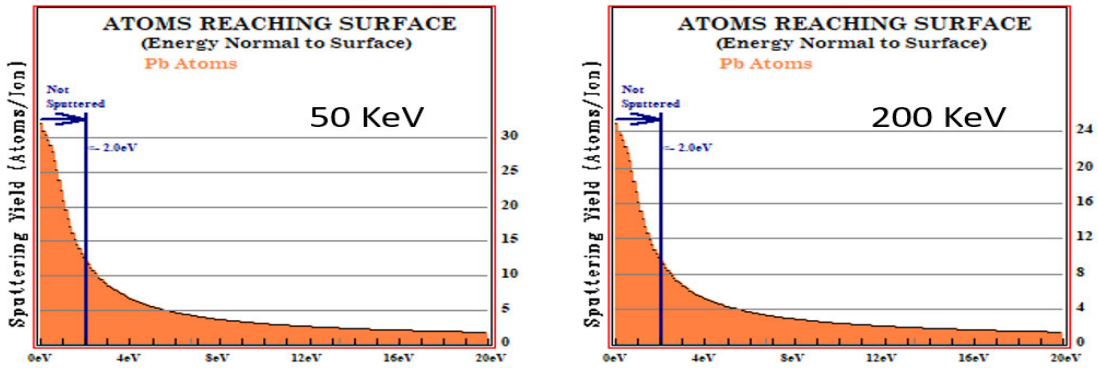

Fig.3.Integral plot of sputtered lead atom yield vs. energy.

Table 1.The Ion distribution data shown in a tabular form

DEPTH Ang	Xe NUmber
30.01	1681.4
60.01	5884.8
90.01	46238
120.01	84069
150.01	158050
180.01	212690
210.01	274910
240.01	315260
270.01	297610
300.01	309380
330.01	319460
360.01	293400
390.01	258930
420.01	215220
450.01	168140
480.01	110130
510.01	100040
540.01	58008
570.01	35309
600.01	31106
630.01	15973
660.01	9247.6
690.01	8406.9

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RESEARCH ARTICLE

Calculation of Potential Curve & Cross Section for Compound Nucleus ^{215}Rn

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ABSTRACT

The driving potential and the fusion cross section have been calculated for the compound nucleus ^{215}Rn. The entrance channel for the formation of the compound nucleus is different and two different reaction mechanism with the same excitation energy. Very interesting result has been found that the fusion cross section is more for ^{16}O based reaction and also the FWHM is wider in the potential profile for the heavy ion compared to light one case.

Keywords: Cross section, potential, NRV, fusion

INTRODUCTION

Starting from long time back people are trying to understand the formation of the compound nucleus (CN) and to study their properties. As the formation and the decay are two independent process suggested by the Bhor called Bhor hypothesis of CN.[1,2] There are many reports which indicated that the Bhorhypothesis is depend on two important condition, the excitation energy (Ex) and the matching of angular momentum. The matching of excitation energy can be done using the control over the incident projectile laboratory energy. The matching of Ex is somewhat can be achieved but the matching of the angular momentum is not easily possible as for different projectile target it is different. It is important to study this entrance channel effect which will form the same compound nucleus with different deformation and excitationenergy[3,4,5].In the present paper we have studied the formation of the ^{215}Rn compound nucleus formed by the two independent channel ^{6}Li+^{209}Bi and the ^{16}O+^{199}Pt. Both having the same input excitation to the compound nucleus but different entrance channel.

CALCULATION AND RESULT

The calculation has been performed using the nuclear reaction video project (NRV)[6]. Here the two differententrance channel has been considered to form the same compound nucleus $^{6}Li+^{209}Bi$ and $^{16}O+^{199}Pt$. The excitation energy has been matched but the angularmomentum matching is difficult. Both the two independent channel leads to the formation of the compound nucleus^{215}Rn. The mass flow for the two systems has been shown the in Fig.1. From Fig.1 one can see that the 3D plot of the potential has been done where the other two axis are the elongation R , and the atomic number for the two system forming the same compound nucleus. One can also see that the upper part of the Fig.1 is for the $^{6}Li+^{209}Bi$ reaction and the lower one is for $^{16}O+^{199}Pt$ reaction. The spread on the atomic number and the potential energy is more for the heavy projectile systemcompared to the light one in addition there is a third peak also present for the $^{6}Li+^{209}Bi$ system. This FWHM will affect the formation cross section as the tunneling probability is completely depending on the height and the width of the potential.

The fusion cross section for the two systems has also calculated using the same NRV code. The calculated fusion cross section has been shwn in Fig.2. The fusion coross section has been calculated using the quantum tunneling method.One can see from the Fig.2 that the cross section is not same even if the same compound nucleus is forming and the same Excitation energy. Another interesting thing is, the fusion cross section is more for the ^{16}O case compared to ^{6}Li.

CONCLUSION

A study has been done for the two system forming the same compound nucleus ^{195}Rn . The same compound has been formed using the two different mode of input. The potential curve has been studied and found that more width in the ^{16}O case compared to the ^{6}Li case. Inaddition the fusion cross has found more for^{16}O induced reaction. This clearly indicates that the even if the two mode of formation is different the same compound there is an effect of entrance channel.

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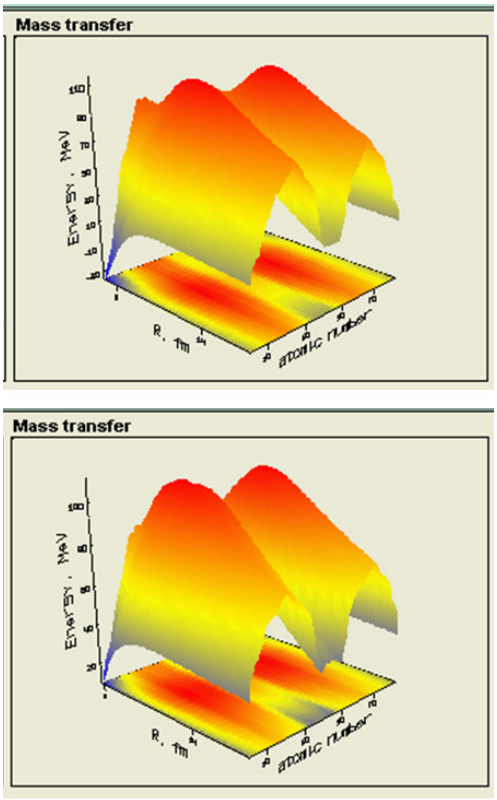

Fig.1 (upper) the potential prediction for the 6Li+209Bi using shell model (lower) Same but for the 16O+^{199}Pt.

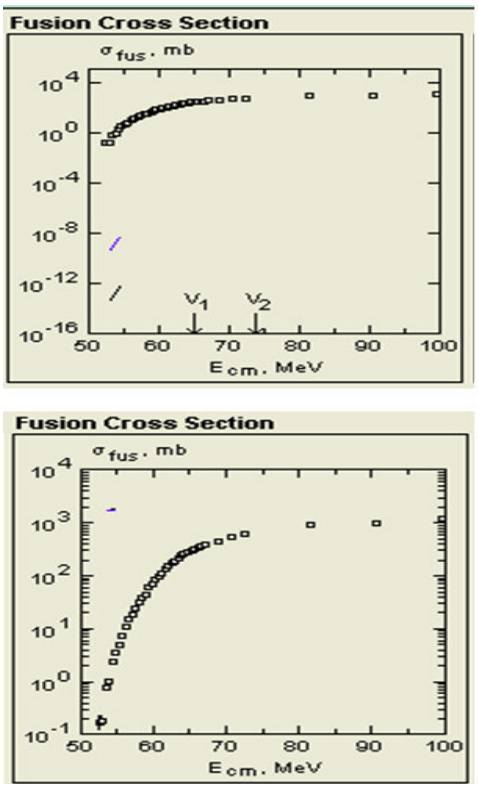

Fig.2 The calculated fusion cross section for the two system using the same two system as indicated in Fig.1.

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RESEARCH ARTICLE

Identification of the N & γ for Scintillator using PSD Method

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ABSTRACT

Neutron detection is one of the important topics since neutrons are closely related with reactors and also they are health hazards. For the detection of neutron people are working hard to synthesize new detection material. Out of many varieties of detection material one of the good material is the scintillators. The big volume Organic/inorganic scintillators are used to detect neutrons. The main problem is the detectors are sensitive to gamma and neutron at the same tie. So one need to filter neutron from gamma. Here an important method has been described to separate these two.

Keywords: PSD, neutron, Scintillator, VME

INTRODUCTION

In the present days peoples are trying to get a clean energy source. The Fusion reaction seems thesolution and many scientists working on fusion project. The fusion reaction direct drive inertialconfinement fusion experiments at the Laboratory for Laser Energetics (LLE) release large amounts ofstored nuclear energy. Most of it is given off as energetic neutrons. The study of neutrons aredemanding subject. The demand for reliable nuclear data , in particular for neutron cross section from 5to 14 MeV, [1] is still interesting to study. More over there is a need for calibrated neutron detectors to be used for reliablecross section measurements. In addition to the above the neutron imaging is another important fieldwhich is evolving which needs more efficient neutron detectors.A Two-body reactions are used to produce a mono energetic neutrons.Therefore in adtion with the existing neutron source the accelerator based source is also important source of neutron.in addition with other reaction like ^{7}Li(p, n)^{7}Be and many others. The reaction has considered and employed for the determination of the efficiency of the neutron detector for a wide range of neutron energies.Inmost of the cases a contamination will possible with intrinsic neutron background.

PROCESS AND RESULTS

The neutron detector has been tested by using the gamma ray source as the detector [2] also sensitive toboth neutron and the gamma ray. A typical data acquisition system with theVME based data acquisition system has been used, we have used the V1720 digitizer. We have developed the algorithm based on the Pulse shape discrimination method (PSD) [3,4]]to distinguish between the neutronand the gamma ray detected by the neutron detector. In addition with the PSD method the sameprogram will also able to analyse the TOF method for the discrimination. To test our PSD analysis program we used the algorithm developed by our group by taking someold data and we found that the n and gamma has been separated out very clearly. Which has been shown in the Fig 1. From the Fig 1 one can see that in both the method (charge comparison andthe TOF) the neutrons and the gamma has been well separated out. We have used the RF source as the deuteron source in our case is gas. To fix the tuningparameter of the RF source, first we have extracted the proton beam by using hydrogen gas in theRF plasma tube and we have extracted the p-beam successfully then transported to the chambernewly installed chamber in the PRIN line with 90% transmission efficiency. The same proton beamhas been used for the elastic scattering angular distribution measurement. After fixing the parameterfor Proton we just replaced the hydrogen gas with deuteron and transported the beam. The RF source has been used to get also pulse beam which will be used for the time of flight (TOF) measurement.

CONCLUSION

A program has been developed for the measurement and identification of the neutron and gamma. The scintillators are sensitive to both neutron and gamma .As the detector is sensitive to both so an algotherim has been developed based on pulse shape discriminazation method has been used to identify the neutron and gamma. A test case has also used for the trilbaisb and found working very nice. The hole thing has been designed for a PRIN project. But it can be used for any other situation where the n,gamma identification will required.

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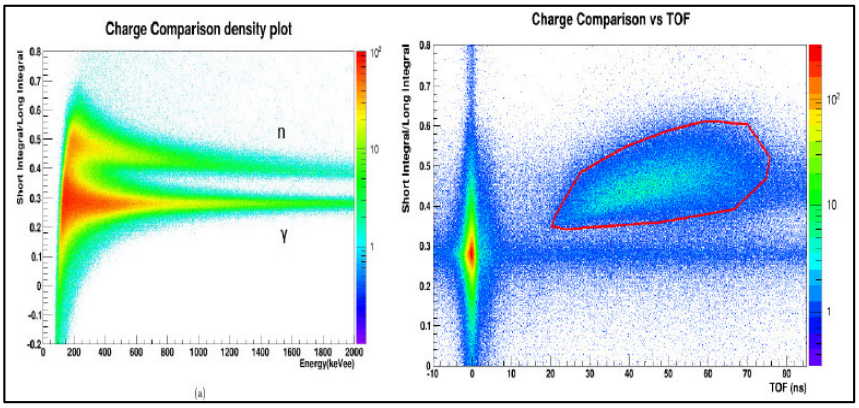

Fig .1. (Left) The Pulse shape discrimination method and (Right) TOF analysis of the previous datausing the newly developed algorithm. Neutron and the gamma are very well separated from both the figure.

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RESEARCH ARTICLE

Simulation of Low Energy Argon-Ion Induced Effects on TiO_2 Nanoparticles using SRIM

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ABSTRACT

Outcome from the irradiation of argon (Ar) ion having the energy of 50 keV on Titanium oxide has been studied using code SRIM (A Monte carlo based calculation). A TiO_2 layer having a thickness of 300 nmwas taken as the target and the simulation results were analyzed. The different outcomes (ion distributions, recoil distributions, etc) has been presented. The detail calculation and behavior of TiO_2 after collision with argonhas been discussed.

Keywords: Monte-Carlo Simulation, SRIM, Titanium oxide nanoparticles, Ion induced defects.

INTRODUCTION

TiO_2 nanoparticles have found wide application in several fields. These are used in food and personal care products[1], catalysts for water pollutant removal[2]as well as heterogenous photocatalyst[3] to name a few. Thus it is important to study their various properties. Here we have simulated an ion irradiation experiment on a layer of TiO_2.

RESULTS AND DISCUSSION

Figure 1 shows the ion track represented by a red dot.A vacancy is created when the ion hits titanium oxide atoms from the target. These holesare due to recoiling TiO_2 atoms and represented by the blue dots. Incident argon ion loses a significant amount of energy[4]after the impact of on TiO_2. If the mass of target atom is quite different than incident ion mass, very low energy is being transferred. With each binary collision, one vacancy is made causing a blue cascade. Hence, these modifications[5]are the consequence of cascade collision and the recoiled target atoms.

Ion Distribution

Distribution of argon ions implantation in the TiO_2 target is shown in Figure 2 where the Y-axis represents concentration of ions in Atoms/volume (incm^3) or Atoms/area (in cm^2) The impurity concentration (atoms/vol) vs target depth during implantationcan be estimated from the product of fluence and this arbitrary concentration unit in the Y-axis. For 50 keV energy the Ion Range is 605 A, Straggle is 243 A, Skewness is 0.1721 and Kurtosis is 2.7422. For an example, for a fluence of 1 X 10^{17}, we can obtain the concentration as the product of data in Y axis and the fluence at the average penetration depth. Here, we obtained the amount as 19 X 10^{21}.

Recoil Distribution

2D Ion/Recoil Distribution plot for the TiO_2 is shown in Figure 3. The plot indicates the TiO_2 atoms that are all knocked outfrom their lattice positions, thus creating voids. The same ion range value is obtained from recoil distribution as shown earlier in the ion distribution plot.

Energy to Recoil

This plot shows how the target damage is being created. Energy from ions or energy absorbed by Titanium and Oxygen atoms are represented in figure 4. Simulation for 'Energy to recoil'claims that the Ti atoms absorbed 68 eV/ion/A(represented by orange colour) and oxygen atoms absorbed 37 eV/ion (represented by black colour).

Ionization

In figure 5collision events of 50 keV argon ion irradiation has been shown. For low energy the predicted range is small which is expected. The width of the distribution is narrower for low energy as compared to high energy. Hence, there is a higher possibility to obtain narrow energy distribution in case of low energy sputtering compared to high energy sputtering.

CONCLUSION

Here, the Monte-Carlo simulation for low energy argon ion (50 keV) on titanium oxidehas been reported. Data for the ion and recoil distribution, energy to recoils and ionization have been obtained from the simulation study, which will aid to the characterization of experimental data. As irradiation experiments are expensive; a proper simulation is helpful to know the irradiation-induced effects prior to the actual experiment. It will reduce the frequency of the experiments thus saving time and expenditure.

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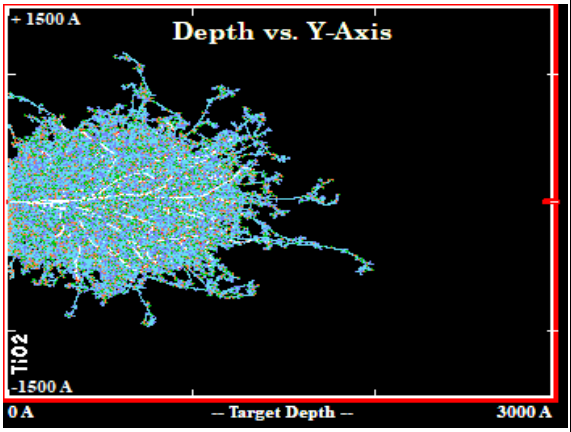

Figure 1.The trajectory of incident Ar ion having 50 keV hitting the target atoms vertically.

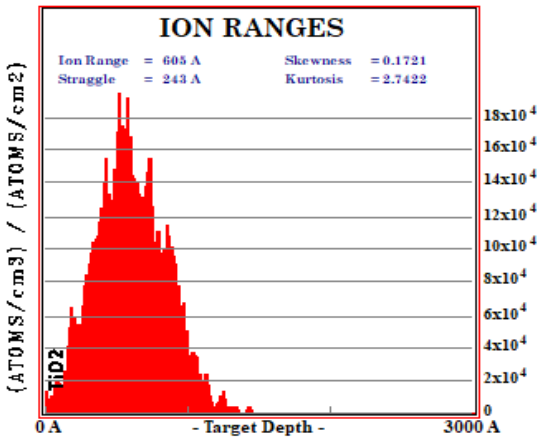

Figure 2. Ion Distribution plot in 2D for 50 keV

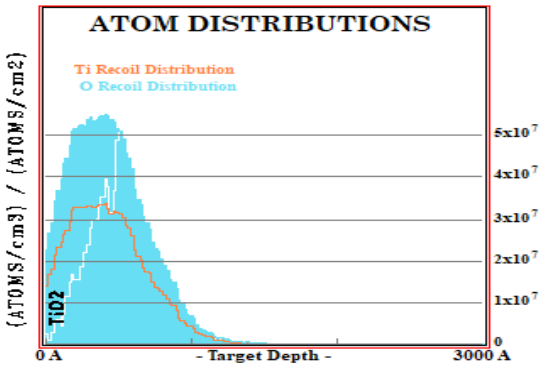

Figure 3.Ion/Recoil Distribution for 50 keV energy in 2D

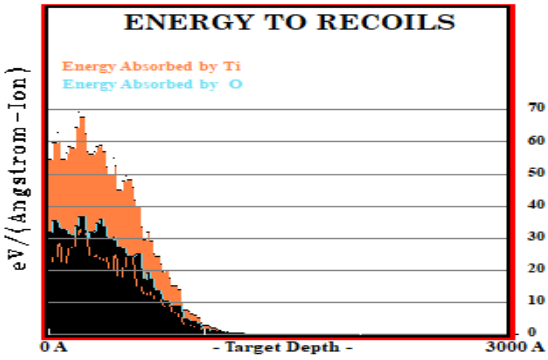

Figure 4.2D Energy to Recoils for 50 keV energy

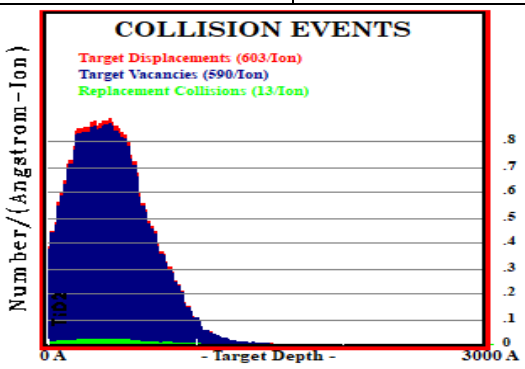

Figure 5.2D Ionization for 50 keV energy

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RESEARCH ARTICLE

In silico Analysis of12αd-Glucose and Dichloro-Ethylene Compatibility in a Blend

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ABSTRACT

The mixture of a substance with another substance results in blend. The compatibility of 12αd-Glucose and Dichloro-Ethylene were studied to form a mixable blend using Biovia Materials Studio. The miscibility of the two substances was demonstrated on free energy of mixing, chi parameter, phase diagram and mixing energy. The results stipulated that the pair can become congruent at both low and high temperature. Phase diagram specify that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were reviewed based on bulk modulus, shear modulus, Young's modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of dichloro-ethylene. The composition of the blend was examined with respect to heat capacity, thermal conductivity and dielectric constant which are permeability properties. The molar volume and density decreased with increase in dichloro-ethylene fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of dichloro-ethylene. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend, In Silico, 12αd-Glucose, Dichloro-Ethylene

INTRODUCTION

Blends or composites are formed with mixing of more than one substance where substances do retain their identity in the mixture. It is obtained that verifying any single parameter or quality in any component is not an easy method. So by combining more than one component it is easier to find the property. Examining of any single property is time taking and a complex process. The blending procedure helps in overcoming the property extraction time. By this method blending procedure helps us in generation of new polymer in an advanced way. Polymer blends can be

achieved by two or more polymers, or fibers and polymer, or particles and polymer. Nano material modified polymers paved the way to multifunctional materials. Polymers combined with carbon based (graphene, carbon nano-tube) nano-materials have accentuated. Biodegradable polymers- natural fiber composites have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials. There we have found that the inorganic additives in polypropylene; that can enhance flame retardancy without raising theweight. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method and this technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio) has been used to identify compatible pairs. The 1st polymer taken is the 12αd-Glucosepolymer of carbohydrate.This polymer is also called as alpha-dextrose. It belongs to the group of organic compounds known as hexoses. These are monosaccharides in which the sugar unit is a six-carbon containing moiety.12αd-Glucoseis a pure weak basic compound. 12αd-Glucoseexists in all living species, ranging from human to bacteria. In yeast, 12αd-Glucoseis involved in the metabolic pathway known asstarch. The 2nd polymer that is chosen is Dichloro-ethylene. It is a polymer under halide group. It is an organo-chloride with formula $C_2H_2Cl_2$.It is highly flammable, colorless liquid with a sharp, harsh odour.It can exist as either of two geometric isomers, cis-1,2-dichloroethylene or trans-1,2-dichloroethylene, but is usually used as a mixture of the two. It is also known as dichloroethene. This polymer is used as base element in the blending procedure in this combination. These polymers are moderately soluble in water. These polymers have limited industrial use. It has a boiling point of 55^0 C. We have blended above two polymers to extrct the properties individually.

MATERIALS AND METHODS

Software Used

Materials studio module of Biovia software (DassaultSystemesof France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology

12αd-Glucoseanddichloro-ethylene were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. 12αd-Glucosewas used as the base and dichloro-ethylene was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of 12αd-Glucoseand dichloro-ethylene were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of ichloro-ethylene on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of 12αd-Glucose and dichloro-ethylene as potential components of a blend was analyzed using Biovia Materials Studio.In this work the use of 12αd-Glucose and dichloro-ethylene potential components of a

composite was analyzed using Biovia Materials Studio. This simulation studio contains Synthia which uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Additive group contribution method were used for a long time to progonostigate the properties of polymers and small molecules. These methods are rapid and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the major drawbacks of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be evaluated.

To prevent this limitation, the method presented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

ENERGY PARAMETES

Free Energy of Mixing: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that 3

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

Where $\Delta G_m = Gibb's\ free\ energy\ of\ mixing$

$\Delta H_m = Enthalpy\ of\ mixing$

$\Delta S_m = Entropy\ of\ mixing$

$T = Absolute\ Temperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the following condition satisfy;

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (up to 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between 12αd-Glucose and dichloro-ethylene with negative value of mixing energy,which may lead to form a particular shape with significantly high effort.

Chi Parameter

The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that

the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

Phase Diagram

The density of binary mixtures can be seen by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:
a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).
b. Fragmented metastable regions existed between binodals and spinodals, and
c. The two-phase separated regions of immiscibility are bordered by the spinodals.
The binodals separated miscible and metastable region, while the spinodals separated the metastable and two-phase region.

When the system enters from single-phase region to the metastable region, the phase difference usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing Energy

A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature.The temperature is vary from 50K to500K for the varying of mixing energy. It is very much possible to mix the two components at any feasible temperature with least mixing energy value.

MECHANICAL PROPERTIES

Bulk modulus

Bulk modulus **is** the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of dichloro-ethylene.

Shear modulus

It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6shows that the shear modulus of the composite increases linearly with increase in mass fraction of dichloro-ethylene.

Young's modulus

It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7shows that the Young's modulus of the composite increases linearly with increase in mass fraction of dichloro-ethylene.

Poisson ratio

It is the ratio of lateral strain to longitudinal strain. Figure 8shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of dichloro-ethylene.

Brittle fracture stress

Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs.Figure 9shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of dichloro-ethylene.

THERMAL PROPERTIES

Heat capacity

It is the amount of heatrequired to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of dichloro-ethylene.

Thermal conductivity

It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of dichloro-ethylene.

Dielectric constant

It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of dichloro-ethylene.

INTENSIVE PROPERTIES

Molar volume

It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with increase in mass fraction of dichloro-ethylene.

Density

Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14shows that the density of the composite decreases linearly with increase in mass fraction of dichloro-ethylene.

Permeability of gas

Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the membrane.

Figure 15 shows that the permeability of oxygen through the composite decreases with increase in mass fraction of dichloro-ethylene. Figure 16 shows that the permeability of nitrogen through the composite decreases with increase in mass fraction of dichloro-ethylene. Figure 17 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of dichloro-ethylene. Thus, the results indicated that an increase in dichloro-ethylene fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of poly12Ød-Glucose and Polydichloro-ethylene to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of dichloro-ethylene.The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of dichloro-ethylene. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in dichloro-ethylene fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases decreased with increase in mass fraction of dichloro-ethylene. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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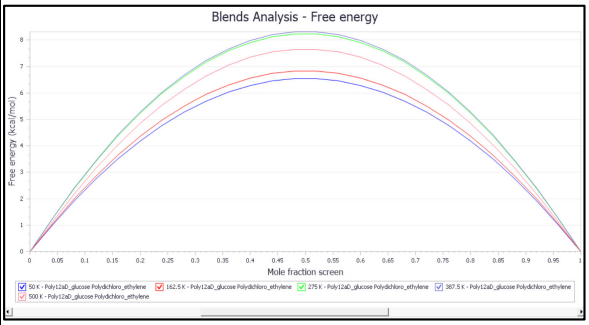

Figure 1. Free energy change with mole fraction of polyethyl12Ød-Glucose Polydichloro-ethylene at differenttemperatures

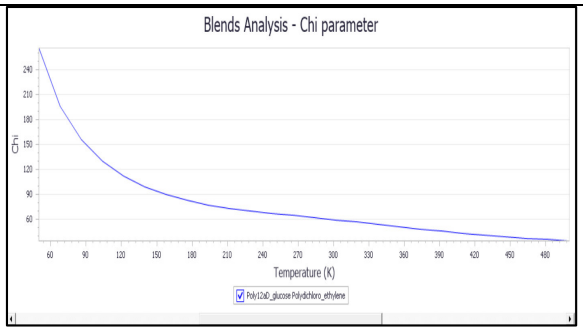

Figure 2. Change in χ (chi) value with temperature

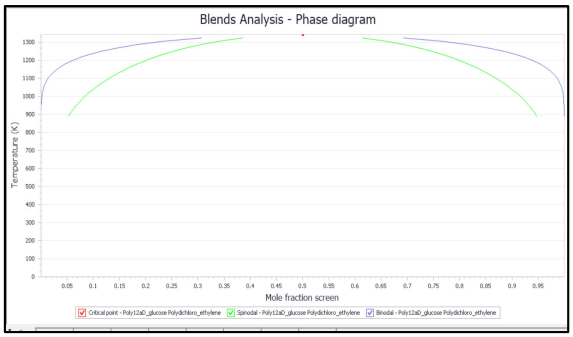

Figure 3 .Phase diagram

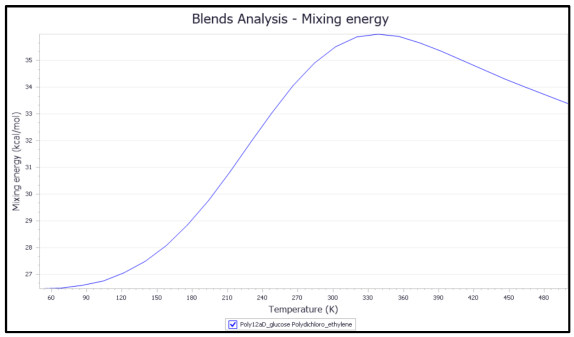

Figure 4Mixing energy

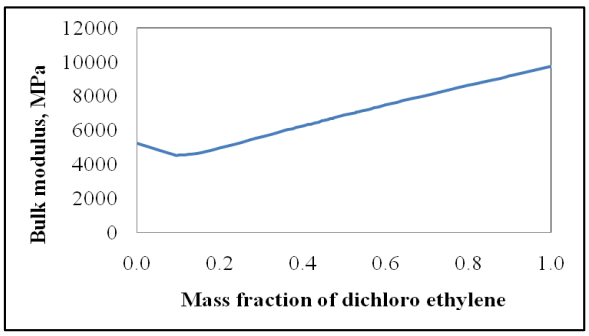

Figure 5 Change in bulk modulus with mass fraction of dichloro-ethylene

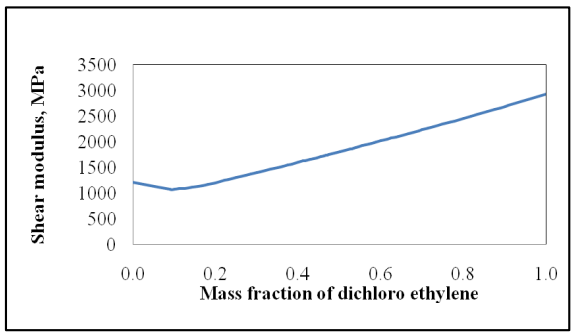

Figure 6 Change in shear modulus with mass fraction of dichloro-ethylene

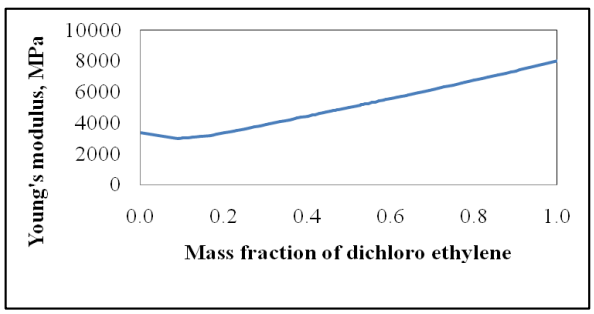

Figure 7 Change in Young's modulus with mass fraction of dichloro-ethylene

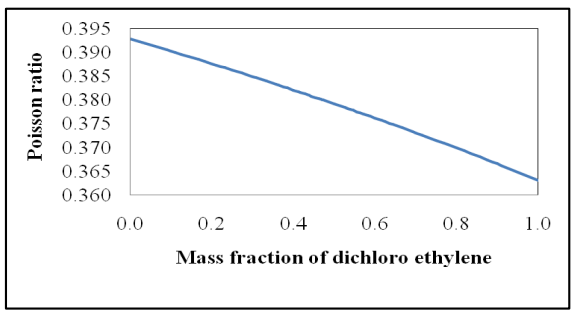

Figure 8 Change in Poisson modulus with mass fraction of dichloro-ethylene

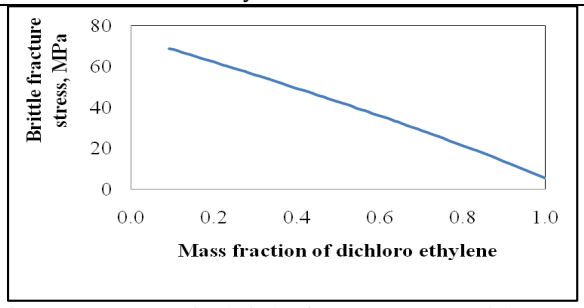

Figure 9 Change in brittle fracture stress with mass fraction of dichloro-ethylene

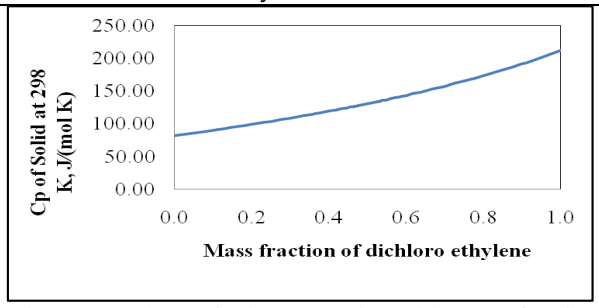

Figure 10 Change in heat capacity with mass fraction of dichloro-ethylene

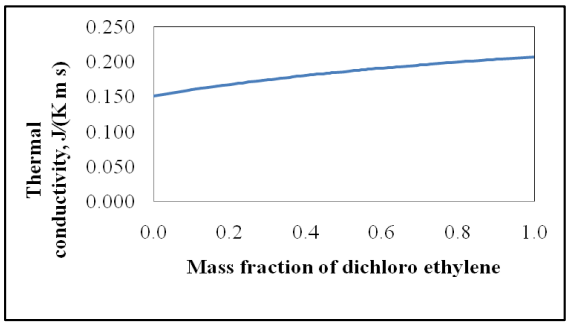

Figure 11 Change in thermal conductivity with mass fraction of dichloro-ethylene

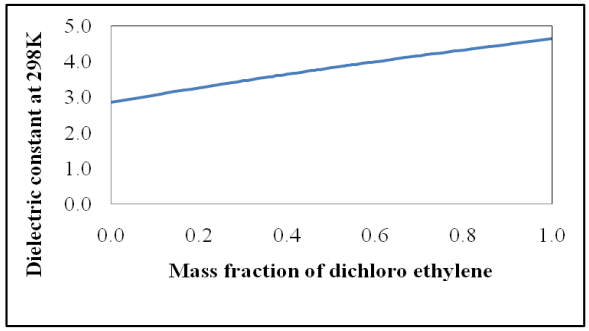

Figure 12Change in dielectric constant with mass fraction of dichloro-ethylene

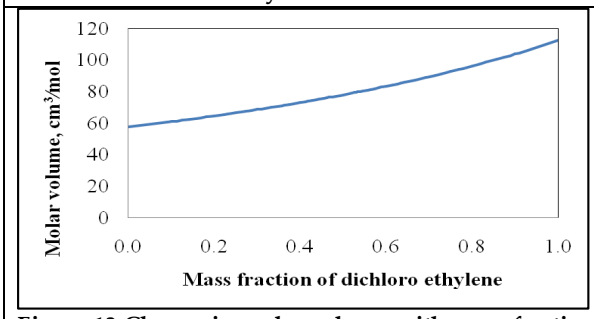

Figure 13 Change in molar volume with mass fraction of dichloro-ethylene

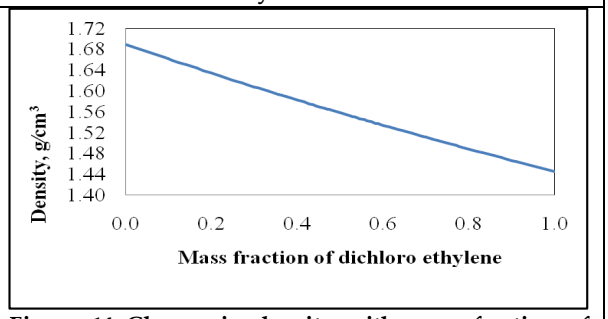

Figure 14 Change in density with mass fraction of dichloro-ethylene

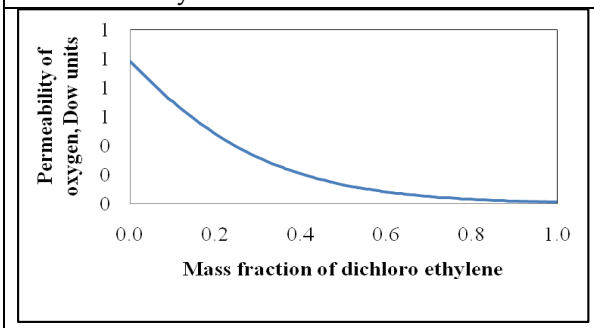

Figure 15 Change in permeability of oxygen with mass fraction of dichloro-ethylene

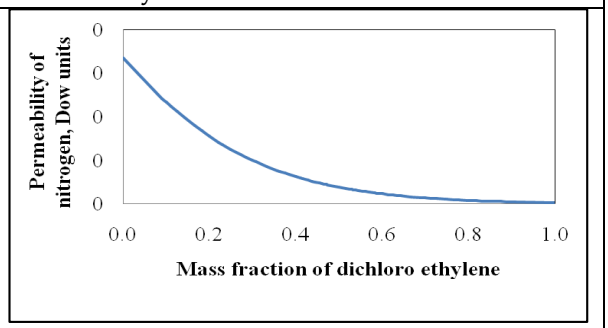

Figure 16 Change in permeability of nitrogen with mass fraction of dichloro-ethylene

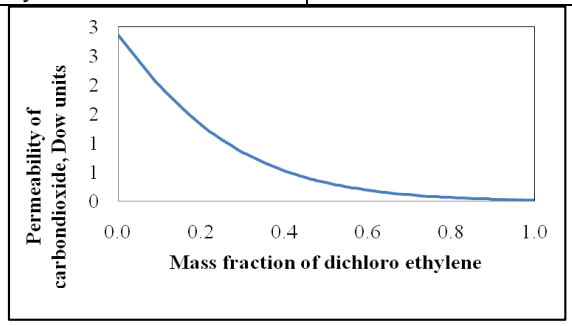

Figure 17. Change in permeability of carbon dioxide with mass fraction of dichloro-ethylene

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RESEARCH ARTICLE

In silico Analysis of Polyvinyl Alcohol and Polyacrylonitrile Compatibility in a Blend

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ABSTRACT

A blend is especially to combine or associate of more than one constituents or the line of demarcation cannot be distinguished. The desired property of a blend is its homogeneity. The selection of polyvinyl alcohol and polyacrylonitrile to form a miscible blend was explored using "Biovia Materials Studio". The compatibility of the two components was studied based on the free energy of mixing, chi parameter, phase diagram, and mixing energy. The results indicated that the pair can become compatible only at high temperatures. Phase diagram indicated that a single phase can be obtained above 575 K which was the critical temperature. The coordination number was found to be 5.82 +/- 0.04. The highest number of configurations concerning energy level was found to be -1.6 kcal/mol. The phase separation might lead to its use as porous material to be used as adsorbent. This study will help determine pairs without performing laboratory experiments saving materials, money, and time.

Keywords: Blend, in silico, polyvinyl alcohol, polyacrylonitrile

INTRODUCTION

Blends or composites are materials containing more than one component. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. The development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nanomaterial modified polymers paved the way for multifunctional materials. Polymers coupled with carbon-based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fireproof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of

lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for the construction of bridges, light rail transit, mining and tunneling, retaining walls, and other waterside buildings. All the above-mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time, and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs. Polyvinyl alcohol (PVA) polymer is one of the promising material due to its easy film formation, adhesiveness, high dielectric strength, and its properties can be controlled by dopant concentrations in different ratios [8, 9]. The PVA has film-forming ability which is widely used in the packaging industry to form strong polymeric films because of their high mechanical strength, easy processability, and environmental stability [10]. The other beauty of PVA is biocompatible, non-toxic, semi-crystalline, hydrophilic, and easily soluble in water [11]. Polyacrylonitrile presents good hydrophobicity, good mechanical property, and has been widely used as film materials [12]. Polyacrylonitrile melts above 300 °C but it degrades before melting [13].

METHODOLOGY AND MATERIALS

SOFTWARE USED: Materials studio module of "Biovia software (Dassault Systemes of France)" was used for analysis. The software builds in standard algorithms and machine learning techniques and to analysis different stage of interaction.

METHODOLOGY: Polyvinyl alcohol and polyacrylonitrile were prepared using the build menu of Materials Studio. The structure of the components was optimized using the components that were used in the blends->calculation menu of Materials studio. Polyvinyl alcohol was used as the base and polyacrylonitrile was used as a screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed.

RESULTS AND DISCUSSION

In this work the use of polyvinyl alcohol acid and polyacrylonitrile as potential components of a blend was analyzed using Biovia Materials Studio.

FREE ENERGY OF MIXING: A blend is said to be miscible if it is homogeneous. The value of free energy is negative of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m - \Delta H_m - T\Delta S_m \quad (1)$$

where ΔG_m = *Gibb's free energy of mixing*

ΔH_m = *Entalpy of mixing*

ΔS_m = *Entropy of mixing*

T = *Absolute temperature*

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpy contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always positive for the temperatures studied. The free energy decreases with an increase in temperature as evident from Eq. 1. The results indicated that the blend will not lead to a homogeneous mixture for the temperature range studied (50 to 500 K). The trend suggested that there might be a possibility of a miscible blend at a very high temperature.

CHI PARAMETER

The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers indicates poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the χ value is high for the temperature range studied (60 to 500 K) indicating demixing. The χ value changes periodically with an increase in temperature. Thus at high temperature there is a possibility to form a miscible blend. The result is in agreement with the free energy of mixing for the blend.

COORDINATION NUMBER

The coordination number Z_{ij} is the number of molecules of type *j* that can be packed around a single molecule of type *i*. The coordination number was calculated for *each* of the possible molecular pairs involved in molecular simulations. The "Blends" module of Materials studio differed from the Flory-Huggins model and used an off-lattice calculation. It assumed that molecules that are not arranged on a regular lattice is expected in the original Flory-Huggins theory. The coordination number is significant only when the components of the binary blend have similar volumes or surface areas. It is difficult to apply the pairs method in defining a coordination number for a binary system in which the components are not similar in size. In this study the coordination number was found to be 5.82 +/- 0.04.

PHASE DIAGRAM

The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. Here we were described three regions of different degree of miscibility:

a. The single-phase miscible region existed above the critical temperature of around 575 K. This value supported the fact that a single-phase blend can be formed at a high temperature (higher than 575 K).

b. Fragmented metastable regions existed between binodal and spinodals, and

c. The two-phase separated regions of immiscibility are bordered by the spinodals.

The binodal separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region. When the system enters from a single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase-separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

ENERGY DISTRIBUTION FOR BLEND

The generation of different orientations using the pairs method may lead to configurations of varying energy levels. Figure 4 shows the plot of frequency (P(E)) against energy levels. It shows that the distribution is somewhat asymmetrical and there is a long, low-energy tail. The number of configurations with energy higher than the peak value decreased significantly. The maximum frequency was observed for the energy level of around -1.6 kcal/mol.

MIXING ENERGY

A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 5 shows that the mixing energy for the system was high for the temperature range studied. The graph indicated that an increase in temperature helped reduce the mixing energy. This result supported the previous observations. The formation of a nonhomogeneous blend with polyvinyl alcohol as a base might help the formation of blend with higher porosity such as hydrogel. This might have an application as adsorbent.

CONCLUSIONS

The possibility of the use of polyvinyl alcohol and polyacrylonitrile to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on the free energy of mixing, chi parameter, phase diagram, and mixing energy. The results indicated that the pair can become compatible at high temperatures. Phase diagram indicated that a single phase can be obtained above 575 K. The coordination number was found to be 5.82 +/- 0.04. The maximum number of configurations concerning the energy level was found to be -1.6 kcal/mol. The phase separation might make it a porous material to be used as an adsorbent. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money, and time.

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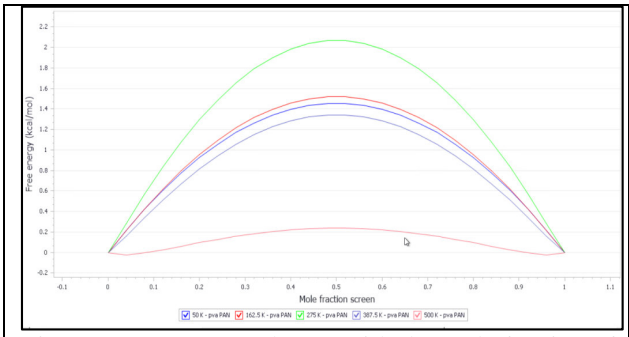

Figure 1. Free energy change with the mole fraction of polyacrylonitrile at different temperatures

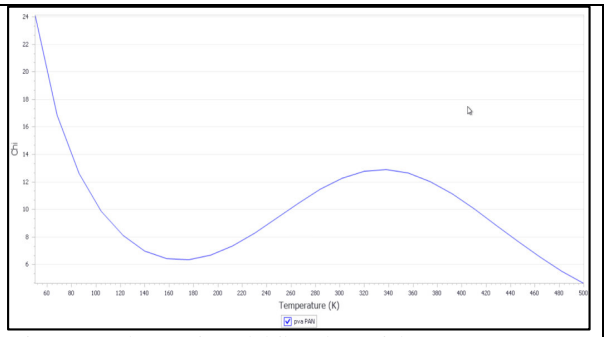

Figure 2. Change in χ (chi) value with temperature

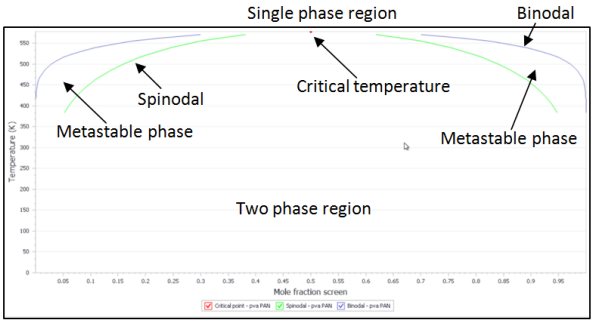

Figure 3. Phase diagram

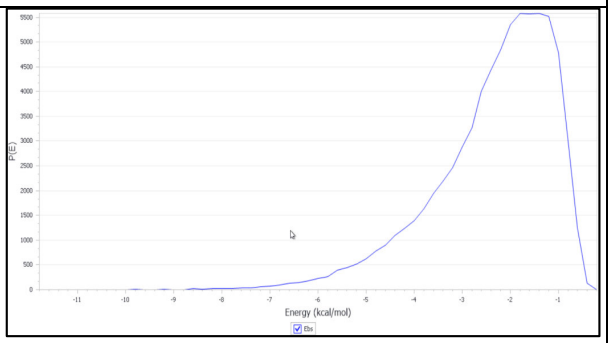

Figure 4. Energy distribution

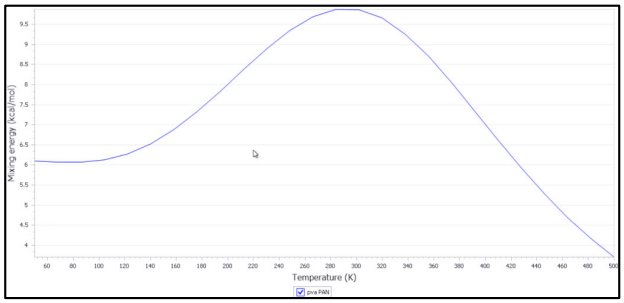

Figure 5. Mixing energy

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RESEARCH ARTICLE

In silico Analysis of Gas Permeability Properties of Polyvinyl Alcohol and Polyacrylonitrile Composite

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ABSTRACT

A blend is a combination of more than one component or constituents. The desired property of a blend is its homogeneity. The composition of polyvinyl alcohol and polyacrylonitrile to provide desired mechanical properties of the blend was explored using Biovia Material Studio. The composition of the blend was analyzed concerning permeability properties. The permeability properties of the composite were studied based on the permeability of oxygen, nitrogen, and carbon dioxide. The results showed that the permeability for all the gases, molar volume decreased and density increased with an increase in mass fraction of polyvinyl alcohol. This study will help determine components of a blend without performing laboratory experiments saving materials, money, and time.

Keywords: polyvinyl alcohol, polyacrylonitrile, *in silico*, permeability

INTRODUCTION

Blends or composites are materials containing more than one component. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. The development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nanomaterial modified polymers paved the way for multifunctional materials. Polymers coupled with carbon-based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fireproof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio

and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for the construction of bridges, light rail transit, mining and tunneling, retaining walls, and other waterside buildings. All the above-mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time, and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs. Polyvinyl alcohol (PVA) polymer is one of the promising material due to its easy film formation, adhesiveness, high dielectric strength, and its properties can be controlled by dopant concentrations in different ratios [8, 9]. The PVA has film-forming ability which is widely used in the packaging industry to form strong polymeric films because of their high mechanical strength, easy processability, and environmental stability [10]. The other beauty of PVA is biocompatible, non-toxic, semi-crystalline, hydrophilic, and easily soluble in water [11]. Polyacrylonitrile presents good hydrophobicity, good mechanical property, and has been widely used as film materials [12]. Polyacrylonitrile melts above 300 °C but it degrades before melting [13].

METHODOLOGY AND MATERIALS

SOFTWARE USED: Materials studio module of "Biovia software (Dassault Systems of France)" was used for analysis. The software builds in standard algorithms and machine learning techniques and to analysis different stage of interaction.

METHODOLOGY: The structures of polyvinyl alcohol and polyacrylonitrile were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of the weight fraction of polyvinyl alcohol on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work, the use of polyvinyl alcohol and polyacrylonitrile use as main components of a composite was analyzed using "Biovia Materials Studio". "BIOVIA Materials Studio" Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. For many years were used Group additive methods to predict the properties of small molecules as well as small polymers. The principal drawback of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome the limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: silicon, sulfur, fluorine, chlorine, bromine, carbon, hydrogen, nitrogen, oxygen.

MOLAR VOLUME: Molar volume define as the volume occupied by one mole of a substance. Figure 1 shows that the molar volume of the composite decreases with an increase in mass fraction of polyvinyl alcohol.

DENSITY: Increase in density indicates a decrease in porosity. A higher porosity will enhance the surface area making it suitable for absorption/adsorption applications. Figure 2 shows that the density of the composite increases with an increase in mass fraction of polyvinyl alcohol.

PERMEABILITY OF GAS: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates a longer time lag for the gas to pass through the membrane. Figure 3 shows that the permeability of oxygen through the composite decreases with an increase in mass fraction of polyvinyl alcohol.

Figure 4 shows that the permeability of nitrogen through the composite decreases with an increase in mass fraction of polyvinyl alcohol. Figure 5 shows that the permeability of carbon dioxide through the composite decreases with an increase in mass fraction of polyvinyl alcohol.

CONCLUSIONS

The possibility of the use of polyvinyl alcohol acid and polyethersulfone to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed concerning permeability properties. The permeability properties of the composite were studied based on the permeability of oxygen, nitrogen, and carbon dioxide. The results showed that the permeability for all the gases, molar volume decreased and density increased with an increase in mass fraction of polyvinyl alcohol. Usually components for blends are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money, and time.

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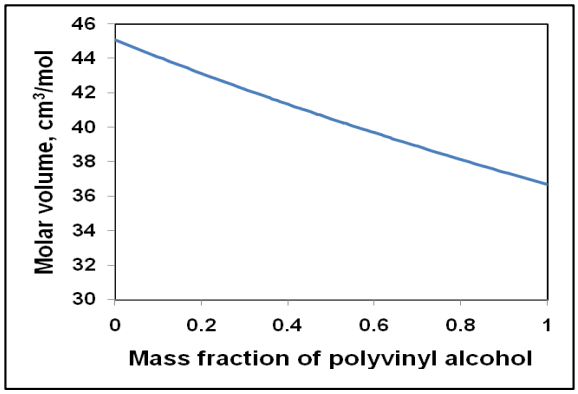

Figure1. Change in molar volume with the mass fraction of polyvinyl alcohol.

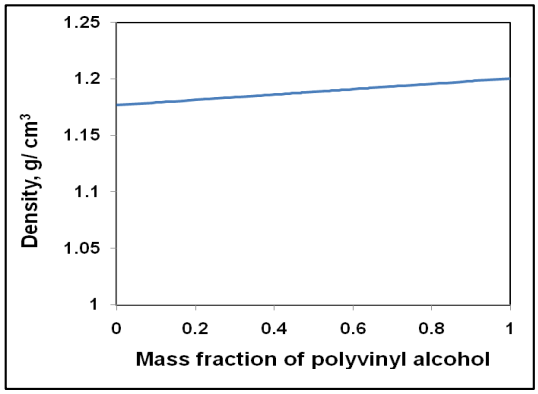

Figure 2. Change in density with the mass fraction of polyvinyl alcohol.

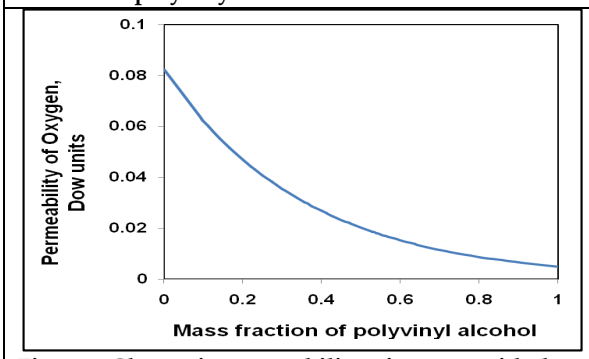

Figure3. Change in permeability of oxygen with the mass fraction of polyvinyl alcohol

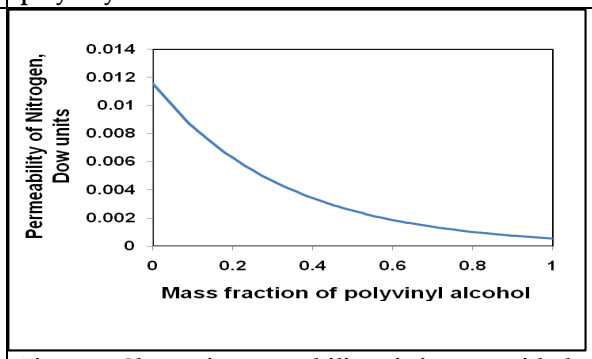

Figure 4. Change in permeability of nitrogen with the mass fraction of polyvinyl alcohol.

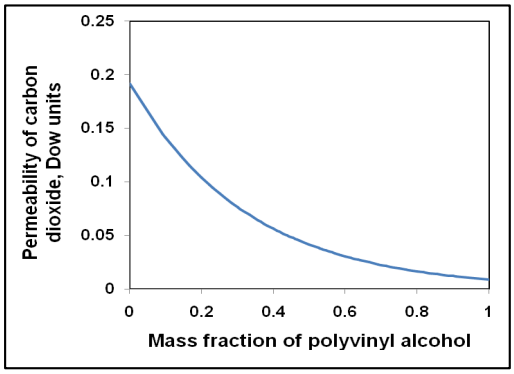

Figure5. Change in permeability of carbon dioxide with the mass fraction of polyvinyl alcohol.

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RESEARCH ARTICLE

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ABSTRACT

A blend is a combination of more than one component or constituents. The desired property of a blend is its homogeneity. The composition of polyvinyl alcohol acid and polyacrylonitrile to provide desired mechanical properties of the blend was explored using Biovia Material Studio. The mechanical properties of the composite were studied based on Young's modulus, Shear modulus, Bulk modulus, Poisson ratio, and Brittle stress fracture. The obtained values indicated that the value of all the properties increased with an increase in mass fraction of polyvinyl alcohol. This study will help determine pairs without performing laboratory experiments saving materials, money, and time.

Keywords: mechanical, in silico, polyvinyl alcohol, polyacrylonitrile

INTRODUCTION

Blends or composites are materials containing more than one component. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. The development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nanomaterial modified polymers paved the way for multifunctional materials. Polymers coupled with carbon-based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fireproof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to resistance and weight ratio to corrosion. So glass fiber reinforced polymers, latex polymer cementitious composites [6] were

developed for the construction of bridges, light rail transit, mining and tunneling, retaining walls, and other waterside buildings. All the above-mentioned examples relied on laboratory experiments. Usually, blends are prepared by trial and error method. Thus it involves wastage of materials, time, and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. Polyvinyl alcohol (PVA) polymer is one of the promising material due to its easy film formation, adhesiveness, high dielectric strength, and its properties can be controlled by dopant concentrations in different ratios [8, 9]. The PVA has film-forming ability which is widely used in the packaging industry to form strong polymeric films because of their high mechanical strength, easy processability, and environmental stability [10]. The other beauty of PVA is biocompatible, non-toxic, semi-crystalline, hydrophilic, and easily soluble in water [11]. Polyacrylonitrile presents good hydrophobicity, good mechanical property, and has been widely used as film materials [12]. Polyacrylonitrile melts above 300 °C but it degrades before melting [13].

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BULK MODULUS: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 1 shows that the bulk modulus of the composites hikes with a hike in a mass fraction of polyvinyl alcohol.

SHEAR MODULUS: Shear modulus is defined as the ratio between the shear stress to shear strain of the particles. It shows the response of the composite to shear deformation. Figure 2 shows that the shear modulus of the composites hikes with a hike in a mass fraction of polyvinyl alcohol.

YOUNG'S MODULUS: It is defined as the ratio between the stress and strain of the particles. It compares the relative stiffness of the composite. Figure 3 shows that the Young's modulus of the composites hikes with a hike in mass fraction of polyvinyl alcohol.

POISSON RATIO: It is the ratio between the lateral strain to longitudinal strain of the particles. Figure 4 shows that the Poisson ratio of the composite hikes with a hike in a mass fraction of polyvinyl alcohol.

BRITTLE FRACTURE STRESS: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 5 shows that the brittle fracture stress of the composite hikes with a hike in a mass fraction of polyvinyl alcohol.

CONCLUSIONS

The possibility of the use of polyvinyl alcohol acid and polyethersulfone to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed concerning permeability properties. The permeability properties of the composite were studied based on the permeability of oxygen, nitrogen, and carbon dioxide. The values indicated that the value of every property increased along with an increase in mass fraction of polyvinyl alcohol. Usually, components for blends are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money, and time.

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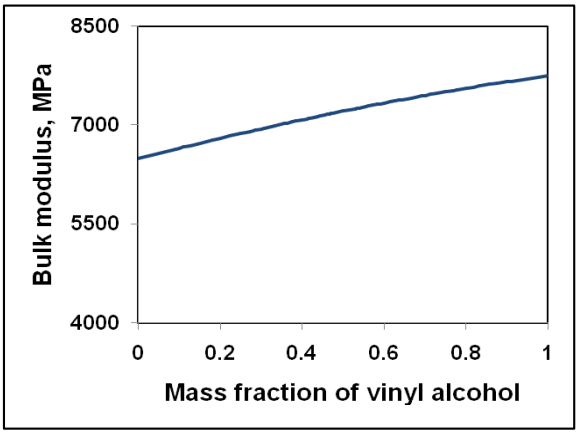

Figure1. Change in bulk modulus with the mass fraction of vinyl alcohol.

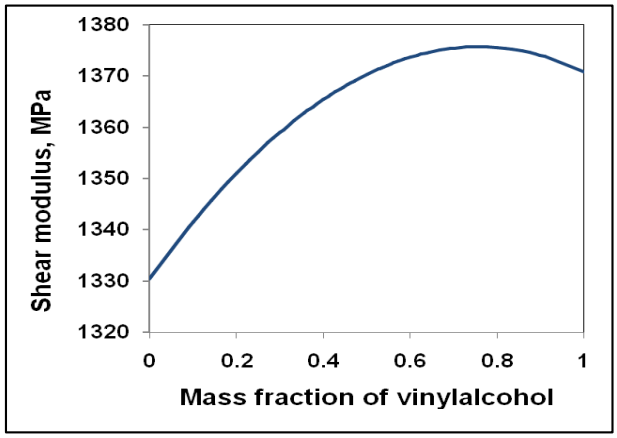

Figure2. Change in shear modulus with the mass fraction of vinyl alcohol

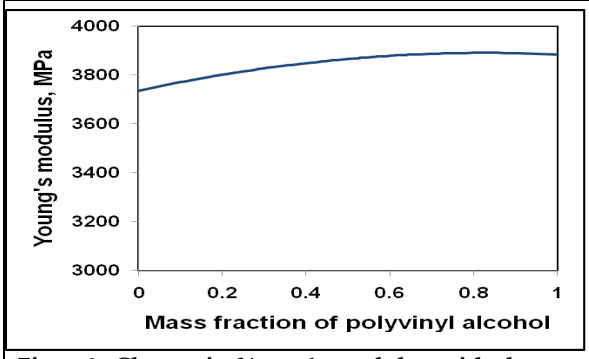

Figure3. Change in Young's modulus with the mass fraction of vinyl alcoho

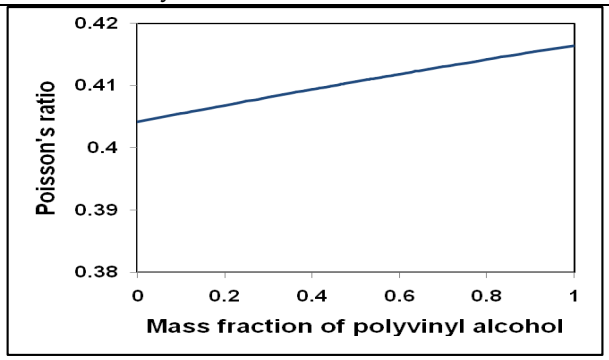

Figure 4. Change in Poisson modulus with the mass fraction of vinyl alcohol

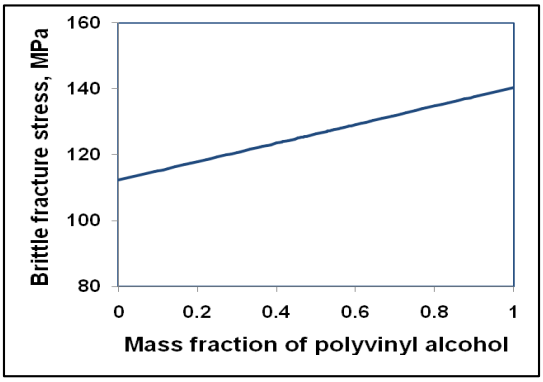

Figure 5. Change in brittle fracture with the mass fraction of vinyl alcohol

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RESEARCH ARTICLE

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of the blend was analyzed concerning heat capacity, dielectric constant and thermal conductivity. The outputs show that heat capacity decreased but thermal conductivity and dielectric constant hikes with a hike in a mass fraction of polyvinyl alcohol. This study will help determine pairs without performing laboratory experiments saving materials, money, and time.

Keywords: thermal, dielectric, polyvinyl alcohol, in silico, polyacrylonitrile

INTRODUCTION

Blends or composites are materials containing more than one component. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. The development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nanomaterial modified polymers paved the way for multifunctional materials. Polymers coupled with carbon-based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fireproof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for the construction of bridges, light rail transit, mining and tunneling, retaining walls, and other waterside buildings. All the above-mentioned examples relied on laboratory experiments.

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METHODOLOGY: The structures of polyvinyl alcohol and polyacrylonitrile were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of the weight fraction of polyvinyl alcohol on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work, the use of polyvinyl alcohol and polyacrylonitrile use as main components of a composite was analyzed using "Biovia Materials Studio". "BIOVIA Materials Studio" Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. For many years were used Group additive methods to predict the properties of small molecules as well as small polymers. The principal drawback of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome the limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: silicon, sulfur, fluorine, chlorine, bromine, carbon, hydrogen, nitrogen, oxygen.

HEAT CAPACITY: Heat capacity is the amount of heat energy required to raise the temperature of one unit of a substance through 1°C. Figure 1 shows the heat capacity (Cp) of the composite decreases with an increase in mass fraction of polyvinyl alcohol.

THERMAL CONDUCTIVITY: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 2 indicate that the thermal conductivity of the composite increases with an increase in mass fraction of polyvinyl alcohol.

DIELECTRIC CONSTANT: Dielectric constant define as the ratio between electric permeability of the material to the electric permeability of free space or air. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 3 shows that the dielectric constant of the composite increases with an increase in the mass fraction of polyvinyl alcohol.

CONCLUSIONS

The possibility of the use of polyvinyl alcohol acid and polyethersulfone to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed concerning permeability properties. The permeability properties of the composite were studied based on the permeability of oxygen, nitrogen, and carbon dioxide. The results indicated that heat capacity decreased but thermal conductivity and dielectric constant hikes with a hike in a mass fraction of polyvinyl alcohol.Usually components for blends are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money, and time.

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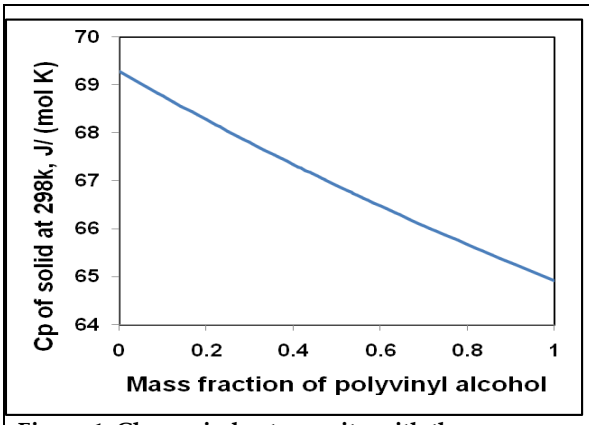

Figure 1. Change in heat capacity with the mass fraction of vinyl alcohol

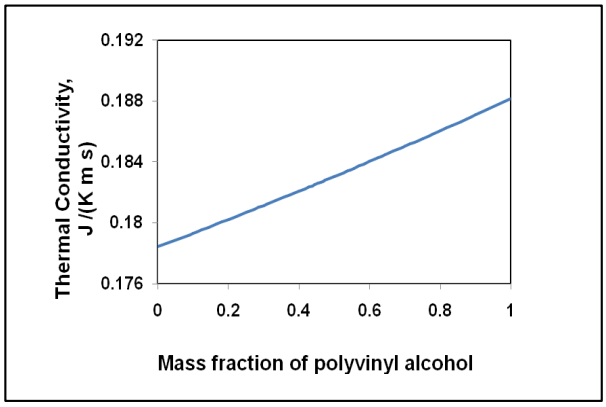

Figure 2. Change in thermal conductivity with the mass fraction of vinyl alcohol.

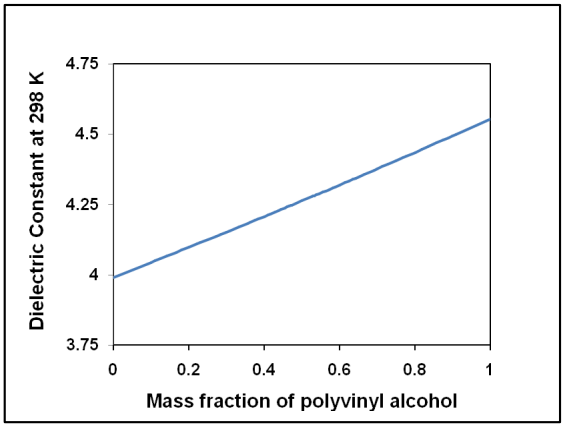

Figure 3. Change in Dielectric constant with the mass fraction of vinyl alcohol.

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6lvn Enzyme using *Tectona grandis* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". For this ongoing pandemic to find out an effective drug against this organism is now a grim theme for virologist. Taking plant material is now trending in virology lab to eradicate the causative organism of this pandemic. Before going to wet lab there will be smart choose of using computational tool for drug discovery. The molecular docking of the bioactive compounds there in plant *Tectona grandis* with " PDB code 6lvn (nCOV 2019 HR2 domain) of SARS-CoV-2"was studied using "Biovia Discovery Studio". And the highest "-CDocker energy and -CDocker interaction energy" value indicated that trans-caffeic acid of *Tectona grandis* extract can be an effective molecule to deactivate the mechanism of metabolic pathway of Heptad repeat 2 domain of "SARS-CoV-2 virus".

Key words: Phytoconstituent, Biovia, Discovery studio, nCOV 2019 HR2 domain, SARS-CoV-2

INTRODUCTION

According to WHO "Coronavirus disease 2019 (COVID-19)" has declared as a pandemic in March 2020 [1][2]. Ignoring nature we can suffer but cannot gain anything great. Since ancient time it has been proved as medicinal plants is nature is gift of God to rural as well as urban people and it has been using drug discovery lab very successfully. For this onging pandemic though some medicines are used to cure the this disease but till now there is no such established curable medicine.[3] We can deal with photochemical present in plant which will be cost effective. [4]. *Tectona grandis* commonly known as teak a tropical hard wood tree species belongs to family Lamiaceae. From literature it is found to be use to cure kidney stone, throat infection, bronchitis disorder, asthama etc. It contains phytochemicals like apigenin, luteolin 7ObetaDglucoside,rosmarinic acid and trans-caffeic acid etc. This study based on the exploring those phytochemicals which are responsible for curing disease cause by COVID-19.

MATERIALS AND METHODS

For this study a software named "BioviaDiscovery studio" used for the analysis of ligand protein interaction for drug discovery. From literature it was found that teak plant contains apigenin, luteolin 7ObetaDglucoside, rosmarinic acid

and trans-caffeic acid etc. It is known be effective against viral infection. Present study was is focused on the isolating the major bioactive compound present in examined plant whichis responsible for blocking the mechanism of "nCOV 2019 HR2 domain" and controlling the life cycle of "COVID-19".

PubChem database was used to find the enzyme list and particular enzyme which are used in molecular docking method. Prepared the protein in this given soft ware after that molecular docking was carried out to find the 3D and 2D structure of Enzyme lingad intraction and the to find strongest tautemeric structure of ligand which attached to which active site of the enzyme. The aminoacid residue of the active site can also be characterized, that can deactivate the "COV 19 HR2". [5]. Thus the high value C-Docker energy and C-Docker interaction and the lowest value of their difference might indicate the key phytochemical which can be chosen for further study in drug discovery.

RESULTS AND DISCUSSION

For molecular docking CDocker method was used. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The conformation of the ligand was identified by "Molecular Dynamic methods".
High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Trans-caffeic acid is the main ligand (bioactive compound) can really prevent the activity of PDB 6lvn enzyme.(Table-1)

CONCLUSIONS

From the recent study it can be concluded that *Tectona grandis* cab be used as anti viral dots due to the presence of major bioactive compound that inhibit the many mechanism of metabolic pathway which is occurred due to the Heptad repeat2 domain. Using "Discovery Studio module of Biovia software", it was identified that trans-caffeic acid can significantly interact with the viral nCOV 2019 HR2 domain.

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Table 1. Results of CDocking of phytochemicals with nCOV 2019 HR2 domain (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remark
1	Apigenin	10.7132	15.5728	4.8596	
2	luteolin 7Obeta-Dglucoside	failed	Failed	failed	
3	rosmarinic acid	-452.783	-127.852	324.931	Minimum inhibition of viral
4	transcaffeic acid	16.7705	17.8908	1.1203	Maximum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6M03 Enzyme using *Tectona grandis* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". Corona virus is consisting of both structural protein and non structural protein. So to discover a potent antiviral drug we can target both these structural and non structural protein. Using "Biovia Discovery Studio" molecular docking can be done using ligand (phytochemicals) of plant material with non structural protein "RCSB PDB 6m03of SARS-CoV-2". And high "-CDocker energy and -CDocker interaction energy" value and the lowest value of difference between these energy indicate that trans-caffeic acid (phytochemical) of teak plant extract can be the potent inhibitor of "SARS-CoV-2 virus".

Key words: Trans-caffeic acid, nonstructural protein, Discovery studio, COVID-19,

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" is a transmittable disease has declared as a pandemic by WHO [1][2]. Now this pandemic is an alarming stage because of its mortality rate due to the deadly virus "CORONA". So to overcome this situation it is a obligatory time to discover a established drug that can be used against this disease as till now there is no such effective medicine found. [3] We can explore photochemical present in plant which has already been using against various alignments that can be used against this viral disorder with a low cost strategy. [4]. *Tectona grandis* belongs to family Lamiaceae. It has been used ti cure various infectous disease like throat infection cold, cough, asthma and also againy dipression, excessive seating, skin disorder ect. It contains like apigenin, luteolin 7O-beta Dglucoside, rosmarinic acid and trans-caffeic acid etc. This study was carried out for finding the phytochemicals present in Teak plant which can be the barrier of the COVID 19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" Dassault System was used for ligand protein interaction analysis.
From literature it was found that the apigenin, luteolin 7ObetaDglucoside, rosmarinic acid and trans-caffeic acid etc. are the main phytoconstituent present in *Tectona grandis* plant. From past curing record it is known to be effective against virus. The recent study was based on the identification of the potent bioactive compound present in this teak plant that can inhibit the activity of enzyme 6m03 (PDB code) nonstructural protein main protease in apo form that can control the "COVID-19". Particular enzymes were identified using Brenda enzyme database. Then preparing Ligand and protein, molecular C-docking was done which identify the exact active site of the enzyme where ligand was bound. By analysing the C-Docker enery and intraction, the potent lingad was identified that seem to block the enzyme of COVID-19 [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Transcaffeic acid is the key phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Tectona grandis* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that transcaffeic acid can significantly interact with the viral 6m03 viral protein that control the lifecycle.

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Table 1. Results of CDocking of phytochemicals with 6m03 viral protein (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Apigenin	19.2625	24.2052	4.940	Minimum inhibition of viral protein
2	luteolin 7ObetaD-glucoside	failed	Failed	Failed	
3	rosmarinic acid	failed	failed	Failed	
4	transcaffeic acid	20.4118	20.1925	0.2193	Maximum inhibition of viral protein

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RESEARCH ARTICLE

Prevention of COVID-19 by Blocking NSP9 RNA Binding Protein using *Helichrysum chasmolycicum* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "NSP9 RNA binding protein of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Hexadecanoic acid of *Helichrysum chasmolycicum* extract can effectively fight against "SARS-CoV-2 virus".

Key words: Discovery studio, Phytochemical, Biovia, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" is one of the most dangerous infectious disease and this is declared as pandemic in March 2020 by WHO [1][2]. While, there is no such relevant cure for this severe disease [3]. Hence, it is the need of the hour to discover the most needed drugs against the emerging pandemic. Several plants have been identified curing various illnesses [4]. The phytochemicals extracted from them will be effective as well as low-cost. *Helichrysum chasmolycicum* belongs to family Asteraceae. This plant constitute phytochemicals like hexadecanoic acid, kaemferol, apigenin, palmitic acid, 3',5-dihydroxy-3,4',7-trimethoxyflavone etc. This study point out the phytochemicals, which can capable to cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. After in silico molecular docking the result reveals that *Helichrysum chasmolycicum* contains hexadecanoic acid, kaemferol, apigenin, palmitic acid, 3',5-dihydroxy-3,4',7-trimethoxy flavone etc. Investigation shows that plants, which come under this family are effective against several viruses. In our investigation, the main objective was to pick up that phytochemical which is unique and capable inhibiting NSP9 RNA binding protein a non structural protein resulting the control of the

COVID 19. To find out numerous enzymes of COVID-19, Brenda database has been used. The 3D structure of ligand (Phytochemical) of plant extract also obtained from PubChem database. Then to find out the significance potency of phytichemicals molecular docking was carried out which shows the effective binding of ligand with active site of function enzyme NSP9 RNA binding protein [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". Lowest value of the difference between -CDOCKER energy and -CDOCKER interaction energy and High positive value of -CDOCKER energy are the principle to identify the drug effective phytochemical. Hexadecanoic acid is the main phytochemical that can actually prevent the enzyme activity (Table-1).

CONCLUSIONS

It concluded on the key phytochemicals of the examined plant that is *Helichrysum chasmolycicum* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Hexadecanoic acid can efficienty interact with the viral NSP9 RNA binding protein and inhibit it's all metabolic pathway resulting in blocking the activity of corona virus inside the host cell.

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Table 1. Results of CDocking of phytochemicals of *Helichrysum chasmolycicum* with NSP9 RNA binding protein

SL NO	LIGAND	-C DOCKER ENERGY	-C DOCKER INTERACTION ENERGY	Difference between -C DOCKER interaction energy and -C DOCKER energy	Remarks
1	Hexadecanoic acid	38.7625	38.9588	0.1963	Maximum inhibition of viral protein
2	3',5-dihydroxy-3,4',7-trimethoxyflavone	11.3438	28.0064	16.6626	
3	Apigenin	19.3234	25.4012	6.0778	
4	Kaemferol	20.0526	24.7887	4.7361	
5	Palmitic acid	-51.4859	10.1787	61.6646	Minimum inhibition of viral protein

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RESEARCH ARTICLE

Computational Study of Polyoxyethylene and Polybutylene Isophthalate Compatibility in a Blend

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ABSTRACT

Combination of two or more components results in the formation of a blend. The compatibility of polyoxyethylene and polybutylene isophthalate were studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram and mixing energy. The results indicated that the pair can become compatible at both low and high temperature. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of oxyethylene. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that the thermal conductivity increased with increase in mass fraction of oxyethylene and other two parameter decreased. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in oxyethylene fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases increased with increase in mass fraction of oxyethylene. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend, in silico, oxides, ester

INTRODUCTION

Blends or composites are formed with combination of more than one components where components do retain their identity in the mixture. As it's very difficult to find multiple properties in a single material, advisable to combine different components thereby improving the quality of the material. Development of a single material with the

desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus it saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method and this technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. The general formula for any polymer of ethylene glycol is $HO-(CH_2CH_2O)_n-H$; used in the manufacture of emulsifiers. Polyoxyethylene is a polymer of ethylene glycol. It has a low toxicity and has been used as the gate insulator in an electric double layer transistor.& due to this transistor it induce superconductivity in an insulators. The polymer is used as a oil or grease coating for various surfaces in aqueous and non aqueous environments. It is used in a variety of products including processed foods, cosmetics , drugs, and other substances that contain PEG . In commercial purpose, for making of skin creams and personal lubricants polyoxyethylene is the base. It is also used in a number of toothpastes as adispersant. In this application , it binds uniformly water . In blood banking, PEG is used to raise the field of detection of antigens and antibodies. It is the basis of a number of laxatives. It is also used as an bonding agent in many pharmaceutical products.

Polybutylene isophthalate is a thermoplastic engineering polymer. As an insulator in the electrical and electronics industries this polybutylene isophthalate is used. It is a thermoplastic semi crystralline polymer , and a type of polyster. It can be treated with flame proofed to make non inflammable. By differential scanning calorimetry the thermal properties of uniformly random polybutylene isophthalate copolyster of various composition and different molecular weight were probed. All copolymers were partially crystalline, and the main effect of coplymerization was a lowering in the amount of crystallinity and a decrease of melting temperature with respect to pure homopolymers. Completely amorphous samples are obtained by rapid extinguishing from the melt which is showed a monotonic decrease of glass transition temperature and a monotonic increase of the heat capacity augmentation with increasing butylenes adipate content in the copolymers.

MATERIALS AND METHODS

SOFTWARE USED: Materials studio module of Biovia software (Dassault Systemesof France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

METHODOLOGY: Polyoxyethylene and Polybutylene isophthalate were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. Polyoxyethylene was used as the base and Polybutylene isophthalate was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data.

The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of Polyoxyethylene and Polybutylene isophthalate were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of Polyoxyethylene on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of Polyoxyethylene and Polybutylene isophthalatepotential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-determined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive method, extreamly fast and easy, were used to predict the properties of polymers and small molecules also. Consequently, they are of greatest usefulness when a rapid approximate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, then the property of that polymer cannot be calculated if a polymer contains a group for which the group contribution cannot be estimated.

To overcome this limitation, the method executed in Synthia uses topological information about polymers in the auguring correlations. The connectivity indices retained from graph theory are hired. Thus, no database of group contributions is required and properties may be forecasted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, sulfur, fluorine, chlorine, bromine and silicon.

ENERGY PARAMETER

FREE ENERGY OF MIXING: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend.

Thermodynamic analysis suggests that

$\Delta G_m = \Delta H_m - T\Delta S_m$ (1)

where $\Delta G_m = Gibb\,s\,free\,energy\,of\,mixing$

$\Delta H_m = Enthalpy\,of\,mixing$

$\Delta S_m = Entropy\,of\,mixing$

$T = Absolute\,temperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$\Delta H_m < T\Delta S_m$ (2)

Figure. 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between Polyoxyethylene and Polybutylene isophthalate with negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

CHI PARAMETER: The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase

separation. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2. shows that the value of x high from temperature ranging from 50Kto 500K .The value of x decreases exponentially with increase in temperature. This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: Phase diagram can be envisaged by the compatibility of binary mixtures c. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:
a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).
b. Between binodals and spinodals region Fragmented metastable regions existed.
c. The two-phase separated regions of immiscibility are bordered by the spinodals.
The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.
When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition

MIXING ENERGY: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature. The temperature is vary from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

MECHANICAL PROPERTIES

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5. shows that the bulk modulus of the composite decreases with increase in mass fraction of oxyethylene.

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite decreases gradually and at a certain mass fraction it becomes zero and then having negative value. After this with increase in mass fraction of Oxyethylene the shear modulus of increase to zero.

Young's modulus: Ratio of stress and strain defined the young's modulus. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite decreases gradually and at a certain mass fraction it becomes zero and then having negative value. After this with increase in mass fraction of Oxyethylene the Young's modulus of increase to zero.

Poisson ratio: Ratio of lateral strain to longitudinal strain is known as the poisson ratio. Figure 8 shows that the Poisson ratio of the composite increases with increase in mass fraction of acrylic oxyethylene.

THERMAL PROPERTIES

Heat capacity: It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 9 shows that the heat capacity (Cp) of the composite decreases with increase in mass fraction of oxyethylene.

Thermal conductivity: Correlation between heat flux per unit area and temperature gradient indicated through the thermal conductrivity. It refers to the intrinsic ability of a material to transfer heat. Figure 10 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of oxyethylene.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 11 shows that the dielectric constant of the composite decreases linearly with increase in mass fraction of oxyethylene

INTENSIVE PROPERTIES

Molar volume: The definition of the molar volume isthe volume occupied by one mole of a substance. Figure 12 shows that the molar volume of the composite decreases with increase in mass fraction of oxyethylene.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 13 shows that the density of the composite decreases linearly with increase in mass fraction of oxyethylene.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the mebrane. Figure 14(a) shows that the permeability of oxygen through the composite increases with increase in mass fraction of oxyethylene. Figure 14(b) shows that the permeability of nitrogen through the composite increases with increase in mass fraction of oxyethylene. Figure 14(c) shows that the permeability of carbon dioxide through the composite increases with increase in mass fraction of oxyethylene. Thus, the results indicated that an increase in oxyethylene fraction increases the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSION

The possibility of use of polyoxyethylene and polybutylene isophthalate to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter , mixing energy and phasediagram. The results indicated that the pair can have very good compatibility at different ranges of temperature. Based on bulk modulus, shear modulus the mechanical properties of the composite were studied , Young' modulus, Poisson ratio . The results indicated that the values of all the properties increased with increase in mass fraction of oxyethylene. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the thermal coductivity increased with increase in mass fraction of oxyethylene whereas the other two parameter decreased. The composition of the blend was analyzed with respect to permeability properties. The molar volume, density, decreased with increase in oxyethylene fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases increased with increase in mass fraction of oxyethylene. Usually components for a blend are identified experimentally. This in silico study will

help determine components of a blend without performing laboratory experiments saving materials, money and time

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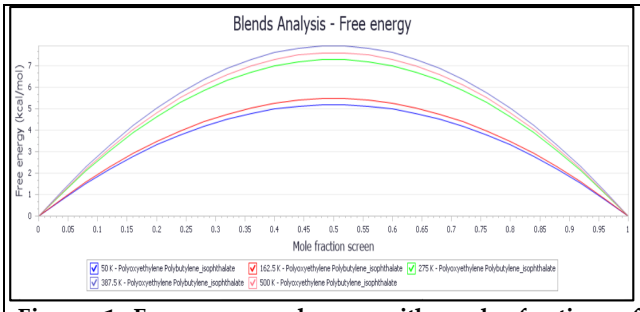

Figure 1 Free energy change with mole fraction of polybutylene isophthalate at different temperatures

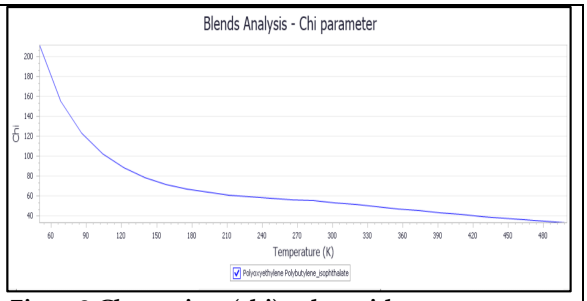

Figure2 Change in χ (chi) value with temperature

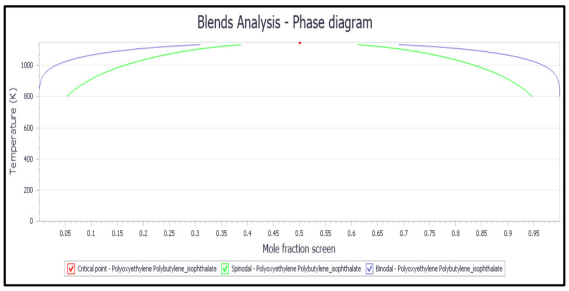

Figure 3 Phase diagram

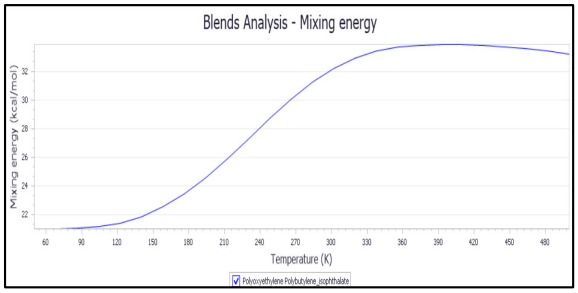

Figure.4 Mixing energy

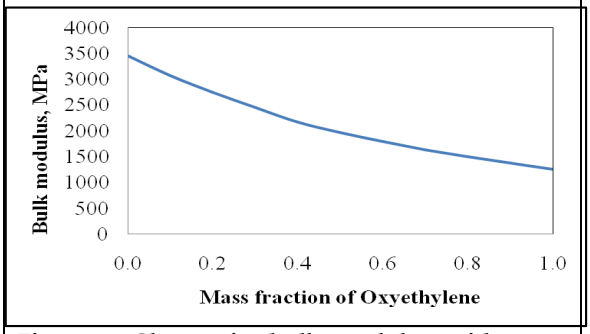

Figure 5 Change in bulk modulus with mass fraction of Oxythylene

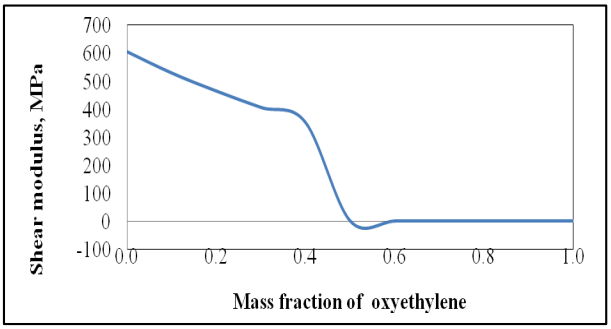

Figure 6 Change in shear modulus with mass fraction of oxyethylene

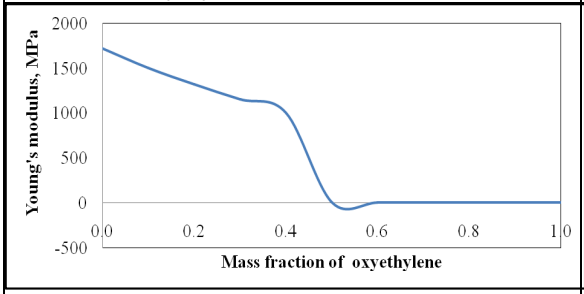

Figure 7 Change in Young's modulus with mass fraction of oxyethylene

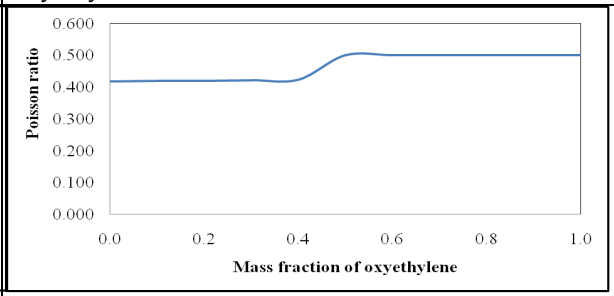

Figure 8 Change in Poisson modulus with mass fraction of oxyethylene

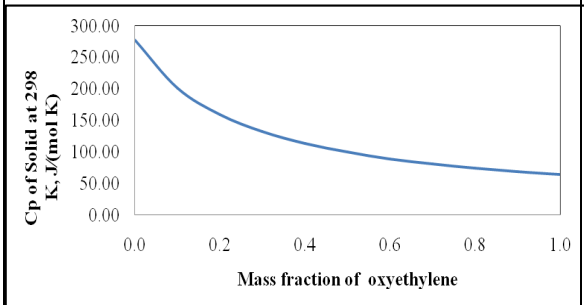

Figure 9 Change in heat capacity with mass fraction of oxyethylene

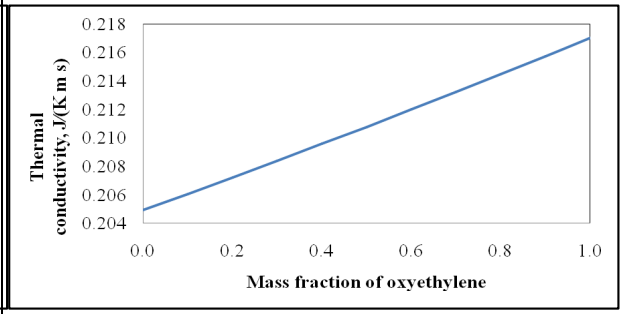

Figure 10 Change in thermal conductivity with mass fraction of oxyethylene

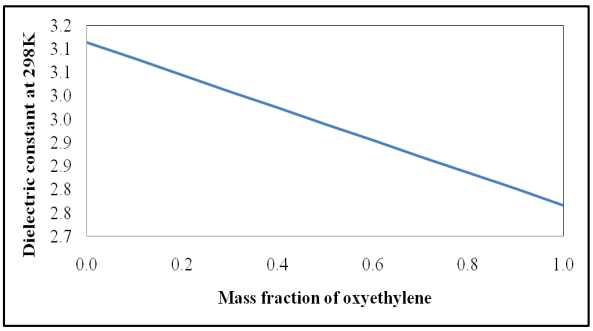

Figure 11 Change in dielectric constant with mass fraction of oxyethylene

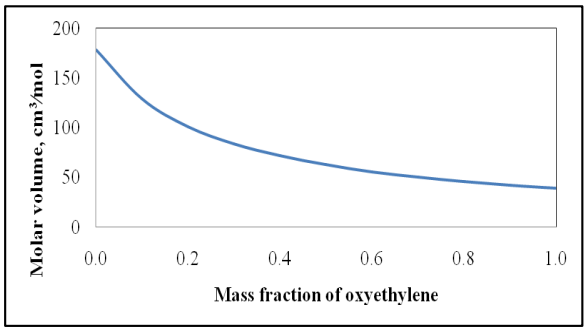

Figure 12 Change in molar volume with mass fraction of oxyethylene

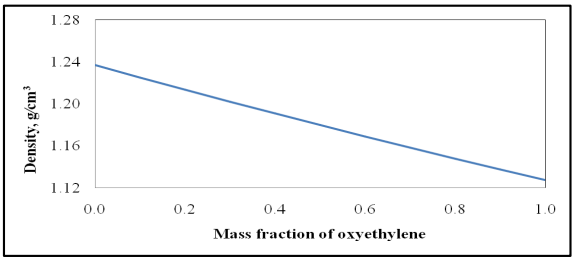

Figure 13 Change in density with mass fraction of oxyethylene

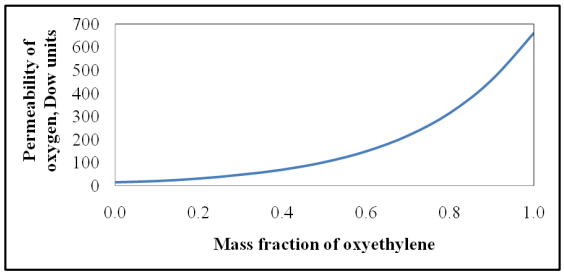

Figure 14(a) Change in permeability of oxygen with mass fraction of oxyethylene

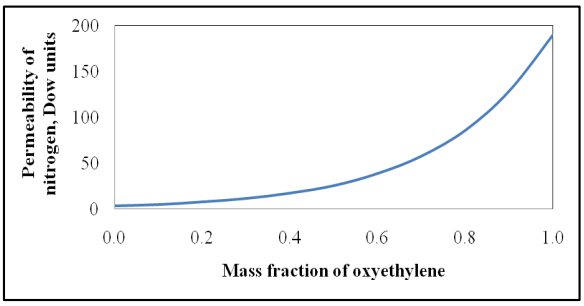

Figure 14(b) Change in permeability of nitrogen with mass fraction of oxyethylene

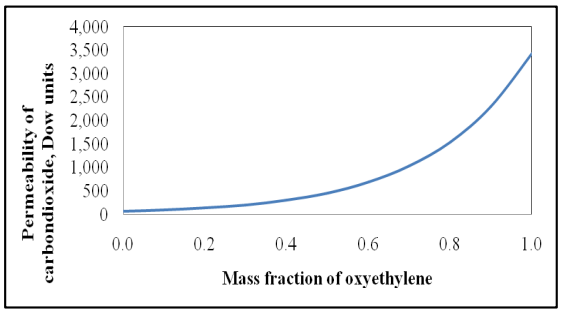

Figure 14(c) Change in permeability of carbon dioxide with mass fraction of oxyethylene

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6M03 using *Velvet bean:* An *In silico* Analysis

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researchers are working seriously to develop drugs or vaccine against COVID-19. The main aim of this study to identify the phytochemicals extracts from the plant *Velvet bean* which can deactivate 6M03 of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of *Velvet bean* were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like bufotenine. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of COVID-19.

Keywords: COVID-19, 6M03, Biovia, *Velvet bean* ,NSP3.

INTRODUCTION

A novel corona virus (nCoV-2019) emerge as contagious disease for human on the month of December, 2019 Wuhan province of China[1] and cause severe acute respiratory syndrome (SARS). On 30th January, 2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. Situation is getting worse with this viral infection and the mortality graph approaches to upward.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [4]. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. Various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir have effect on treatment of COVID. The less effective of these drugs motivated to examine the restraint of COVID-19 protease by

Indian herbal plants [5]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc.[6]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry.The leaves of bean have the following phytochemicals like alkaloids,tannins,saponin and phenolic compounds.The main objective of this article to identify the phytochemicals of *Velvet bean* responsible for inhibiting COVID-19 6M03) by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software ((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Velvet bean* contains various phytochemicals like genistine and Bufotenine. It has been reported that fabacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[7,8].

COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that 6M03 is involved in replication of virus. By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Velvet bean* were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value shows the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of 6M03 of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b)small difference between -CDOCKER energy and -CDOCKER energy interaction.

High positive values of C-Docker energy are6.57799 and the difference with Cdocker interaction energy 11.82361 are presented in table-I.TableI also represented the difference in energy which are vasicinone, vasicine, peganine. From these findings it is found that Bufotenine can effectively deactivate 6M03, thereby interrupting viral replication. Vasicine, vasicinone, peganine can less effectively inhibit the viral replication as negative -CDocker energy but shows

positive -CDocker interaction energy. Thus, the key phytochemicals Bufotenine can prevent COVID-19 caused by 6M03 of virus.

CONCLUSIONS

It was reported that *Velvet bean* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like Bufotenine can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with 6M03 of COVID-19. It was found that Bufotenine of *Velvet bean* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus.. From this study it can be concluded that phyochemical Bufotenine provide the medicinal importance to *Velvet bean* that can act against COVID-19 caused by 6M03.

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Table 1. C-Docking score of different phytochemicals with 6M03 of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Bufotenine	6.57799	18.4016	11.82361
2	Genistine	Failed	Failed	-

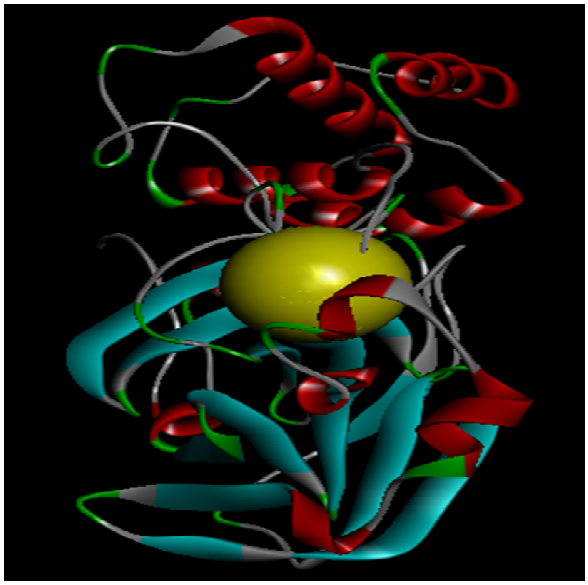

Figure 1. Binding site of 6M03

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) using *Velvet bean:* An *In silico* Analysis

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researchers are working seriously to develop drugs or vaccine against COVID-19. The main aim of this study to identify the phytochemicals extracts from the plant velvet bean (*Mucuna pruriens*) which can deactivate ADP ribose phosphatase of NSP3(6VXS) of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of velvet bean were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like Dopamine and Bufotenine. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of COVID-19.

Keywords: COVID-19,6VXS, Biovia, *Mucuna pruriens*, NSP3.

INTRODUCTION

A novel corona virus (nCoV-2019) emerge as contagious disease for human on the month of December,2019 Wuhan province of China[1] and cause severe acute respiratory syndrome (SARS). On 30th January,2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. Situation is getting worse with this viral infection and the mortality graph approaches to upward.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [4]. Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel coronavirus, there exists no vaccines, so far which has

been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. Various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir have effect on treatment of COVID. The less effective of these drugs motivated to examine the restraint of COVID-19 protease by Indian herbal plants [5]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc.[6 The velvet bean (*Mucuna pruriens*) belongs to the family *Fabaceae* and a common plant found in tropical and sub-tropical regions of the world. It is viewed as a suitable dietary source because of its high edible protein content (23–35%) and comparable with that of soybean, rice bean, and lima bean . Additionally, Velvet bean contain a high portion of L-Dopa, which is helpful for treating Parkinson's disease. The main objective of this article to identify the phytochemicals of *Mucuna pruriens* responsible for inhibiting COVID-196VXS) by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Mucuna pruriens*contains dopamine,genistein,behenic acid and bufotenine etc. It has been reported that Acanthacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[7,8].COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that6VXS is involved in replication of virus.

By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Mucuna pruriens*were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value shows the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of6VXS of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b) small difference between -CDOCKER energy and -CDOCKER energy interaction.

High positive values of C-Docker energy are 21.184 and the difference with Cdocker interaction energy 2.4672 are presented in table-I. Table I also represented the difference in energy which are dopamine and buftomine. From these findings it is found that dopamine and buftomine can effectively deactivate6VXS, thereby interrupting viral replication. Vasicine, vasicinone, peganine can less effectively inhibit the viral replication as negative -CDocker energy but shows positive -CDocker interaction energy. Thus, the key phytochemicals dopamine and buftomine can prevent COVID-19 caused by6VXS of virus.

CONCLUSIONS

It was reported that *Mucuna pruriens* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like dopamine and buftomine can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with6VXS of COVID-19. It was found that dopamine and buftomine of *Mucuna pruriens*can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The following phytochemicals like Vasicine, vasicinone, peganine were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals dopamine and buftomine provide the medicinal importance to *Mucuna pruriens*that can act against COVID-19 caused by6VXS.

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Table 1. C-Docking score of different phytochemicals with 6VXS of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Behenic acid	FAILED	FAILED	14.61877
2	Genistein	FAILED	FAILED	14.49826
3	Dopamine	18.9338	18.571	14.73767
4	Bufotenine	19.1272	24.6582	error

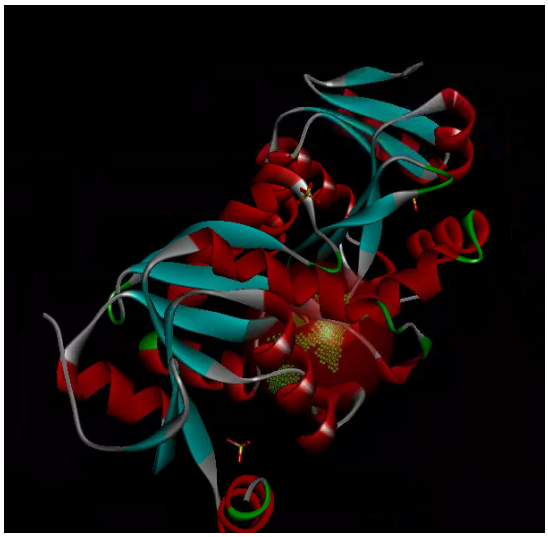

Figure 1. Binding site of 6VXS ADP ribose phosphatase of NSP3

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Nucleocapsid Protein (6M3M) using *Adhatoda vasica:* An *In silico* Analysis

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Received: 19 Mar 2020 Revised: 21 Apr 2020 Accepted: 23 May 2020

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researchers are working seriously to develop drugs or vaccine against COVID-19. The main aim of this study to identify the phytochemicals extracts from the plant *Adhatoda vasica* which can deactivate 6M3M of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of *Adhatoda vasica* (Vasak) were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like quercitin. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of COVID-19.

Keywords: COVID-19, 6M3M, Biovia, *Adhatoda vasica*, NSP3.

INTRODUCTION

A novel corona virus (nCoV-2019) emerge as contagious disease for human on the month of December, 2019 Wuhan province of China[1] and cause severe acute respiratory syndrome (SARS). On 30th January, 2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. Situation is getting worse with this viral infection and the mortality graph approaches to upward.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [4]. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there

exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. Various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir have effect on treatment of COVID. The less effective of these drugs motivated to examine the restraint of COVID-19 protease by Indian herbal plants [5]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc.[6]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry.The leaves of vasak have the following phytochemicals like alkaloids,tannins,saponin and phenolic compounds.The main objective of this article to identify the phytochemicals of *Adhatoda vasica* responsible for inhibiting COVID-19 6M3M) by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Adhatoda vasica* contains vasicin, vasicinone, peganin, quercetin , kaempferol, etc. It has been reported that Acanthacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[7,8].

COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that 6M3M is involved in replication of virus. By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Adhatoda vasica* were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value shows the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of 6M3M of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b)small difference between -CDOCKER energy and -CDOCKER energy interaction.

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CONCLUSIONS

It was reported that *Adhatoda vasica* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like Quercitin can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with 6M3M of COVID-19. It was found that Quercitin of *Adhatoda vasica* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The following phytochemicals like Vasicine, vasicinone, peganine were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals Quercitin provide the medicinal importance to *Adhatoda vasica* that can act against COVID-19 caused by 6M3M.

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Table 1. C-Docking score of different phytochemicals with 6M3M of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Quercitin	21.184	23.6512	2.4672
2	Peganine	4.29333	18.9121	14.61877
3	Vasicine	2.09314	16.5914	14.49826
4	Vasicinone	1.60423	16.3419	14.73767
5	Vasicine acetate	error	error	error

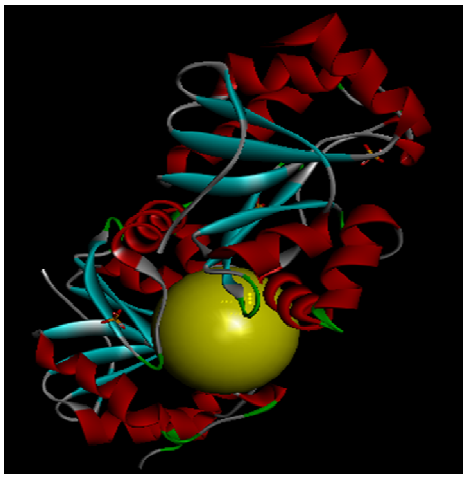

Figure 1. Binding site of 6M3M (nucleocapsid protein N-terminal RNA binding domain)

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6LNV Enzyme using *Eclipta prostrate* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "2019-nCoV HR2 Domain" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Pentadecane of Eclipta extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

Coronavirus has become a critical public issue across the global since December 2019 which was suspected to be originated from a wet market in Wuhan, Hubei province, China [1, 2, 3]. As of 24thof April 2020, more than 2.6 million cases have been reported in 213 countries and territories. SARS-CoV-2 belongs to the beta corona-virus genus, closely related to the previously identified severe acute respiratory syndrome corona-virus (SARS-CoV) [4]. Their phytochemicals will be low-cost but effective. *Eclipta prostrate* several phytochemicals. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

For the *in silico* molecular docking, BIOVIA's Discovery Studio docking method [11] was used for molecular docking. The catalytic pocket of the RdRp protein was specified and targeted for binding of the ligand. CDOCKER Energy and CDOCKER Interaction Energy signify the affinity of the ligands with the protein receptors. Basically, high positive values of the CDOCKER Energy, CDOCKER Interaction Energy and a diminutive difference between the CDOCKER Energy and CDOCKER Interaction Energy are considered to be the most favourable [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Pentadecane is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Eclipta* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Pentadecane can significantly interact with the viral HR2 Domain.

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Table 1. Results of CDocking of phytochemicals with HR2 Domain (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	6,10,14-trimethyl-2-pentadecanone	31.198	35.4829	4.2849	
2	7,11-Dimethyl-3-methylene-1,6Z,10-dodecatriene	-31.5171	26.0956	57.6127	Minimum inhibition of viral protein
3	octadea-9-enoic acid	27.3052	43.9134	16.6082	
4	Phytol	11.5501	38.5206	26.9705	
5	Pentadecane	32.6039	34.34	1.7361	Maximum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6lvn Enzyme using *Helichrysum chasmolycicum* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "6lvnenzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Luteolin of *Helichrysum chasmolycicum* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a serious illness that has caused pandemic across the globe [1][2].However, specific drugs for curing the disease is yet to be identified [3]. This necessitates the need to explore phytochemicals or active compounds present in plants which can be a potential drug to cure the pandemic. Several medicinal plants with different phytochemicals can be used for drug development [4]. These drugs will be safe and cost effective. *Helichrysum chasmolycicum* belongs to Asteraceae. It contains hexadecanoic acid,luteolin, Apigenin,oleic acid,palmitic acid and quercetin 3-O-β-Dglucopyranoside etc.This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"BioviaDiscovery studio" module (DassaultSystemes of France) was used for analysis. Published works showed that *Helichrysum chasmolycicum* contains hexadecanoic acid, luteolin, Apigenin, oleic acid,palmitic acid and quercetin 3-O-β-Dglucopyranoside etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting 6and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has

been used to identify the phytochemical from the plant extract, thatcan deactivate the 6lvnviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

Table 1 shows that Luteolin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Helichrysum chasmolycicum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatluteolin can significantly interact with the viralprotein 6lvn.

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Table 1. Results of CDocking of phytochemicals with 6lvn (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Hexadecanoic acid	-222.839	-93.8606	128.978	

2	oleic acid	-248.497	-93.6308	154.866	Minimum inhibition of viral protein
3	Apigenin	10.7132	15.5728	4.8596	
4	Luteolin	13.2361	15.7976	2.5606	Maximum inhibition of viral protein
5	Palmitic acid	failed	failed	Failed	
6	quercetin 3OβD-glucopyranoside	failed	failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6M03 Enzyme using *Moringa oleifera* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "6M03 enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that4-hydroxyl-4-methyl-2-pentanone of *Moringa oleifera* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a serious disease and has severely affected the global health situation [1][2]. Selective medicines are not yet identified for the treatment of this pandemic [3] Phytochemicals produced from plants can be used for suitable drug formulations to treat the virus [4]. The drugs formulated from these phytochemicals will be safe to use and highly effective. *Moringa oleifera* belongs to family Moringaceae. It contains phytochemicals like 3-ethyl-2,4-dimethylpentane, 4-hydroxyl-4-methyl-2-pentanone, 4, 8, 12, 16-tetramethyl heptadecan-4-olide, 9-octadecenoic acid and hexadecanoic acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"BioviaDiscovery studio" module (DassaultSystemes of France) was used for analysis. Published works showed that Moringaoleiferacontains 3-ethyl-2,4-dimethylpentane, 4-hydroxyl-4-methyl-2-pentanone, 4, 8, 12, 16-tetramethyl heptadecan-4-olide, 9-octadecenoic acid and hexadecanoic acid etc. It is known that plants belonging to this family

are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-19.
Brenda enzyme database was used to list different enzymes found in COVID-19.
Molecular docking method has been used to identify the phytochemical from the plant extract, which can deactivate the 6M03viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".
High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.
Table 1 shows that 4-hydroxyl-4-methyl-2-pentanone is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Moringa oleifera* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that4-hydroxyl-4-methyl-2-pentanonecan significantly interact with the viral protein 6M03.

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Table 1.Results of CDocking of phytochemicals of *Moringa oleifera* with 2019-nCoV 6M03

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	3-ethyl-2,4-dimethylpentane	9.91055	18.1992	8.28865	Minimum inhibition of viral protein
2	4-hydroxyl-4-methyl-2-pentanone	17.9442	18.4675	0.5233	Maximum inhibition of viral protein
3	4,8,12,16-tetramethylheptadecan-4-olide	FAIL		NA	
4	9-octadecenoic acid	FAIL		NA	
5	hexadecanoic acid	FAIL		NA	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6M3M Enzyme using *Helichrysum chasmolycicum* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytoconstituents with with "6M3M enzyme of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive estimations of "- CDocker energy and - CDocker interaction energy" showed that hexadecanoic acid of *Helichrysum chasmolycicum* concentrate can successfully battle against "SARS-CoV-2 virus".

Keywords: Phytoconstituent, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus diseases 2019 (COVID-19)" has sabotaged the entire world. It has been broadcasted as a pandemic [1][2], be that as it may, till now there is no proper cure of "COVID-19" [3]. There is a need to distinguish drugs against the infection. There are various traditional plants rewarding different diseases [4]. Their phytoconstituents will be minimal effort yet compelling. *Helichrysum chasmolycicum* has a place with family Asteraceae. It contains a few phytochemicals that may assist with inhibiting SARS-coV-2 infection for example hexadecanoic acid, kaemferol, aspigenin etc. This examination distinguishes those phytoconstituents which can cure the "COVID-19 attack".

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.
From the review of literature, it is realized that plants having a place with this family Asteraceae are powerful against infections. This work is focused around the recognizable proof of the specific phytochemical liable for inhibiting 6M3M enzyme and controlling of COVID-19.
"Brenda enzyme database was used to list different enzymes found in COVID-19".

The Molecular docking method has been used to identify the phytoconstituent from the plant extract, that can deactivate the 6M3M enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

Table 1 revealed that Hexadecanoic acid is the phytoconstituent that can really avert COVID-19 attack.

CONCLUSIONS

It was identified that *Helichrysum chasmolycicum* has effective against the "COVID-19 attack". Utilizing "Discovery Studio module of Biovia programming", it was recognized that Hexadecanoic acid can act together with the viral 6M3M enzyme

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Table 1. Results of CDocking of phytoconstituent with 6m3m enzyme i.e. receptor.

Sl No.	Ligand	- C docker energy	- C docker interaction energy	Difference between - C docker interaction energy and - C docker energy	Remarks
1	Hexadecanoic acid	41.9423	38.5978	3.3445	Highest inhibition
2	3',5-dihydroxy-3,4',7-trimethoxyflavone	15.5968	31.6696	16.0728	Lowest inhibition
3	Apigenin	24.0931	29.2745	5.1814	
4	Kaemferol	25.7611	31.9523	6.1912	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6M03 using *Velvet bean:* An *In silico* Analysis

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researchers are working seriously to develop drugs or vaccine against COVID-19. The main aim of this study to identify the phytochemicals extracts from the plant *Velvet bean* which can deactivate 6M03 of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of *Velvet bean* were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like dopamine. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of COVID-19.

Keywords: COVID-19, 6M03, Biovia, *Velvet bean* ,NSP3.

INTRODUCTION

A novel corona virus (nCoV-2019) emerge as contagious disease for human on the month of December,2019 Wuhan province of China[1] and cause severe acute respiratory syndrome (SARS). On 30th January,2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. Situation is getting worse with this viral infection and the mortality graph approaches to upward.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [4]. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies

because of a tiny virus. Various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir have effect on treatment of COVID. The less effective of these drugs motivated to examine the restraint of COVID-19 protease by Indian herbal plants [5]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc.[6]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry.The leaves of bean have the following phytochemicals like alkaloids,tannins,saponin and phenolic compounds.The main objective of this article to identify the phytochemicals of *Velvet bean* responsible for inhibiting COVID-19 6M03) by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software ((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Velvet bean* contains various phytochemicals like behenic acid and Dopamine. It has been reported that fabacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[7,8]. COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that 6M03 is involved in replication of virus.

By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Velvet bean* were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value shows the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of 6M03 of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b) small difference between -CDOCKER energy and -CDOCKER energy interaction.

High positive values of C-Docker energy are6.57799 and the difference with Cdocker interaction energy 11.82361 are presented in table-I.TableI also represented the difference in energy which are vasicinone, vasicine, peganine. From

these findings it is found that Dopamine can effectively deactivate 6M03, thereby interrupting viral replication. Thus, the key phytochemicals Dopamine can prevent COVID-19 caused by 6M03 of virus.

CONCLUSIONS

It was reported that *Velvet bean* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like Dopamine can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with 6M03 of COVID-19. It was found that Dopamine of *Velvet bean* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. From this study it can be concluded that phyochemical Dopamine provide the medicinal importance to *Velvet bean* that can act against COVID-19 caused by 6M03.

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Table 1. C-Docking score of different phytochemicals with 6M03 of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Dopamine	11.4945	11.9946	0.5001
2	Behenic acid	Failed	Failed	-

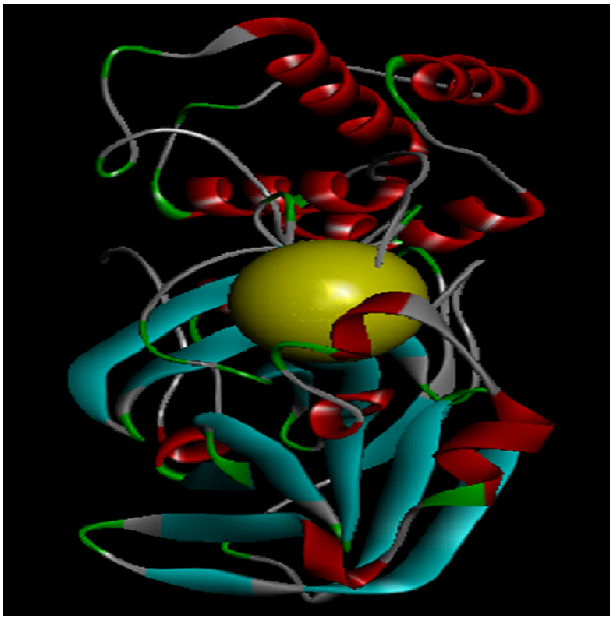

Figure 1. Binding site of 6M03

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6VXS Enzyme using *Aloe vera* Extract: An *In silico* Analysis

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ABSTRACT

The emerging of corona virus disease is caused by severe acute respiratory syndrome corona virus 2 (SARS Cov-2) with has worsened the public health and economy. Structurally, this virus is composed of RNA and some proteins like N protein,S-protein and envelope and hemagglutinin-esterase dimer. Entry of these viral proteins in human body may cause severe damages to heart, kidney, gastrointestinal system, liver, and central nervous systems. As no specific medicines or vaccines are available to combat this deadly virus, researchers throughout the globe are working seriously to develop proper drugs to neutralize the negative impact of viral proteins. This study focuses on identification of phytochemicals from plant extract which has the capability to fight against COVID-19 by deactivating ADP ribose phosphatase of NSP3 of COVID-19 which is reported to be very crucial for the viral replication in to the host cell. The molecular docking was studied by the Biovia discovery studio. This docking was done by Biovia Discovery studio to analyze the interaction of phytochemicals of Aloe-vera with 6VXS of NSP3 protein. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like quercitin and kaempferolcan. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of ADP ribose phosphatase of NSP3 of COVID-19.

Keywords: Phytochemicals ,aloe-vera, Biovia, Discovery studio, COVID-19

INTRODUCTION

A novel corona virus (nCoV-2019) emerges with a unique characteristic of human-to-human transmission on December 2019 in Wuhan province of China[1] and cause severe acute respiratory syndrome (SARS) .This infection has marked as dead-threatening to numerous people around the world within short period of time. On 30th January,2020 World Health Organisation has issued public health emergency of international concern under

International Health regulations [2]. As per the global statistics, the mortality rate is doubled in just 7 days with this deadly virus. Globally more than 3 million people have been already confirmed with COVID-19 positive along with 274,488 death reports as on 10th May, 2020 (WHO reports). The Indian scenario of COVID-19 is also painful. More than 41, 000 people are enlisted with active cases and 2109 people have been already passed away. By the time, situation is getting worse with this viral infection and the mortality graph approaches to upward and incomplete number of COVID-19 positive cases because the published number is only related to the laboratory confirmation.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects . Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. To battle this dangerous COVID-19, various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir, and so on, have been attempted and found with certain therapeutic impact in vitro. In any case, the clinical medication response isn't very empowering and toxicity stays an unavoidable issue causing severe effects. This motivated us to examine the restraint of COVID-19 protease by Indian herbal plants [4]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values . Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc. [5]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry.Among different medicinal plants , Aloe vera (*Aloe barbadensis miller*) plant has been known and utilized for a prolonge time for its excellence, therapeutic and healthy skin properties. It belongs to family "Liliaceae" and is a shrubby,xerophytic, delicious and green shading plant . Aloe vera contains 75 possibly active phytochemicals , including vitamins (A, C and E), enzymes, sugars, minerals (calcium, copper, magnesium, manganese, potassium, sodium and zinc), saponins, salicylic acid etc [6,7]. All these have anti-inflammatory activity and lupeol additionally has pain relieving properties. The main objective of this article to identify the phytochemicals of *Aloe barbadensis miller* responsible for inhibiting COVID-19 ADP ribose phosphatase of NSP3 by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that Aloe vera (*Aloe barbadensis miller*)contains aloe-emodin,anthraquinone,cinnamic acid,salicylic acid,aloin and glucomannan were considered for the study. etc. It has been reported that Liliaceae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[8].

Papain-like protease (PLpro) of COVID-19

COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that ADP ribose phosphatase of NSP3 (PDB Id 6vws) is involved in replication of virus. By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of Aloe vera (*Aloe barbadensis miller*)were

downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value show the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of ADP ribose phosphatase of NSP3 of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b)small difference between -CDOCKER energy and -CDOCKER energy interaction.

High positive values of C-Docker energy are25.0075 and the difference with Cdocker interaction energy 4.7246 are presented in table-I.TableI also represented the difference in energy which are aloe-emodin,anthraquinone,cinnamic acid,salicylic acid,aloin and glucomannan. From these findings it is found that Aloe-emodin can effectively deactivate 6vxs, thereby interrupting viral replication.On the other hand, anthraquinone shows the second highest affinity towards ADP ribose phosphatase of NSP3 of COVID-19 and therefore, it has the potential to deactivate the enzyme. cinnamic acid and salicylic acid,can less effectively inhibit the viral replication as negative -CDocker energy but shows positive -CDocker interaction energy. Thus, the key phytochemicals Aloe-emodin can prevent COVID-19 caused by 6vxs of virus.

CONCLUSIONS

It was reported that *Aloe barbadensis miller* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals aloe-emodin can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with ADP ribose phosphatase of NSP3 of COVID-19. It was found that Aloe-emodin of *Aloe barbadensis miller* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The other phytochemicals of this plants like anthraquinone,cinnamic acid,salicylic acid,aloin and glucomannan were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals aloe-emodin provide the medicinal importance to *Aloe barbadensis miller* that can act against COVID-19 caused by ADP ribose phosphatase of NSP3.

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Table 1. C-Docking score of different phytochemicals with ADP ribose phosphatase of NSP3 of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Aloe-emodin	25.0075	29.7321	4.7246
2	Anthraquinone	13.6454	19.3660	5.7206
3	cinnamic acid	17.0733	21.9162	4.8429
4	salicylic acid	18.2504	24.6911	6.4407
5	Aloin & Glucomannan	Failed	Failed	

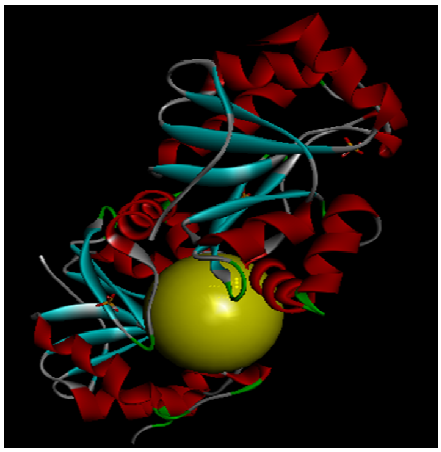

Figure 1. Receptor binding site of ADP ribose phosphatase of NSP3 of COVID-19

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RESEARCH ARTICLE

COVID-19 Prevention by blocking ADP Ribose Phosphatase Enzyme using *Psidium guajava* (Guava) Extract: An *In silico* Analysis

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ABSTRACT

A pandemic disease is produced by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) named as Corona virus disease 2019 (COVID-19) cause infection in human being. It has been a source of fright and anguish worldwide which is ensuing thousands of demises and affecting millions of people as an ongoing epidemic every day. This study focuses on identification of phytochemicals from plant extract which has the potency to resist against COVID-19 by deactivating ADP Ribose phosphatase enzyme. The molecular docking of the phytochemicals with the microbial enzyme was studied using "Biovia Discovery Studio". The strength of the interaction was evaluated based on -CDocker energy and -CDocker interaction energy. High positive values for both the parameters indicated that the phytochemical citric acid can effectively deactivate the enzymatic metabolic activity of COVID-19 virus.

Key words: Phytochemical, Biovia-Discovery studio, COVID-19, SARS-CoV-2, -CDocker

INTRODUCTION

A pandemic situation was spread all over world with serious fatal implications for countries with ageing human populations mostly caused by a new strain of corona virus is the large family among virus identified as novel Corona virus. The transmittable disease resulting in the ongoing 2019–20 corona virus is named "Corona virus disease 2019 (COVID-19)" A Public Health Emergency of International Concern (PHEIC) on 30 January 2020, and a pandemic on 11 March 2020 [1] [2]was declared by the World Health Organization (WHO) in view the accreditation of 2019–20 corona virus outbreak. It has escalated globally since December 2019, when the first cases of these epidemic were reported at Wuhan, the capital of China's Hubei province [3][4]. More than millions of people infected and thousands demised according to the statistical analysis has since touched however the total number of COVID-19 cases is not known. According to geographic regions in the virus any kind of preventive or molecular drugs or vaccine could not been developed yet unfortunately due to continuous mutation. However, scientists from all over world fully engaged for the investigation of vaccines or drugs for established treatment.

The ultimate source of number of drugs and modern drugs is nature that have been derived from thousands of years. The modern scientific technique so far derived the medicinal value of the plants lies on chemical substances that produce from any part of it defined as phytochemicals. These are produced as secondary metabolites protect plants from potential threats like bacteria, fungi, virus and from predators which have definite physiological action on the human body while consume can be used for therapeutic purpose. The phytoextracts from various medicinal plants have shown numerous medicinal properties like anti-oxidant, anti-inflammatory, anti-cancer, anti-microbial, anti-diabetes action etc [9] can be provided to be safe and cost effective.

Psidium guajava (guava) belongs to family Myrtaceae is popularly known for medicinal value that the extraction of it's leaves is used to cure disease like diarrhea, diabetes, for lowering chloresterol level, cold and cough and skin diseases, for weight loss, cancer etc. [11], [12], [13]. The phytochemicals of this plant is composed like Malonic acid, Ascorbic acid, Kaempftrol, Catechin, Gallic acid and citric acid etc. This present investigation focuses on exploring the possibility of using phytochemicals of *Psidium guajava* in curing the disease caused by COVID-19. However, any specific phytochemical responsible to cure COVID—19 is not yet reported.

MATERIALS AND METHODS

Software used

This study was analysed by using software "Biovia-Discovery studio" module (Dassault Systemes of France).

Methodology

List of phytochemicals: *Psidium guajava* contains Malonic acid, Ascorbic acid, kaempftrol, Catechin, Gallic acid and Citric acid etc is reported from literatures. It has already been established that different plants belonging to Myrtaceae family has potential to fight against microbes/viruses. The aim of this work was to identify the particular phytochemical that may responsible for inhibiting and controlling of COVID-19.

List of Enzyme in (COVID-19): The cycle of COVID-19 for survival is regulated by number of enzymatic action was searched and collected the list of enzyme by using "Brenda enzyme database". It has been found that ADP Ribose phosphatase enzyme (protein database code 6w6y) is involved in metabolic cycle in order to survive.

Molecular docking: The identification of phytochemicals of Psidium guajava has been established by using "molecular docking method" for CDocker protocol of Biovia software under "receptor-ligand interaction".

RESULTS AND DISCUSSION

The molecular interaction for the phytochemicals found in the Psidium guajava was performed by -CDOCK method is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy. The active site of the ADP Ribose phosphatase enzyme was appeared as light green color under "receptor-ligand interaction". The ligand conformations were obtained by Molecular Dynamic methods. The -CDOCKER energy with high positive value and small difference between -CDOCKER energy and -CDOCKER interaction energy is identified as best criteria for drug. The molecular docking of ADP Ribose phosphatase-Citric acid interaction has established with the highest positive value of -CDOCKER energy 33.2042 and small value of the difference 3.335 between -CDOCKER interaction energy and -CDOCKER energy followed by Gallic acid (shown in Table 1). Thus, the results is indicated towards Citric acid can effectively prevent COVID-19 attack.

CONCLUSIONS

From the present study of molecular docking it was identified that *Psidium guajava* (Guava) plant has possible phytochemical responsible for medicinal action against COVID-19 attack. Using molecular docking through "Discovery Studio module of Biovia software",it was identified that Citric Acid has potency that can significantly interact with the vital enzyme of COVID-19 caused by SARS-CoV-2 and may provide the medicinal values of *Psidium guajava* (Guava) for curing the pandemic disease.

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Table 1. Results of CDocking of phytochemicals with 6w6y (receptor)

SL NO	LIGAND	-CDOCKER ENERGY	-CDOCKER INTERACTION ENERGY	Difference between-CDOCKER interaction energy and -CDOCKER energy	Remarks
1	MALONIC ACID	24.6939	21.3776	3.3163	
2	ASCORBIC ACID	10.2796	27.3893	17.1097	Least effective
3	KAEMPFEROL	23.419	27.9579	4.5389	
4	CATECHIN	22.3351	29.6932	7.3581	
5	GALLIC ACID	27.5569	24.0019	3.555	Second best inhibition
6	CITRIC ACID	33.2042	29.8692	3.335	Maximum inhibition

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) from SARS CoV-2 of using *Prunus dulcis* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase of NSP3 of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Catechin of Prunus dulcis extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

The 2019 Novel coronavirus (2019-nCoV) threatens public health [1, 2], Specific drugs have not been discovered [3]. It's high time to identify medicines against the virus. Medicinal plants are exploited for treating various diseases [4]. The phytochemicals are essentially cost effective. *Prunus dulcis* belongs to family Rosaceae. *Prunus dulcis* is a rich source of nutrients because of phytochemicals including phenolic compounds, phytosterols, flavonoids, phenolic acids, vitamins and fatty acids.etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"BioviaDiscovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Prunus dulcis* belongs to family Rosaceae. *Prunus dulcis* is a rich source of nutrients because of phytochemicals including phenolic compounds, phytosterols, flavonoids, phenolic acids, vitamins and fatty acids.etc. It is known that plants belonging to this family are effective against viruses. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the ADP ribose phosphatase of NSP3 viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Catechin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Catechin plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Catechin can significantly interact with the ADP ribose phosphatase of NSP3.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase of NSP3 (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Methylquercetin	16.7667	28.983	12.2163	Minimum inhibition of viral protein
2	Catechin	23.4794	30.4109	6.9315	Maximum inhibition of viral protein
3	Vanillic acid	19.7045	21.3169	1.6124	
4	Kaempferol	20.9951	27.1805	6.1854	
5	Resveratrol	18.7727	27.6062	8.8335	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 using *Adhatoda vasica* (Vasak) Extract: An *In silico* Analysis

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ABSTRACT

Now the emerging novel coronavirus (2019-nCOV) from Wuhan, China, has created a pandemic situation throughout the globe that worsens the public health and economy. The structural determination shows that the virus is composed of RNA based proteins like N-proteins, S-proteins, envelope and haemagglutinin estaerase dimer. The association of proteins of these viruses with the human creates severe respiratory issue along with affecting the heart, kidney, gastrointestinal system, liver, and central nervous systems. As no specific medicines or vaccines are available to combat this deadly virus, researchers throughout the globe are working seriously to develop proper drugs to neutralize the negative impact of viral proteins. The main aim of this study to identify the phytochemicals extracts from the plant *Adhatoda vasica* which can deactivate enzyme 6vxs of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of *Adhatoda vasica* (Vasak) were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like quercitin and kaempferolcan. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of ADP ribose phosphatase of NSP3 of COVID-19.

Keywords: COVID-19, Biovia, Biovia, *Adhatoda vasica* ,NSP3.

INTRODUCTION

A novel corona virus (nCoV-2019) emerge with a unique characteristic of human-to-human transmission on December 2019 in Wuhan province of China [1] and cause severe acute respiratory syndrome (SARS). This infection has marked as dead-threatening to numerous people around the world within short period of time. On 30th January, 2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. As per the global statistics, the mortality rate is doubled in just 7 days with this deadly virus.

Globally more than 3 million people have been already confirmed with COVID-19 positive along with 274,488 death reports as on 10th May, 2020 (WHO reports). The Indian scenario of COVID-19 is also painful. More than 41, 000 people are enlisted with active cases and 2109 people have been already passed away. By the time, situation is getting worse with this viral infection and the mortality graph approaches to upward and incomplete number of COVID-19 positive cases because the published number is only related to the laboratory confirmation.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [7]. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. To battle this dangerous COVID-19, various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir, and so on, have been attempted and found with certain therapeutic impact in vitro. In any case, the clinical medication response isn't very empowering and toxicity stays an unavoidable issue causing severe effects. This motivated us to examine the restraint of COVID-19 protease by Indian herbal plants [4]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc. [5]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry. The main objective of this article to identify the phytochemicals of *Adhatoda vasica* responsible for inhibiting COVID-19 by ADP ribose phosphatase of NSP3 by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Adhatoda vasica* contains vasicin, vasicinone, peganin, quercetin , kaempferol, etc. It has been reported that Acanthacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[6,7].

Papain-like protease (PLpro) of COVID-19: COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that ADP ribose phosphatase of NSP3 (PDB Id 6vws) is involved in replication of virus.

By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Adhatoda vasica* were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value show the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of ADP ribose phosphatase of NSP3 of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b)small difference between -CDOCKER energy and -CDOCKER energy interaction.

High positive values of C-Docker energy are15.4280 and the difference with Cdocker interaction energy 9.1167 are presented in table-I.TableI also represented the difference in energy which are kaempferol, vasicinone, vasicine, peganine. From these findings it is found that quercitin can effectively deactivate 6vxs, thereby interrupting viral replication.On the other hand, kaempferol shows the second highest affinity towards ADP ribose phosphatase of NSP3 of COVID-19 and therefore, it has the potential to deactivate the enzyme. Vasicine, vasicinone, peganine can less effectively inhibit the viral replication as negative -CDocker energy but shows positive -CDocker interaction energy. Thus, the key phytochemicals quercitin can prevent COVID-19 caused by 6vxs of virus.

CONCLUSIONS

It was reported that *Adhatoda vasica* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like quercitin and kaempferol can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with ADP ribose phosphatase of NSP3 of COVID-19. It was found that quercitin of Adhatoda vasicacan have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The following phytochemicals like Vasicine, vasicinone, peganine were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals quercitin and kaempferol provide the medicinal importance to *Adhatoda vasica* that can act against COVID-19 caused by ADP ribose phosphatase of NSP3.

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Table 1. C-Docking score of different phytochemicals with ADP ribose phosphatase of NSP3 of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Vasicine	-1.4622	18.0087	19.4709
2	Vasicinone	-0.8565	13.6178	14.4743
3	Peganine	-1.4936	17.5796	19.0732
4	Quercitin	15.4280	24.5447	9.1167
5	Kaempferol	14.8936	26.6799	11.7863

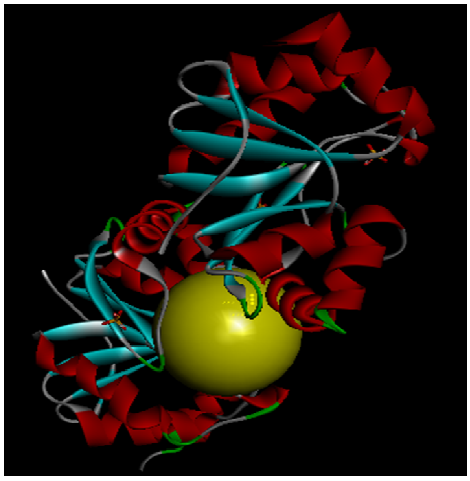

Figure 1. Receptor binding site of ADP ribose phosphatase of NSP3 of COVID-19

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP-Ribose Phosphatase of NSP3 from SARS CoV-2(6W6Y) of using *Prunus dulcis* L. Extract: An *In-silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytoconstituents with "6W6Y of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Kaempferol and vanillic acid of *Prunus dulcis* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: Phytoconstituent, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has caused severe illness among people worldwide [1][2], However, still there are no drugs available to cure the pandemic [3].The bioactive componds present in plants could be a good source of pharmaceutical drugs. They have the potential to be an effective medicine against the virus [4]. They will be really effective and reliable towards fighting this deadly virus. *Prunus dulcis* belongs to family Rosaceae. It contains catechin, vanillic acid, kaempferol,resveratrol etc.

MATERIALS AND METHODS

"Biovia Discovery studio module (Dassault Systemes of France) was used for analysis". Published works demonstrated that *Prunus dulcis* contains phytoconstituent methylquercetin, catechin, vanillic corrosive, kaempferol, resveratrol and so forth. It is realized that plants having a place with this family are powerful against infections. This work is centered around distinguishing proof of the specific phytochemical liable for restraining 6W6Yand controlling of COVID-19. "Brenda enzyme database was used to list different enzymes found in COVID-19".

Molecular docking strategy has been utilized to recognize the phytochemical from the plant extricate, which can deactivate the NSP3 (6W6Y) viral protein. The nitty gritty technique has been portrayed somewhere else [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". "High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug". Table 1 Revealed that Kaempferol is the phytoconstituents that can really prevent COVID-19 attack.

CONCLUSIONS

It was distinguished that *Prunus dulcis* plant can prevent COVID-19 attack. Utilizing "Discovery Studio module of Biovia software", it was recognized that kaempferol can altogether connect with the viralNSP3 (6W6Y).

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Table 1. Results of CDocking of phytoconstituents with NSP3 (6W6Y)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Catechin	17.0889	24.7572	7.6683	
2	Vanillic acid	19.9233	26.0681	6.1448	
3	Kaempferol	19.3442	24.2207	4.8765	High inhibition of viral protein
4	Resveratrol	10.1838	18.2689	8.0851	Low inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Apo-Like Protease (6M03) from SARS CoV-2 using *Allium sativum* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Apo-like protease of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Caffeic acid of *Allium sativum* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic; however, till now there is no established treatment [1, 2, 3]. There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4]. Theirphytochemicals will be low-cost but effective. *Allium sativum* belongs to familyAmaryllidaceae. *Allium sativum* extract is used to cure disease like fungal, viral, bacterial, myotic and parasitic infection. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"BioviaDiscovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Allium sativum* contains like caffeic acid, coumaric acid, feluric acid, sinapic acid and vanilic acid, etc. It is known that plants belonging to this family are effective against viruses. Molecular docking method has been used to identify the phytochemical from the plant extract, which can deactivate the apo-like protease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Caffeic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Allium sativum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Caffeic acid can significantly interact with the viral apo-like protease.

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Table 1. Results of CDocking of phytochemicals with apo-like protease (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	caffeic acid	24.2825	24.1918	0.0907	Maximum inhibition of viral protein
2	coumaric acid	19.6106	21.1553	1.5447	
3	feluric acid	19.9883	26.0522	6.0639	
4	sinapic acid	18.3908	26.2627	7.8719	Minimum inhibition of viral protein
5	vanilic acid	16.6591	19.8459	3.1868	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Apo-Like Protease (6M03) from SARS CoV-2 of using *Aloe barbadensis* Extract: An *In silico* Analysis

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. The main objective of this article is to identify the phytochemicals as ligands which has the capability to deactivate Apo like proteases from SARS CoV-2(6M03) that help for the growth of the virus. Molecular docking of phytochemicals with the viral proteinss can be studied by the Biovia Discovery studio. The interaction of molecule was determined by the energy of -CDocker and-CDocker interaction respectively. More is the negative energy means high positive scores of these two parameters indicates that aloeemodin can effectively inhibit the viral metabolic activity than other phytochemicals present in aloevera It can be predicted that these molecules can interfere with the infection phase of SARS-CoV-2 virus.

Keywords: *Aloe vera*, Phytochemicals, COVID-19, Biovia, SARS-CoV-2

INTRODUCTION

Globally, COVID-19 is considered as an infectious communicable serious pandemic disease . It is imparting life risk consequences for aged people in various countries. On 30th January,2020 The World Health Organization(WHO) has declared that coronavirus outbreak is a Public Health Emergency of International Concern [1,2] This epidemic were first preliminary reported at Wuhan city of China in December 2019 and gradually spread its tentacles worldwide. [3][4]. According to WHO a confirmatory case is that "if a person has undergone with laboratory confirmation of COVID-19 infection"[5]. Unfortunately till today no vaccine and preventive molecular drugs has developed to fight against this disease [6] . Nature has been a source of many medicines in the form of chemicals, enzymes and proteins present in the plantsthrough which modern drugs have been derived [7]. The chemical substances produce by plant has some medicinal that can regulate or affect the human physiology are called as phytochemicals. These chemicals can be used as therapeutic purposes and theses phytochemicals can extract from seed,barks,leaves, fruits and flowers

etc. 8] . These phytochemicals are have various medicinal properties like anti-oxidant, anti diabetic, anti-cancer and anti inflammatory. These molecules can serve as the initiators of production of pharmaceuticals which are Safe and cost effective [9]. About 25% of pharmaceutical drugs available in the market are of botanical origin and the beneficial effects are evaluated by invitro bioassay or experiments using animal models [10]. *Aloe barbadensis* belonging to family *Asphodelaceae* is known to cure many fungal, viral, bacterialand parasitic infection.It is one of the earliest known medicinal plant which is used for health benefits that has sulphur containing compounds in the form of phytochemicals.The main objective of this study to identify phytochemicals present in *Aloe barbadensis* to cure the corona virus disease COVID-19 by inhibiting its metabolism.

MATERIALS AND METHODS

Biovia software (Dassault Systems of France) having Discovery Studio tool was analysed the molecular level interaction between the phyochemicals and enzymes. This software helps in prediction of molecular interaction through machine learning Plant produces phytochemicals as secondary metabolites to protect them from predators and plants usually fights against the micro organisms.Apo-like proteases from SARS CoV-2 (PDB:- 6M03) is a Hydrolase enzyme that play a very crucial for the survival and multiplication of this virus. Molecular interaction between the viral protein and phytochemicals which form a covalent bond to inhibit viral growth.Biovia discovery studio was used for analyzing the molecular interaction to identify the phytochemicals. Phytochemicals were selected from the plant and sdf file downloaded from the website. And PDB code of protein was downloaded from RCSB website. Active site as receptor cavity of this enzyme was selected as "receptor cavity" protocol found under tool "receptor-ligand interaction". For C-Docking in Biovia Discovery studio, enzyme molecule was treated as the receptor molecule and the phytochemical was treated as the ligand. Both "-CDOCKER_ENERGY" and "-CDOCKER_INTERACTION_ENERGY" were determined the strength of molecular docking. High C-Docker score considered as the efficient interaction between the phytochemicals and the viral enzyme. Therefore, high positive values predict the effect of phytochemicals on treatment of COVID-19.

RESULTS AND DISCUSSION

Active site of the 6M03 appears as light green color in fig.1. It is an insilico-based molecular docking method and optimized for accuracy. -CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the nonbonded interaction that exists between the protein and the ligand. The criteria for best interaction was chosen based on a) high positive value of -CDOCKER energy and b)small difference between -CDOCKER energy and -CDOCKER interaction energy. Apoprotease and aloe emodin interaction value is represented in Table-1 and has the highest positive score of -CDOCKER energy 14.1305 kcal/mole and small value of the difference 4.7675 kcal/mole between - C DOCKER interaction energy and - C DOCKER energy. Thus, the results indicated that aloe emodin can effectively deactivate Apoprotease thereby interrupting thehydrolase activity whichprocess the amino-terminal end of the replicase polyprotein to generate two or three replicase productsof the virus . Higher positive values for aloe emodin indicated that it was the most active ingredient against SARS-CoVvirus. Thus, the key phytochemicals aloe emodin preventing COVID-19 caused by SARS-CoV2 virus,

CONCLUSIONS

From this it is concluded that Aloe *barbadensis* has anti-viral properties against COVID-19. It is found that Aloe emodin of *Aloe barbadensis*, which can have an interaction with the viral protein Apo-like proteases significantly to prevent COVID-19. From the molecular docking analysis, It is found that aloe emodin can effectively interact with viral protein to deactivate the viral function. Othe phytochemicals do not much influence on viral protein molecule

to stop their life cycle. Therefore, it can be concluded aloe emodin present in *Aloe barbadensis* has the medicinal values which will be help for curing COVID-19.

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Table 1. C-Docker results of phytochemicals of *Aloe barbadensis* with Apoprotease

SL NO	Phytochemicals	- C Docker energy	- C Docker interaction energy	Difference between - C Docker interaction energy and - C Docker energy	Remark
1	Aloe emodin	14.1305	18.898	4.7675	Maximum inhibition of viral protein
2	Babalocin	Failed	Failed	-	

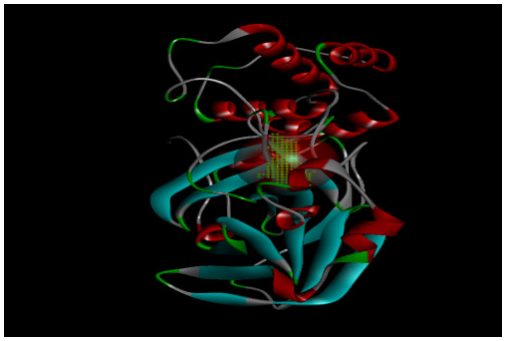

Figure 1. Active site of 6M03

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking COVID-19 Enzyme using *Terminalia arjuna* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19) is an infectious disease produced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". "Molecular docking of the phytochemicals with the microbial enzyme was studied using Biovia Discovery Studio". "Strength of the interaction was evaluated based on -CDocker energy and -CDocker interaction energy". "High positive values for both the parameters indicated that out of different phytochemicals (luteolin) can effectively deactivate the enzymatic metabolic activity thereby interrupting the life cycle of (SARS-CoV-2) virus". "This study focuses on identification of phytochemicals from plant extract has the capability to fight against COVID-19 by deactivate (COVID-19) enzyme which is reported to be very crucial for the survival of the organism".

Keywords: Phytochemicals, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" is communicable syndrome declared by "World Health Organization (WHO) accredited the 2019–20" corona virus outbreak a "Public Health Emergency of International Concern (PHEIC) on 30 January 2020, and a pandemic on 11 March 2020" resulting severe fatal implications for countries [1], [2]. Some of the first cases of the epidemic reported in "December 2019 at Wuhan, the capital of China's Hubei province, which has since escalated globally".[3][4] . First case of this epidemic was report in Dec. 2019 at "Wuhan, the capital of China's Hubei province" have been seeing as escalate globally [3][4]. However, total numbers COVID 19 cases not known [5]. Any kinds of preventives or medicine has not manufacturing so far "due to continuous mutation according to geographic regions for this virus" [6].

Natural plants have good sources of remedial agent since hundreds of years and notable figure of advance drugs have been derived from "natural source" [7]. Therapeutic values of plant s lie chemicals called phytochemicals can be derived from any part of plants derivatives were used for therapeutic purposes [8]. Many plants derivatives and their extracts were revealed many medicinal properties i.e. antioxidant, antiinflammatory, anticancer, antimicrobial

and antidiabetes action etc. [9]. Along with diverse source of usual produce by plants have new chemical substances served primary material for numbers "of old and new pharmaceutical products while proving to be secure price valuable".

"Medicinal plants" are the base of many drugs prescribed by today. "About 25% of modern pharmaceutical drugs have botanical origins". "Research needs in the field of medicinal plants are huge, but are balanced by the potential health benefits and the enormous size of the market. Research into the quality, safety, biological activity, and clinical efficacy of the numerous plants in common usage is required". "Newly emerging scientific techniques and approaches have been used in the growing area of medicinal plant researches, for the investigation of constituents and determination of biological activity of medicinal plants". Proof for beneficial effects of selected plants is generally based on experiments demonstrating a biological activity in a relevant in vitro bioassay or experiments by using animal model.[10] Plants to facilitate demonstrated anticancer, antioxidant, anti-inflammatory, immunostimulatory, and antimicrobial properties have received research attention.

Terminalia arjuna is belonging to family Combretaceae. *Terminalia arjuna* foliage extract used to heal disease like (SARS-CoV-2). The plant is known to contain phytochemicals like luteolinetc. "This study" focus on explore the prospect of using these phytochemicals in curing the disease caused by COVID-19. However, there is no report to identify "the specific phytochemical responsible to cure COVID – 19". "Coronavirus disease 2019 (COVID-19) is a transmittable disease instigated by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)".[11] "However, it is possible to control the disease by inhibiting the metabolic pathway of the microorganism". "This study focuses on the identification of the phytochemical of (luteolin) responsible to cure COVID-19 caused by(SARS-CoV-2) by inhibiting the protien pathway".

MATERIALS AND METHODS

Software used

"Discovery studio module of Biovia software (Dassault Systemes of France) was used for analysis". "The software utilizes machine learning techniques to predict the level of molecular interaction".

Methodology

List of phytochemicals: "Phytochemicals are produced by plants as secondary metabolites to protect themselves from predators. The potential threats to plants include bacteria, viruses, fungi etc. When these plants or their parts are consumed by humans these phytochemicals fight off threats to health. Some phytochemicals have been used as poisons and others as traditional medicine. Published works showed that *Terminalia arjuna* contains (luteolin) etc. It has already been established that different plants belonging to (Combretaceae) family has potential to fight against microbes/viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-19".

Enzyme found in (COVID-19): "It has been reported that COVID-19has various metabolic cycles for its survival. These metabolic cycles are regulated by different enzymes". "Brenda enzyme database was used to identify and list different enzymes found in COVID-19". It has been found that (COVID-19) enzyme (6M03) is involved in luteolin, arjungenin, luteolincycle in order to survive.

Molecular docking: "Molecular docking method has been used to identify the phytochemical from the plant extract, that act as a ligand and form a strong covalent bond with the bacterial protein to successfully inhibit the microbe". "The Discovery studio module of Biovia software was used for identifying molecular interaction and

perform molecular docking". "In this process initially sdf files for the phytochemicals found in the *Terminalia arjuna* plant were downloaded from the website". Then "protein database code of the enzyme was identified from the website". The "active site of the enzyme" was identified via "receptor cavity" protocol found under "receptor-ligand interaction" menu. Molecular docking was done using the CDocker protocol of Biovia software under "receptor-ligand interaction". "The enzyme molecule was treated as the receptor molecule and the phytochemical was treated as the ligand". The "-CDOCKER_ENERGY and -CDOCKER_INTERACTION_ENERGY were used as indicator for the quality of molecular docking". The value is highly positive of those indicators presented a good interaction between the ligand and the receptor. Thus, the "interactions with high values might indicate the major phytochemical responsible for curing the disease".

RESULTS AND DISCUSSION

Figure-1 shows the active site of the (COVID-19) enzyme appears as light green in colour. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm". "It is a grid-based molecular docking method and optimized for accuracy". The "ligand" conformations were obtained by "Molecular Dynamic methods." "-CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the nonbonded interaction that exists between the protein and the ligand.The criteria for best interaction was chosen based on a) high positive value of -CDOCKER energy and b)small difference between -CDOCKER energy and -CDOCKER interaction energy".

Table 1 shows "(C-Docker Ligand Energy)-(C-Docker Energy) interaction has the highest positive value of -CDOCKER energy(27.3559) and small value of the difference (22.2711) between - C DOCKER interaction energy and - C DOCKER energy followed by (5.0848)". "Thus, the results indicated that (luteolin) can effectively deactivate (COVID-19) enzyme thereby interrupting the metabolic pathway of the virus"." Higher positive values for luteolin indicated that it was the most active ingredient against (SARS-CoV-2) virus". "On the other hand, luteolin can deactivate the enzyme to a small extent (negative -CDocker energy but positive -CDocker interaction energy)". As a result key phytochemicals preventing "COVID-19 caused by (SARS-CoV-2) virus" is Luteolin.

CONCLUSIONS

The study identified that *Terminalia arjuna* has "medicinal action against COVID-19". "This study was carried out to find the phytochemical responsible for its medicinal action". By using "Discovery Studio module of Biovia software, molecular docking operation was performed to identify the phytochemical (luteolin), which can have a significant interaction with the vital enzyme (COVID-19) of the virus". It establish (luteolin) can have strong interaction with the enzyme followed by (COVID-19) successfully inhibiting the metabolic cycle of the microbe. (luteolin) were found to be not much effective in deactivating the enzyme of the microbe. Thus, this study concluded the presence of (luteolin) canprovide the medicinal values to (*Terminalia arjuna*) against "COVID-19 caused by(SARS-CoV-2)".

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Table 1. Results of CDocking of phytochemicals with Luteolin

S.L NO	LIGAND	(-)CDOCKER ENERGY	(-) CDOCKER LIGAND ENERGY	DIFFERENCE
1	Arjunetin	FAIL		NA
2	arjungenin	FAIL		NA
3	Arjunolic Acid	FAIL		NA
4	arjunone	FAIL		NA
5	luteolin	22.2711	27.3559	5.0848
6	Terminic Acid	FAIL		NA

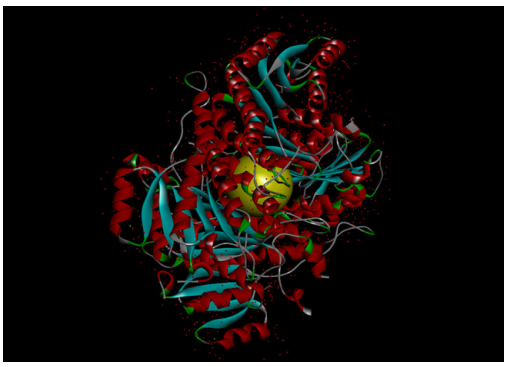

Figure 1. Active site of COVID-19enzyme

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RESEARCH ARTICLE

COVID19 Prevention by Blocking nCoV HR2Domain (6lvn) of using *Trigonella foenum-graecum* L Extracts: An *In silico* Analysis

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ABSTRACT

"Corona virus disease 2019 (COVID-19)" produced "severe acute respiratory syndrome coronavirus 2(SARS CoV 2)". "Molecular docking" of phytochemicals interactions with "microbial enzyme were studied by using Biovia Discovery Studio". "High positive values for both the parameters of -CDocker energy and –Cdocker" energy indicated lysinecan out of different photochemical of *Trigonella foenum-graecum* L. extract can effectively deactivate the deactivating nCoV HR 2 Domain in that way interrupt "SARS CoV 2 virus".

Keywords: Phytochemicals, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" has declared by "World Health Organization (WHO) as pandemic disease [1][2]. First case of this epidemic was report in Dec. 2019 at "Wuhan, the capital of China's Hubei province" have been seeing as escalate globally [3][4]. However, total numbers COVID 19 cases not known [5]. Any kinds of preventives or medicine has not manufacturing yet "due to continuous mutation according to geographic regions for this virus" [6]. Natures of plants have been good sources "medicinal agent" since long period of time and notable numbers of modern medicines has been imitative from it [7]. Therapeutic values of plants lie chemicals called phytochemicals can be derived from any part of plants derivatives were used for therapeutic purposes [8]. Many plants derivatives and their extracts were revealed many medicinal properties i.e. antioxidant, antiinflammatory, anticancer, antimicrobial and antidiabetes action etc. [9]. Along with diverse source of usual produce by plants have new chemical substances served primary material for numbers of old and new pharmaceutical products while proving to be secure price valuable. Evidences from valuable property of selected plants are usually based on experiment indicating organic "activity in a relevant in-vitro bioassay or experiments using animal models" [10]. *Trigonella foenum-graecum* L belongs to family: Fabaceae. Extraction from the leaves and seeds of fenugreek considered safe and are found to have potential therapeutic explicabilities in the treatments and managements of diabetes, cancer, toxicities, cardiovascular diseases, physical injuries, and hormonal imbalance [11]. Plants are known

to contain phytochemicals like Lysine, Sapogenins, Trigonelline, Diosgenin and Galactomannan etc. The experiment revise focus scheduled explore opportunity by "phytochemicals in curing the disease COVID 19" and also identification of the phytochemical of *Trigonella* responsible to cure COVID19 cause by "(SARS-CoV-2)" inhibit nCoV HR2 Domain. However, till now, no report is prepared of identify the specific "phytochemicals" responsible to cure "COVID 19".

MATERIALS AND METHODS

Software Used

"Discovery studio module of Biovia software (Dassault Systemes of France) was used for analysis". Software utilized "machine learning techniques" to predict the level of molecular interaction.

Methodology

List of phytochemicals: Production of "phytochemicals" used secondary metabolites to defend from their predators. Published works showed that *Trigonella* contains Lysine, Sapogenins, Trigonelline, Diosgenin and Galactomannan. Diverse plants belonging to family: Fabaceae have enormous potentials for fight against microbes/viruses has already been established. This piece of work focused to identify particular phytochemicals responsible for inhibit and control of COVID19.

Enzyme found in SARS CoV 2: "COVID 19" utilize different "metabolic cycles for its survival" as reported. The "metabolic cycle were controlled by different enzymes". "Brenda enzyme database was used to identify and list different enzymes found in COVID 19". This was observed 2019-nCoV HR2 Domain protein (PDB: 6lvn) is involved in the fusion of the viral membrane with the host cell membrane**.**

Molecular docking: "Molecular docking methods was used to identify the phytochemical from the plant extract that act as a ligand and form a strong covalent bond with the bacterial protein to successfully inhibit the microbes". "The Discovery studio module of Biovia software was used for identifying molecular interaction and performs molecular docking". Firstly sdf files were downloaded for the phytochemical found in the *Trigonella* plant then "protein database code of the enzyme" identify from the website. "Active site of enzyme was identified via receptor cavity protocol found under receptor-ligand interaction menu. Molecular docking was done by using the CDocker protocol of Biovia software" under "receptor-ligand interaction". "-CDOCKER_ENERGY and "-CDOCKER_INTERACTION_ENERGY" was use an indicator for the quality of "molecular docking". The high positive values indicated good interaction between the ligand and receptors. Thus, interactions with high values might indicate the major phytochemical responsible for therapeutic.

RESULTS AND DISCUSSION

Figure-1 showed active site of 6lvn which appear light green in colour. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy" and "ligand" conformation was obtain "Molecular Dynamic methods."

"-CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the nonbonded interaction that exists between the protein and the ligand. The criteria for best interaction was chosen based on a) high positive value of -CDOCKER energy and b)small difference between -CDOCKER energy and -CDOCKER interaction energy".

Table-1 shown 6lvn-Lysine interaction had "high positive valued of –CDOCKER" energy15.0491 and small valued of the differences noticed 0.0964 between -CDOCKER interaction energy and -CDOCKER energy was followed by scopoletin. Therefore results indicate that Lysine can effectively neutralize 6lvn, in that way interrupting the fusion of the viral membrane with the host cell membrane of virus. Higher positive values for Lysine indicates the majority active ingredient against "SARS-CoV-2 virus". On the other hand Lysinecan neutralize the enzyme to a small extent "(negative -CDocker energy but positive -CDocker interaction energy)". As a result the key phytochemicals preventing "COVID-19 caused by SARS-CoV-2virus" was Lysine.

CONCLUSIONS

The study was identified as *Trigonella* plants have remedial action against to COVID 19 carried out for remedial actions by "Discovery Studio module of Biovia software, molecular docking operation was performed to identify the phytochemical have a significant interaction with vital enzyme nCoV HR2 Domain of virus". It had been found that Lysinecan contain strong interaction with the enzyme followed in *Trigonelle* productively inhibiting the "metabolic cycle of the microbe". Thus, this study could explain that the presence of Lysine can provide medicinal values to *Trigonella* against "COVID 19 caused by (SARS-CoV-2)".

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Table- 1. Results of "CDocking of phytochemicals" with 6lvn

Sl. No	LIGAND	- CDOCKER ENERGY	- CDOCKER INTERACTION ENERGY	Difference between - CDOCKER interaction energy and - CDOCKER energy
1	LYSINE	15.0491	15.1455	-0.0964
2	COUMARIN	4.99157	8.05347	-3.0619
3	TRIGONELLE	14.3356	13.7424	0.5932
4	SCOPOLETIN	8.31507	12.6148	-4.29973
5	FENUGREEKINE	error		

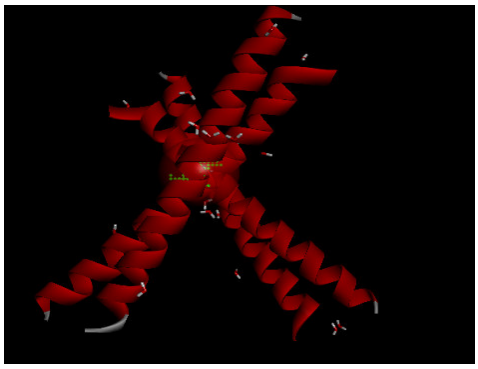

Figure 1. Active site of 6lvn

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Non-Structural Protein 9 of SARS CoV-2 using *Bhringraj* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "non-structural protein 9 of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated thatHeptadecane of*Bhringraj*extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[6]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[9] Their phytochemicals will be low-cost but effective. *Bhringraj* belongs to family Asteraceae. It contains6,10,14-trimethyl-2-pentadecanone, 7,11-Dimethyl-3-methylene-1,6Z,10-dodecatriene, octadea-9-enoic acid,Phytol, Pentadecane, Heptadecane etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that bhringarajcontains 6,10,14-trimethyl-2-pentadecanone, 7,11-Dimethyl-3-methylene-1,6Z,10-dodecatriene, octadea-9-enoic acid,Phytol, Pentadecane, Heptadecaneetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting non-structural protein 9and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the non-structural protein 9viral protein. The detailed method has been described elsewhere.

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Heptadecane is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that guava plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatheptadecane can significantly interact with the viralnon-structural protein 9.

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Table 1. Results of CDocking of phytochemicals with non-structural protein 9 (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	6,10,14-trimethyl-2-pentadecanone	20.1835	20.297	0.1135	
2	7,11-Dimethyl-3-methylene-1,6Z,10-dodecatriene	12.5627	30.546	17.9833	
3	octadea-9-enoic acid	25.5068	35.1775	9.6707	
4	Phytol	6.25999	33.6672	27.40721	Minimum inhibition of viral protein
5	Pentadecane	34.193	35.5291	1.3361	
6	Heptadecane	36.4839	37.6824	1.1985	Maximum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Nsp9 Replicase Enzyme using *Ficus religiosa* (Peepal), Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "non-structural protein 9 (Nsp9) of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated thatbergaptol of *Ficus religiosa* (Peepal) extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is caused by a deadly virus that has affected the health of people worldwide and been considered as a pandemic [1] [2].But, there is no specific treatment till now [3]. Plants contain a good source of phytochemicals which can be used for potential drug development against the disease [4]The drugs which will produced using these phytochemicals will be very effective and of low cost. *Ficus religiosa* belongs to family Moraceae. It contains phytochemicals like lanosterol, beta sitosterolglucoside, bergaptol, bergapten, stigmasterol, etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Ficus religiosa* contains lanosterol, beta sitosterol glucoside, bergaptol, bergapten, stigmasterol, etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Nsp9 and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate the Nsp9viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that bergaptol is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Ficus religiosa* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatbergaptol can significantly interact with the viral protein Nsp9.

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Table 1. Results of CDocking of phytochemicals with Nsp9 (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1.	lanosterol	failed	failed	failed	
2.	Beta sitosterolglucoside	failed	failed	failed	
3.	Bergapten	3.0332	14.8539	11.8209	Minimum inhibition of viral protein
4.	Bergaptol	11.8936	18.5632	6.6696	Maximum inhibition of viral protein
5.	stigmasterol	failed	failed	failed	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Nsp9 Replicase Enzyme using *Trigonella foenum-graecum* (Meethi) Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the bioactive substance present in the plant with "Nsp9 replicase enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". The positive value of "-CDocker energy and -CDocker interaction energy" in high amount revealed that Scopoletin extract can significantly inhibit the action of "SARS-CoV-2 virus".

Keywords: Bioactive substance, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)"has frighten the total globe. It has been declared as an epidemic. [1][2], However human being is still struggling to overcome this as there is no established treatment .[3]There is a need to select medicines against the virus. Medicinal plants are helpful in treating many harmful disease.[4]. The bio active substances present in the plant will pave new way for drug discovery .And these drugs would be very low in cost and these are effective. Fenugreek (Methi) belongs to family Fabaceae. It contains lysine, coumarin, trigonelle, scopoletin, fenugreekine, nicotinic acid, saponins, and L-trytophan etc. This study identifies the bioactive substance which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio module (Dassault Systemes of France) was used for analysis". Previous published works showed that Fenugreek contains lysine, coumarin, trigonelle, scopoletin, fenugreekine, nicotinic acid, saponins, and L-trytophan etc etc. It is known that plants belonging to this family are effective against viruses. This work is focused on selection of the particular bio active substance responsible for inhibiting Nsp9 replicase enzyme and controlling of COVID-19. "Brenda enzyme database was used to list different enzymes found in COVID-19" . Molecular docking

method has been used to identify the phytochemical from the plant extract, that can deactivate the. Nsp9 replicase. The detailed method has been illustrated in some other place [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". "High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the benchmarks to recognize the drug". Table 1 shows that Scopoletin is the secondary metabolite that can really prevent COVID-19.

CONCLUSIONS

It has concluded that the Fenugreek plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was examined that Scopoletin can effectively deactivate the enzyme Nsp9 replicase of the virus.

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Table 1. Results of CDocking of bioactive substance with "Nsp9 replicase enzyme

SL NO	LIGAND	-C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Lysine	25.5317	27.5391	2.0074	
2	Coumarin	11.983	15.1731	3.1901	Low inhibition of viral protein
3	Trigonelle	25.0151	26.1777	1.1626	
4	Scopoletin	11.3411	15.5079	4.1668	High inhibition of viral protein
5	Fenugreekine	Error			
6	Nicotinic acid	16.8338	19.8805	3.0467	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Nsp9 RNA Binding Protein using *Psidium guajava* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Nsp9 RNA Binding Protein of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Citric acid of Nsp9 RNA Binding Protein extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic; however, till now there is no established treatment [1, 2, 3]. There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4]. *Psidium guajava* belongs to family Myrtle. Leaves of *Psidium guajava* extract is used to cure diseases like diarrhea, diabetes, cough, cataracts, high colestreol, heart and cancer. Phytochemicals like malonicacid, ascorbic acid, kaempferol, catechin, Gallic acid and citric acid etc. are found in the *Psidium guajava*. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"BioviaDiscovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Psidium guajava* contains malonicacid, ascorbic acid, kaempferol, catechin, Gallic acid and citric acid etc. It is known that plants belonging to this family are effective against viruses. Molecular docking method has been used to identify the phytochemical from the plant extract, which can deactivate the Nsp9 RNA Binding Protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Citric acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Psidium guajava* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Citric acid can significantly interact with the viral Nsp9 RNA Binding Protein.

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Table 1. Results of CDocking of phytochemicals with Nsp9 RNA Binding Protein (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	GALLIC ACID	22.2036	18.838	3.3656	
2	MALONIC ACID	22.4483	17.937	4.5113	
3	CITRIC ACID	33.334	28.4567	4.8773	Maximum inhibition of viral protein
4	KAEMPFEROL	20.0083	24.8975	4.8892	
5	CATECHIN	21.6986	27.7805	6.0819	
6	ASCORBIC ACID	7.54137	27.983	20.4416	Minimum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking NSP15 Endoribonuclease Enzyme using Methi *(Trigonella foenum-graecum)* Extract: an in silico analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" usually occurred due to "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the bioactive substance with "NSP15 Endoribonuclease, enzyme of SARS-CoV-2"was examined using "Biovia Discovery Studio". The positive values of "-CDocker energy and -CDocker interaction energy"in higher grades reflected that Fenugreek extract can effectively fight against"SARS-CoV-2 virus".

Keywords: Bioactive substance, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has engulfed the total universe. It has been declared as a pandemic.[1][2],Till now there is no established way of treating the disease has been discovered .[3]There is a need to design drug against this virus. There are a number of medicinal plants treating various infectious diseases.[4]The photoactive substance present in the plant will be low-cost and effective. Fenugreek (Methi) belongs to family Fabaceae .It contains lysine, coumarin, trigonelle, scopoletin, fenugrekine, etc as itsbioactive substance. This study involves identification of those bioactive which can slow down the process of COVID-19 and heal it.

MATERIALS & METHODS

"BioviaDiscovery studio module (Dassault Systemes of France) was used for analysis". Literature review showed that Fenugreek contains lysine, coumarin, trigonelle, scopoletin, fenugrekine, etc etc. It is known that plants belonging to this family shows a strong inhibition capacity towards viruses. This work is focused in recognizing of the particular bioactive substance responsible for restraining, NSP15 Endoribonuclease, enzyme activity and controlling of COVID-19. "Brenda enzyme database was used to list different enzymes found in COVID-19". Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the NSP15 Endoribonuclease, enzyme of the virus . The nitty –gritty of the process has been depicted elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". "High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the bench mark in selection procedure of the drug". Table 1 shows that s the bioactive substances that can really cure COVID-19 .

CONCLUSIONS

It was concluded that fenugreek plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was well observed that Scopoletin was very active in suppressing the NSP15 Endoribonuclease, enzyme.

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Table 1. Results of CDocking of phytochemicals with NSP15 Endoribonuclease, enzyme

SL NO	LIGAND	-C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Lysine	17.7642	17.877	0.1128	
2	Coumarin	9.41487	12.566	3.1512	
3	Trigonelle	15.9321	15.148	-0.784	Less inhibition of viral protein
4	Scopoletin	13.3346	17.165	3.8301	More inhibition of viral protein
5	Fenugreekine	Error			
6	Nicotin acid	10.4695	12.557	2.0877	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Nucleocapsid Protein N-terminal RNA Binding Domain (6M3M) of using *Trigonella foenum-graecum* Extract: An *In-silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "nucleocapsid protein N-terminal RNA binding domain (6M3M) which is reported to be very crucial for the survival of the organism, of SARS-CoV-2".The molecular docking of the phytochemicals with microbial enzyme was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Lysine of *Trigonella* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Theirphytochemicals will be low-cost but effective. *Trigonella Foenum-graecum* L belongs to family Fabaceae.The consumption of the seeds as a spice results in different medicinal effects such as hypocholesterolemic, antidiabetic, hepatoprotective, antibacterial, anthelmintic, anticancer, and galactogogue. It containsFlavonoids, saponins, pyridine alkaloids, and steroidal sapogenins which are some of the phytochemicals present in that plant .This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Trigonella* contains contains Lysine, Sapogenins, Trigonelline, Diosgenin, Galacto mannan etc. It has already been established that different plants belonging to Fabaceae family has potential to fight against microbes/viruses. .

It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibitingthat nucleocapsid protein N-terminal RNA binding domain (PDB: 6M3M) areresponsible for RNA binding [17] and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the nucleocapsid protein N-terminal RNA binding domain (PDB: 6M3Mviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".
High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.Table 1 shows that Lysine is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Trigonella* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatLysine can significantly interact with the viralnucleocapsid protein N-terminal RNA binding 6M3M Protein

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Table 1. Results of CDocking of phytochemicals with 6M3M

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Lysine	20.3635	20.3401	0.0234	
2	Coumarin	10.9507	14.0904	3.1397	Minimum inhibition of viral protein
3	Trigonelle	21.0697	20.3537	0.716	Maximum inhibition of viral protein
4	Scopoletin	15.4112	20.143	4.7318	
5	Fenugreekine	error			
6	Nicotin acid	13.2469	15.4093	2.1624	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Nucleocapsid Protein N-terminal RNA Binding Domain Enzyme using *Prunus dulcis* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "nucleocapsid protein N-terminal RNA binding domain enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Catechin of *Prunus dulcis* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2.

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" has put the entire world in risk, being declared as pandemic [1, 2], No specific drugs has been discovered yet [3]. Specific medications against this deadly virus need to be developed. Plants are bestowed with phytochemicals which presumably are effective against several diseases [4]. Phytochemicals are cost effective and also act specifically against the disease causing agents. *Prunus dulcis* belongs to family Rosaceae. It contains methyl quercetin methyl quercetin, catechin, vanillic acid, kaempferol, resveratol, etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Prunus dulcis* contains methyl quercetin methyl quercetin, catechin, vanillic acid, kaempferol, resveratol, etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting nucleocapsid protein N-terminal RNA binding domain enzyme and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the nucleocapsid protein N-terminal RNA binding domain enzyme. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Catechin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Prunus dulcis* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Catechin can significantly interact with the nucleocapsid protein N-terminal RNA binding domain enzyme.

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Table 1. Results of CDocking of phytochemicals with nucleocapsid protein N-terminal RNA binding domain enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Methyl quercetin	17.9855	30.9655	12.98	Minimum inhibition of viral protein
2	Catechin	24.4273	31.0106	6.5833	Maximum inhibition of viral protein
3	Vanillic acid	15.4835	16.7611	1.2776	
4	Kaempferol	21.6643	26.4227	4.7584	
5	Resveratrol	16.5034	24.9676	8.4642	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Papain-Like Protease (6W9C) from SARS CoV-2 of using *Prunus dulcis* L. Extract: An *In-silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytoconstituents with "protease (6W9C)ofSARS-CoV-2"was studied using "Biovia Discovery Studio". High positive estimations of "- CDocker energy and - CDocker interaction energy" showed that Vanillic acid of *Prunus dulcis* L. concentrate can successfully battle against "SARS-CoV-2 virus".

Keywords: Phytoconstituent, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus diseases 2019 (COVID-19)" has sabotaged the entire world. A pandemic situation has aroused around the world.[1][2]. Till now there is no proper cure of "COVID-19" [3].Phytochemicals derived from plants could be an alternative approach to solve this problem. They can be used as potential drugs to get rid of this viral infection.[4]. *Prunus dulcis* L. contains a few phytochemicals that may assist with inhibiting SARS-coV-2 infection for example Vanillic acid, Kaemferol, and so on. This examination distinguishes those phytoconstituents which can cure the "COVID-19 attack".

MATERIALS AND METHODS

"Biovia Discovery studio module (Dassault Systemes of France)" was used for analysis. From the review of literature, it is realized that plants having a place with this family Rosaceae are powerful against infections. This work is focused around the recognizable proof of the specific phytochemical liable for inhibiting papain-like protease from SARS CoV-2(PDB: 6W9C) and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. The molecular docking strategy has been utilized to identify the phytochemicals from

the plant extract, which can deactivate the Papain-like protease from SARS CoV-2(PDB: 6W9C) viral protein. The point by point technique has been depicted somewhere else [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 revealed that Vanillic acid is the phytoconstituent that can actually avert COVID-19 attack.

CONCLUSIONS

It was identified that *Prunus dulcis* is effective against the "COVID-19 attack". Utilizing "Discovery Studio module of Biovia programming", it was recognized that Vanillic acid can interact with the viral papain-like protease from SARS CoV-2.

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Table 1. Results of CDocking of phytoconstituentwith Papain-like protease from SARS CoV-2(PDB: 6W9C) i.e. receptor.

Sl No.	Ligand	- C docker energy	- C docker interaction energy	Difference between - C dockerinteraction energy and - C docker energy	Remarks
1	Methylquercetin	19.3005	31.2871	11.9866	Lowest inhibition
2	Catechin	28.3525	38.9144	10.5619	
3	Vanillic acid	19.5644	21.6802	2.1158	Highest inhibition
4	Kaempferol	25.7611	31.9523	6.1912	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking SARS-CoV-2 Enzyme using Guava Leaf Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals constituents with "SARS-CoV-2 enzyme" was studied using "Biovia Discovery Studio". The value of "-CDocker energy and -CDocker interaction energy" in higher grades of positive value give an indication that guava leaf can be significant in defeating"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has created a pandemic situation. The "World Health Organization (WHO)" has officially recognised coronavirus upsurge as a "Public Health Emergency of International Concern (PHEIC)".[1][2],Human being is trying his best to overcome this uncontrolled situation, however he is helpless as there is no established course of treatment .[3]Nature has provided a large no of plants and from this there are a number of medicinal plants used in healing process of disease.[4]. These plants have secondary metabolites which could be well utilised for low-cost drug discovery. Guava belongs to family Myrtaceae. Its extract is used to cure many diseases. The plant contains phytochemicals constituents like malonic acid, ascorbic acid, kaempferol, catechin, gallic acid, citric acid etc. This study involves identifies and selection of thos e phytochemicals constituents which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Previous literature give information that guava leafcontains malonic acid, ascorbic acid, kaempferol, catechin, gallic acid, and citric acid It is known that plants belonging to Myrtaceae family are effective against viruses. This work is focused on identification

of the particular phytochemical responsible for inhibiting and controlling of COVID-19. ''Brenda enzyme database was used to list different enzymes found in COVID-19''. Molecular docking method has been used to recognize and select the secondary metabolite from the plant extract that can inactivate the viral protein. The process is illustrated in some other article.[5]

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". "High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug''. Table 1 shows that citric acid is the phytochemical constituents that can really cure COVID-19 .

CONCLUSIONS

It was well identified that guava plant can check COVID-19. Using "Discovery Studio module of Biovia software", it was well recognized that citric acid plays a major role in inhibiting enzyme SARS-CoV-2.

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Table 1. Results of CDocking of phytochemicals with 6LNV (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	MALONIC ACID	21.9192	18.0545	3.8647	
2	ASCORBIC ACID	6.16268	28.3171	22.15442	Least effective
3	KAEMPFEROL	25.7684	34.0574	8.289	
4	CATECHIN	29.6306	37.0988	7.4682	Second against the virus
5	GALLIC ACID	25.6526	23.5091	2.1435	
6	CITRIC ACID	34.2647	27.4092	6.8555	Best results

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking SARS-CoV-2 Enzyme using *Psidium guajava*, Guava Leaf Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "SARS-CoV-2 enzyme"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Citric acid of *Psidium guajava* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2.

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic; however, till now there is no established treatment [1, 2, 3]. There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4]. Their phytochemicals will be low-cost but effective. *Psidium guajava* belongs to myrtle family (Myrtaceae). It contains malonic acid, ascorbic acid, kaempferol, catechin, gallic acid, citric acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"BioviaDiscovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Psidium guajava* contains malonic acid, ascorbic acid, kaempferol, catechin, gallicacid, citric acid etc. It is known that plants belonging to this family are effective against viruses. Molecular docking method has been used to identify the phytochemical from the plant extract, which can deactivate the SARS-CoV-2 enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Citric acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Psidium guajava* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Citric acid can significantly interact with the viral SARS-CoV-2 enzyme.

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Table 1. Results of CDocking of phytochemicals with SARS-CoV-2 enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	MALONIC ACID	18.0881	13.3259	4.7622	
2	ASCORBIC ACID	3.27671	20.3881	17.11139	Minimum inhibition of viral protein
3	KAEMPFEROL	17.2574	22.8827	5.6253	
4	CATECHIN	21.3625	30.9284	9.5659	
5	GALLIC ACID	23.3843	19.641	3.7433	
6	CITRIC ACID	26.8969	21.6098	5.2871	Maximum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Tyrosine Phenol-Lyase(6M03) of using *Trigonella foenum-graecum* L Extract: An *In silico* Analysis

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. The main objective of this article is to identify the phytochemicals as ligands which has the capability to deactivate tyrosine phenol-lyase from SARS CoV-2(6M03) that help for the growth of the virus.Molecular docking of phytochemicals present in methi (*Trigonella foenum*) interact with the viral proteins can be studied by the Biovia Discovery studio. The interaction of molecule was determined by the energy of -CDocker and -CDocker interaction respectively. More is the negative energy means high positive scores of these two parameters indicate that Trigonelle can effectively inhibit the viral metabolic activity than other phytochemicals present in methi. It can be predicted that these molecules can interfere with the infection phase of SARS-CoV-2 virus.

Keywords: *Trigonella foenum*, phytochemical, Biovia, Discovery studio, COVID-19.

INTRODUCTION

Globally, COVID-19 is considered as an infectious communicable serious pandemic disease. It is imparting life risk consequences for aged people in various countries. On 30th January,2020 The World Health Organization(WHO) has declared that coronavirus outbreak is a Public Health Emergency of International Concern [1,2] This epidemic were first preliminary reported at Wuhan city of China in December 2019 and gradually spread its tentacles worldwide. [3, 4]. According to WHO a confirmatory case is that "if a person has undergone with laboratory confirmation of COVID-19 infection"[5]. Unfortunately till today no vaccine and preventive molecular drugs has developed to fight against this disease [6]. Nature has been a source of many medicines in the form of chemicals, enzymes and proteins present in the plantsthrough which modern drugs have been derived [7]. The chemical substances produce by plant

has some medicinal that can regulate or affect the human physiology are called as phytochemicals. These chemicals can be used as therapeutic purposes and theses phytochemicals can extract from seed,barks,leaves, fruits and flowers etc.[8].These phytochemicals are have various medicinal properties like anti-oxidant, anti diabetic, anti-cancer and anti inflammatory. These molecules can serve as the initiators of production of pharmaceuticals which are Safe and cost effective [9].About 25% of pharmaceutical drugs available in the market are of botanical origin and the beneficial effects are evaluated by invitro bioassay or experiments using animal models [10].

Trigonella foenum-Graecum L belongs to familyFabaceae. It is reported that *Trigonella* has been used for curing many diseases like gastrointestinal disorder, diabetes, cancer and other infectious diseases [11]. This plant contains phytochemicals like Lysine Sapogenins, Trigonelline, Diosgenin Galactomannan etc. The main objective of this study to identify phytochemicals present in Trigonella *foenum* (methi) to cure the corona virus disease COVID-19 by inhibiting its metabolism.

MATERIALS AND METHODS

Biovia software (Dassault Systems of France) having Discovery Studio tool was analysed the molecular level interaction between the phyochemicals and enzymes. This software helps in prediction of molecular interaction through machine learning [12]. Plant produces phytochemicals as secondary metabolites to protect them from predators and plants usually fights against the micro organisms. Published works shows that *Trigonella* contains contains phytochemicals like Lysine, Sapogenins, Trigonelline, Diosgenin and Galactomannan etc. Plants belong to family *Fabaceae*family have capacity to inhibit infection of viruses and according to this identification of the particular phytochemical responsible can inhibit multiplication COVID-19. tyrosine phenol-lyase from SARS CoV-2 (PDB:-6M03) is a Hydrolase enzyme that play a very crucial for the survival and multiplication of this virus.

Molecular interaction between the viral protein and phytochemicals which form a covalent bond to inhibit viral growth.Biovia discovery studio was used for analyzing the molecular interaction to identify the phytochemicals. Phytochemicals were selected from the plant and sdf file downloaded from the website. And PDB code of protein was downloaded from RCSB website. Active site as receptor cavity of this enzyme was selected as “receptor cavity” protocol found under tool "receptor-ligand interaction". For C-Docking in Biovia Discovery studio, enzyme molecule was treated as the receptor molecule and the phytochemical was treated as the ligand. Both “-CDocker_energy” and “-C Docker Interaction energy” were determined the strength of molecular docking. High C-Docker score considered as the efficient interaction between the phytochemicals and the viral enzyme. Therefore, high positive values predict the effect of phytochemicals on treatment of COVID-19.

RESULTS AND DISCUSSION

Active site of the 6M03 appears as light green color in fig.1. It is an insilico-based molecular docking method and optimized for accuracy. - CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the nonbonded interaction that exists between the protein and the ligand. The criteria for best interaction was chosen based on a) high positive value of -CDOCKER energy and b)small difference between -CDOCKER energy and -CDOCKER interaction energy. Molecular interaction between 6M03 and trigonelle has shown the highest positive score of -CDocker energy 20.717and least difference 0.2342 between - C DOCKER interaction energy and - C DOCKER energy followed by Lysine.

Thus, the results indicated that Trigonelle can effectively deactivate protein thereby interrupting thehydrolase activity whichprocess the amino-terminal end of the replicase polyprotein to generate two or three replicase

products of the virus. Higher positive values for Trigonelle has indicated that it was the most active ingredient against SARS-CoVvirus. On the other hand, lysine, coumarin and Scopoletin can deactivate the enzyme to a small extent. Thus, the key phytochemicals preventing COVID-19 caused by SARS-CoVvirus is Trigonelle followed by lysine.

CONCLUSIONS

From this it is concluded that methi has anti-viral properties against COVID-19. It is found that Trigonelle of *Trigonella foenum*, which can have an interaction with the viral protein tyrosine phenol-lyase significantly to prevent COVID-19. From the molecular docking analysis, It is found that Trigonelle can effectively interact with viral protein followed by lysine to deactivate the viral function. Other phytochemicals present in this plant have not much influence on viral protein molecule to stop their life cycle. Therefore, it can be concluded Trigonelle molecule present in *Trigonella foenum* has the medicinal values which will be help for curing COVID-19.

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Table 1. Results of molecular interaction of C-Docking with 6M03 and phytochemicals

SL NO	LIGAND	- C Docker Energy	- C Docker interaction energy	Difference between - C Docker interaction energy and - C Docker energy
1	Lysine	17.5088	17.0059	0.5029
2	Coumarin	10.0084	13.1506	3.1422
3	Trigonelle	20.717	20.9512	0.2342
4	Scopoletin	12.4053	16.3782	3.9729
5	Fenugreekine	error		

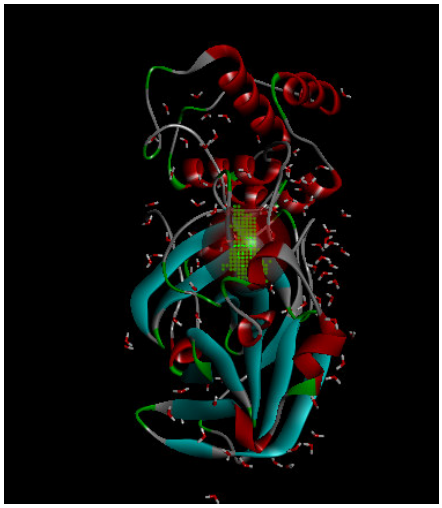

Figure 1. Receptor binding site of 6M03

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RESEARCH ARTICLE

In silico Analysis of Poly13α D-Galactose and Polyvinyl Chloride Compatibility in a Blend

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ABSTRACT

Combination of two or more components results in the formation of a blend. The compatibility of Poly13αd-Galactoseand polyvinyl chloride were studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram andmixingenergy.The results indicated that the pair can become compatible at both low and high temperature. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of ethylene phthalate. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of acrylic acid. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of acrylic acid. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend,In Silico, Poly13αd-Galactose,Polyvinyl Chloride.

INTRODUCTION

When more than one component combine by keeping their identity in the mixture then blend or composites are formed. As it is challenging to find multiple properties in a single material, it is desirable to combine distinctive components thereby enhancing the quality of the material. Development of a single material with the desired

property concerns significant research and time. A blend utilizes the vantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby downgrading the cost of development of products with desired properties.When two or more polymers, or fibers and polymer, or particles and polymer are combined then polymer blend can also be made.

Nano material modified polymers paved the way to multifunctional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method andthis technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. 13αd-Galactoseexists in both open chain and cyclic form.The open chain form has a carbonyl at the end of the chain.Four isomers are cyclic, two of them with a pyranose (six membered)ring, two with a furanose(five membered)ring.In the cyclic form there are two isomers, named alpha and beta,since the transition from the open chain form to the cyclic form involves the creation of new sterio-center at the site of the open chain carbonyl. Vinyl chloride is also called chloro ethane. It is an organochloride with the formula H_2C=CHCL. It is among top twenty largest petrochemicals in the world production. It comes under the class of flammable liquid.

MATERIALS AND METHODS

Software Used

Materials studio module of Biovia software (DassaultSystemesof France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology

Poly13α d-Galactose and polyvinyl chloride were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. Poly13α d-Galactosewas used as the base and polyvinyl chloride was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of Poly13α d-Galactose and polyvinyl chloride were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of Poly13αd-Galactoseon the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of Poly13αd-Galactose and polyvinyl chloride as potential components of a blend was analyzed using Biovia Materials Studio. In this work the use of Poly13αd-Galactoseand polyvinylchloride as potential

components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

ENERGY PARAMETES

Free Energy of Mixing

A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m - \Delta H_m - T\Delta S_m \quad (1)$$

Where $\Delta G_m = Gibb's\ free\ energy\ of\ mixing$

$\Delta H_m = Enthalpy\ of\ mixing$

$\Delta S_m = Entropy\ of\ mixing$

$T - Absolute\ temperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy increases with increase in temperature (up to 275 K) as evident from Eq. 1 and free energy decreases with increase in temperature. The results indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between Poly13α-d-Galactose polyvinyl chloride with negative value of mixing energy,which may lead to form a particular shape with significantly high effort.

Chi Parameter

The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that

the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

Phase Diagram

The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:
a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K). b. Fragmented metastable regions existed between binodals and spinodals, and
c. The two-phase separated regions of immiscibility are bordered by the spinodals.
The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.

When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing Energy

A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature.The temperature is vary from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

MECHANICAL PROPERTIES

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of vinyl chloride.

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6shows that the shear modulus of the composite increases linearly with increase in mass fraction of vinyl chloride.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7shows that the Young's modulus of the composite increases linearly with increase in mass fraction of vinyl chloride.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8shows that the Poisson ratio of the composite decreases linearly with increase in mass fraction of vinyl chloride.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9shows that the brittle fracture stress of the composite decreases with increase in mass fraction of vinyl chloride.

THERMAL PROPERTIES

Heat capacity: It is the amount of heatrequired to raise the temperature of unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of vinyl chloride.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11shows that the thermal conductivity of the composite increases slightly with increase in mass fraction of vinyl chloride.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of vinyl chloride.

INTENSIVE PROPERTIES

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite increases linearly with increase in mass fraction of vinylchloride

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14shows that the density of the composite increases linearly with increase in mass fraction of vinyl chloride.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the membrane.

Figure 15 shows that the permeability of oxygen through the composite decreases with increase in mass fraction of vinyl chloride. Figure 16 shows that the permeability of nitrogen through the composite decreases with increase in mass fraction of vinyl chloride. Figure 17 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of vinyl chloride. Thus, the results indicated that an increase in acrylic acid fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of Poly13d-Galactose and vinyl chloride to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of vinyl chloride. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of vinyl chloride. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in vinyl chloride fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases decreased with increase in mass fraction of vinyl chloride. Usually

components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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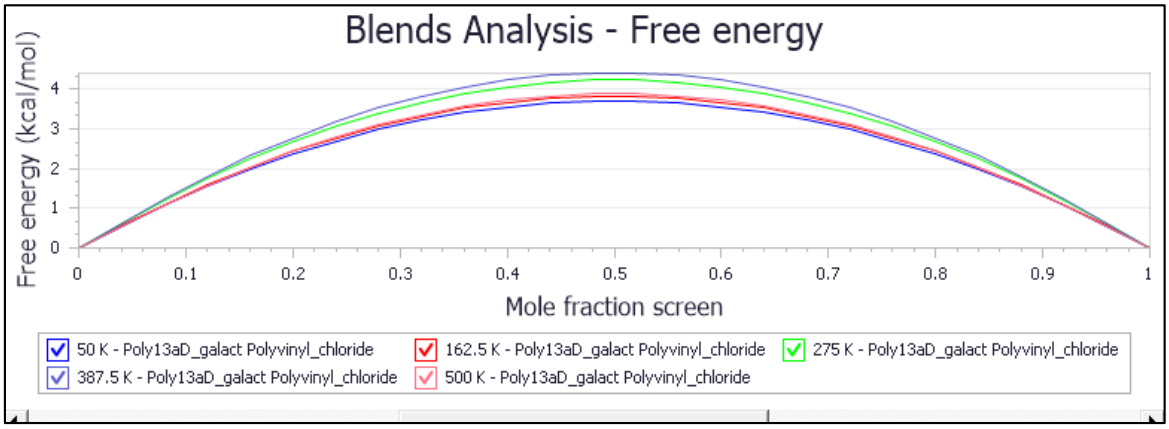

Figure 1. Free energy change with mole fraction of Poly13$_\alpha$ d-Galactose polyvinyl chloride at different temperatures

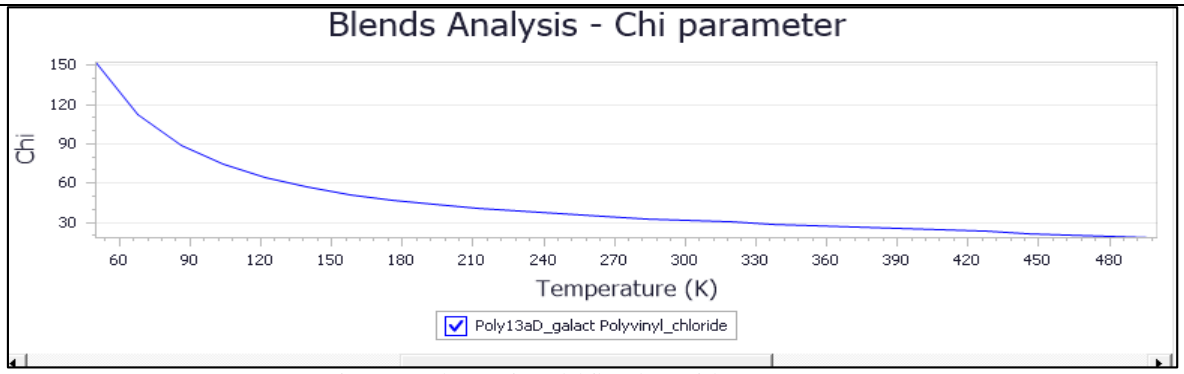

Figure 2. Change in χ (chi) value with temperature

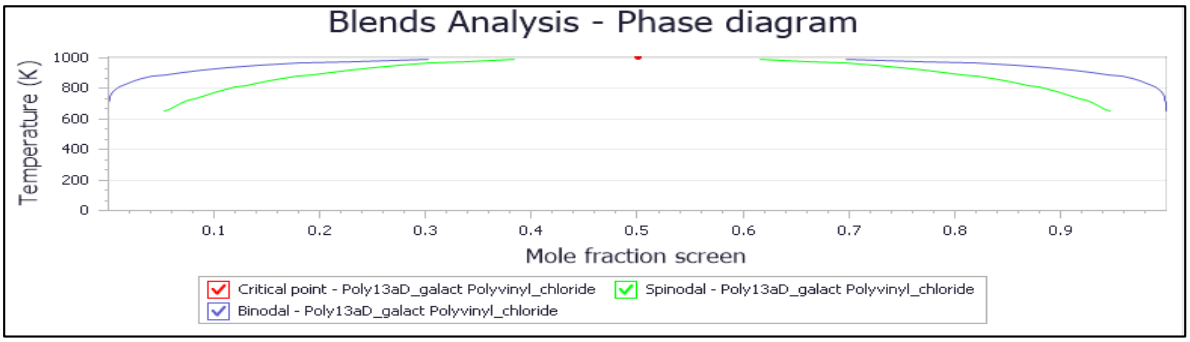

Figure 3 Phase diagram

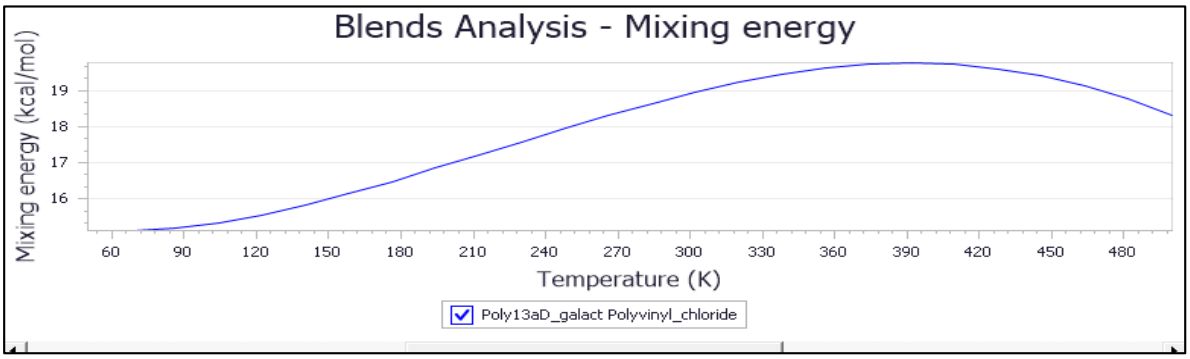

Figure 4 Mixing energy

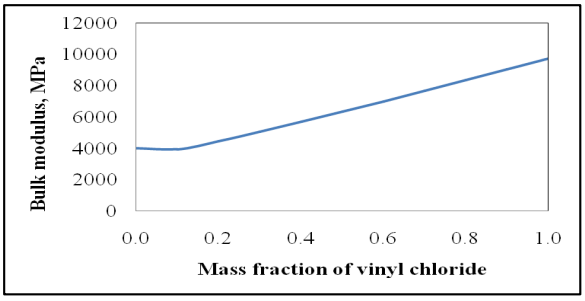

Figure 5. Change in bulk modulus with mass fraction of vinyl chloride.

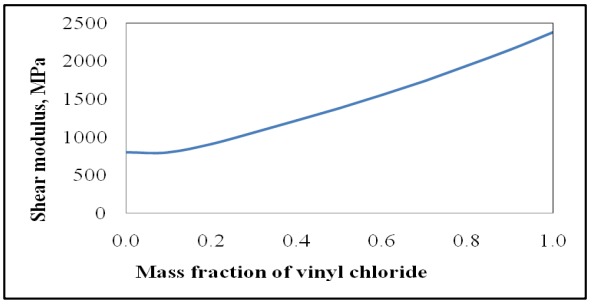

Figure 6. Change in shear modulus with mass fraction of vinyl chloride.

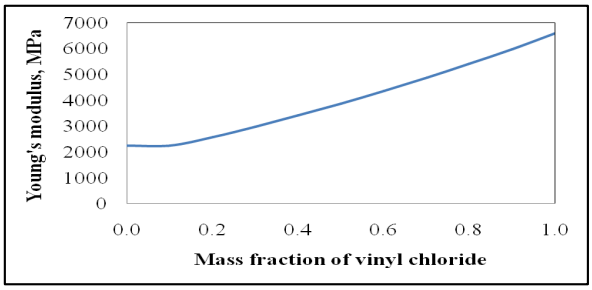

Figure 7. Change in Young's modulus with mass fraction of vinyl chloride.

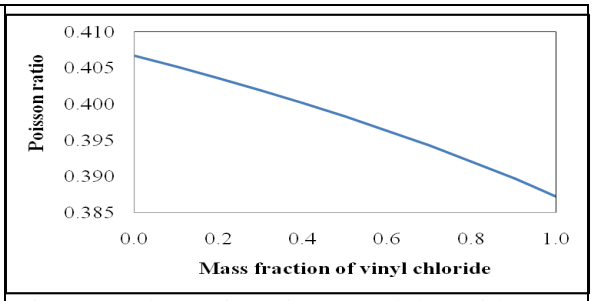

Figure 8. Change in Poisson modulus with mass fraction of vinyl chloride.

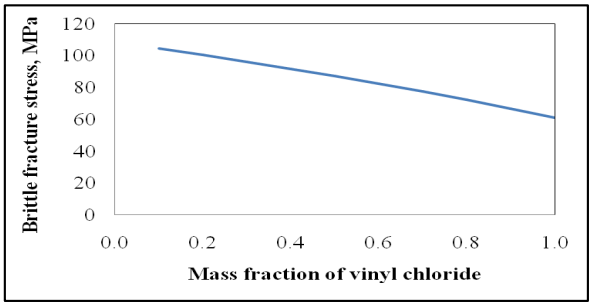

Figure 9. Change in brittle fracture stress with mass fraction of vinyl chloride.

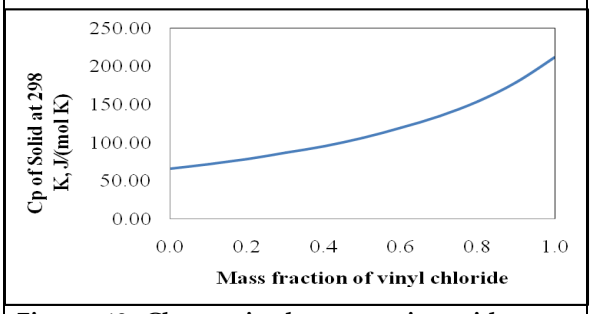

Figure 10 Change in heat capacity with mass fraction of vinyl chloride.

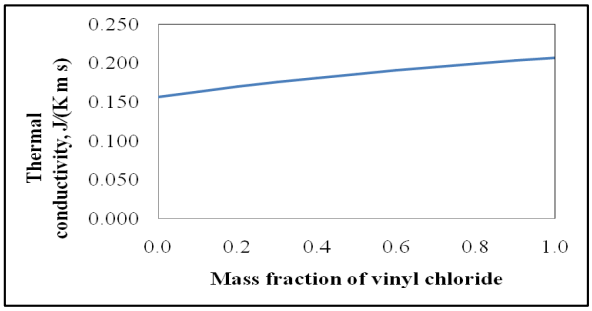

Figure 11. Change in thermal conductivity with mass fraction of vinyl chloride.

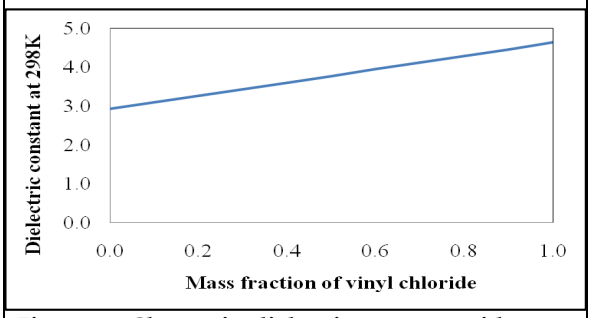

Figure 12 Change in dielectric constant with mass fraction of vinyl chloride.

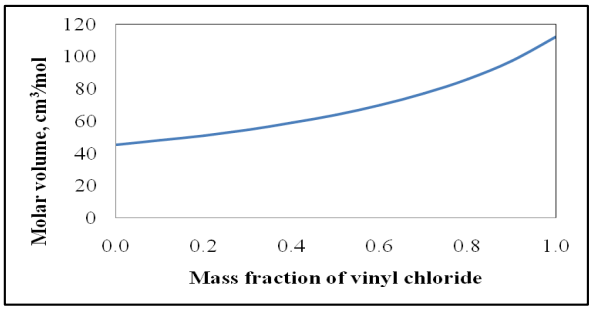

Figure 13. Change in molar volume with mass fraction of vinyl chloride.

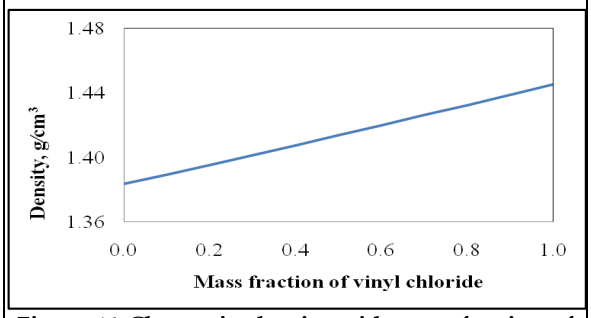

Figure 14 Change in density with mass fraction of vinyl chloride.

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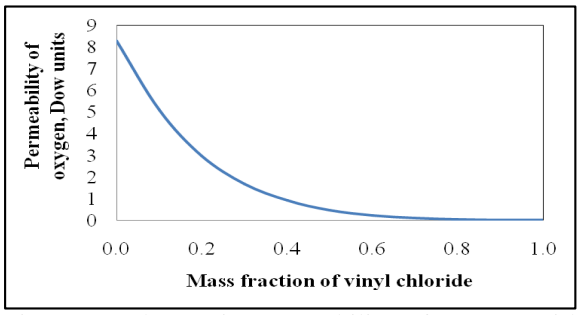

Figure 15 Change in permeability of oxygen with mass fraction of vinyl chloride.

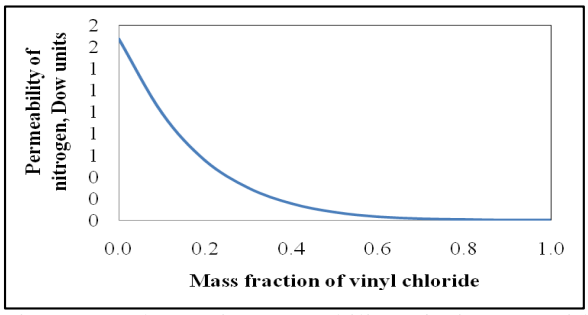

Figure 16 Change in permeability of nitrogen with mass fraction of vinyl chloride.

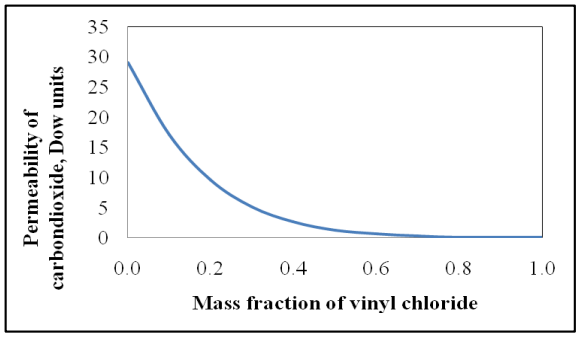

Figure 17 Change in permeability of carbon dioxide with mass fraction of vinyl chloride.

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RESEARCH ARTICLE

In silico Analysis of Benzimidazole and Urea Compatibility in a Blend

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ABSTRACT

Blends are formed by mixing of two or more components. With the help of Biovia Material Studio the compatibility of Benzimidazole and Urea were studied. Basing upon the free energy of mixing, chi parameter, phase diagram and mixing energy the compatibility of the two component present in the blend can be described. It shows the composite holds good at different temperature. All the mechanical property like bulk modulus, young's modulus, shear modulus, Poisson ratio, brittle stress fractures said that all are decrease with increase the mass fraction of base Benzimidazole. The permeability property of composites towards nitrogen gas, carbon dioxides, oxygen gas all have zero value till the mass fraction reached to 0.8 but after that there were sudden rise in permeability. The molar volume increase and the dielectric constant decrease for the composite.

Keywords: Insilico, blend, Material Studio, Benzimidazole and Urea

INTRODUCTION

When two components combine with each other and form a mixture and in the mixture the component retain its property is known as blend or composite. As we know a single component have not multiple property so blends are very helpful to produce a single component with multiple properties. For developing a material with multiple properties takes time and money also. To overcome this problem blends are best choice. Sometime in the polymer chemistry blends are prepared by combining polymer with polymer, polymer with fibre particle with polymer etc.
Modified polymers that is polymer with Nano particles help to construct a material with multiple functional properties for example Polymers coupled with graphene or carbon Nano-tube [1]. Biodegradable polymers for example natural fibre composites [2] helps to increase the mechanical property and water resistance. Now a day researchers are working on fire proof materials [3]. There have been invented that inorganic additives in polypropylene can increase flame retardant capacity without increasing the weight [4]. Researchers are working to produce a composite material to increase the efficiency of fuel used for transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fibre reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges,

light rail transit, mining and tunnelling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments. Trial and error technique to develop blend is cost effective and less time consuming technique. Thus to develop new blends researchers have focus on the use of in silico approach. To identify compatibility between polymer pairs a Software called Materials Studio has been used [7]. In silico analysis describes the simplest type of simulation of complex polymer molecule.

Benzimidazole's Chemical formula is $C_7H_6N_2$. IUPAC name is 1H-1,3-Benzimidazole. It is a heterocyclic aromatic compound composed of benzene with imidazole ring and a colour less solid. It is used as fungicide, analgesic, antiviral, cardiovascular drugs and also used as dye preparation.Urea is also known as carbamide with chemical formula NH_2CONH_2. It is colourless, odorless, water soluble solid. It is used in agricultural industry as fertilizerplywood for marine use, explosives.The rate of mixing of different component of polymer blends are depend upon temperature. Sometime both have same value of temperature dependence or sometime both have different values[8]. Polyvinyl alcohol (PVA) and polymethyl methacrylate (PMMA) was used for blending and studied the composition compatibility by the atomistic and mesoscopic method. Here PVA contain greater than 60 wt %. The Flory-Huggins interaction parameter confirm the blend compatibility. Also the calorimetric experiment and solubility parameter of the polymer supports the blend compatibility [9]. The blend compatibility of polyvinylidene fluoride(PVDF) with polymethyl methacrylate (PMMA) or polyisopropyl methacrylate (PiPMA) were studied by DSC-FTIR method. The PVDF and PMMA are miscible and PVDF and PiPMA are immiscible[10].

MATERIALS AND METHODS

SOFTWARE USED

For the whole simulation process Material Studio of Biovia Software (Dassaultsystemes of France) was used. This software use machine learning technique and standard algorithm to calculate the value of interaction.

METHODOLOGY

In Material Studio there is a build menu present. By the help of this Benzimidazole and Urea were prepared. By the help of blend calculation menu present in Material Studio the structures were optimised. After all this process the analysis menu was used to calculate and generate the various data. After analysing all the data, the compatibility of the components forming the blend was analysed. After this the structures of both the polymers were fed to Synthia menu of Material Studio and allowed to run. Various type of property was seen in a tabular form and graphs were generate.

RESULT AND DISCUSSION

Here the blend was prepared by using Benzimidazole polymer and Urea polymer as potential component. Here Benzimidazole was taken as base (maximum amount by wt %) and Urea was taken as screen (minimum amount by wt %) . Biovia Material Studio Synthia uses structure-property relation to calculate the properties of polymers.The most popular method is group additive method which is very fast and comfortable for use. This method was used for many years. But the drawback of this process is it can't calculate the property of those polymer which contain a group whose groupcontribution value can't beestimated.To overcome this drawback , Biovia Material Studio synthia is used and for this no group contribution value is required

FREE ENERGY OF MIXING

The symbol for free energy is ΔG. We know that if the free energy value is more negative then the reaction is spontaneous.

$\Delta G_m = \Delta H_m - T\Delta S_m$
ΔG_m = Gibb's free energy of mixing
ΔH_m= Enthalpy of mixing
ΔS_m = Entropy of mixing
T = Absolute temperature

The entropy of mixing is increase in case of blend so the value of $T\Delta S_m$ is always positive. Therefore the free energy value depends upon the enthalpy of mixing ΔH_m.If $\Delta H_m < T\Delta S_m$i.e the enthalpy of mixing is greater than$T\Delta S_m$ then both the polymers can mix to form a blend.**Figure 1** shows that free energy increase by increase temperature upto 275K. Further increase in temperature the free energy increases. The results shows that a homogeneous blend can form within the temperature range 50K to 500K.

CHI PARAMETE

High value of chi for chemically dissimilar polymer describes unfavourable for mixing and low value of chifor chemically similar polymer. Figure 2shows that the value of chi decrease exponentially with increase in temperature

Phase Diagram

Figure 3 shows the variation of phase of the two components at different temperature and composition.The compatibility of the two components can be studied by the phase diagram. There are three regions of different degree of miscibility. Above the critical temperature the single phase miscible region existed. Metastable regions existed between binodals and spinodals. The binodals separate the miscible and meta stable region and the spinodals separate the metastable and two phase region.

Mixing energy

Small value of mixing energy always favours the mixing process.so the temperature at which mixing energy is low can chosen for mixing. The graph shows that when temperature increase at first mixing energy increase then further decrease with increase in temperature and becomes zero at 340K and further increase in temperature mixing energy increase sharply which is clear from figure-4.

Bulk modulus

Bulk modulus is the change in volume by change in pressure. Figure 5 shows that bulk modulus decrease linearly with increase mass fraction of Benzimidazole.

Shear modulus

It is the ratio between shear stress to shear strain. It describes the response towards shear deformation of the blend. Figure 6 shows that the shear modulus decrease with increase of mass fraction of Benzimidazole.

Young's modulus

It is known as ratio between stress and strain. It describes the relative stiffness of the blend. Figure 4.7 shows the young's modulus decrease with increase of mass fraction of Benzimidazole.

Poisson ratio

It is the ratio between lateral strain to longitudinal strain. Figure 8 shows linear decrease of poisson ratio with increase of mass fraction of Benzimidazole.

Brittle fracture stress

Brittle fracture is the sudden rapid cracking of a material under stress. Figure 9 shows that brittle fracture decrease slightly with increase with mass fraction of Benzimidazole.

Heat capacity

The amount of heat required for a given mass of substance to produce a unit change in temperature without change of phase is known as heat capacity. Figure 10 shows that increase of heat capacity with increase in mass fraction of Benzimidazole.

Thermal conductivity

It indicates the correlation between heat flux per unit area and temperature gradient. It tells about the heat transfer ability of a material. Figure 11 shows that the thermal conductivity decreases linearly with increase of mass fraction of Benzimidazole.

Dielectric constant

It is the ratio of electric permeability of material to the electric permeability of free space. Figure 12 describes the dielectric constant decrease with increase of mass fraction of Benzimidazole.

Molar volume

Volume occupied by one mole a substance is known as molar volume. Figure 13 shows that molar volume increase with increase of mass fraction of Benzimidazole.

Density

Porosity decrease with increase of density. Surface which is highly porous has the high value of adsorption or absorption. Figure 14 shows density decrease slightly with increase of mass fraction of Benzimidazole.

Permeability of oxygen

At first Permeability of oxygen is zero for mass fraction value 0.8 but after that sudden rise in permeability occur when mass fraction reaches above 0.8.

Permeability of nitrogen gas

At first Permeability of nitrogen is zero for mass fraction value 0.8 but after that sudden rise in permeability occur when mass fraction reaches above 0.8.

Permeability of carbon dioxide

At first Permeability of carbon dioxide gas is zero for mass fraction value 0.8 but after that sudden rise in permeability occur when mass fraction reaches above 0.8.

CONCLUSION

Basing upon the value of free energy, chi parameter, phase diagram, mixing energy the compatibility between the two components are studied and reach on a conclusion that both the components have good compatibility at various ranges of temperature. The mechanical property like bulk modulus, young's modulus, shear modulus, Poisson ratio indicates that all the mechanical property decrease with increase mass fraction of Benz-Imidazole. The compatibility of the two components also analysed on the basis of heat capacity, thermal energy, dielectric constant and the result was heat capacity increase and both the thermal energy and dielectric constant decrease sharply and slightly respectively. There are also some permeability properties of the composite towards nitrogen, oxygen, carbon dioxide described that the blend was not permeable till the mass fraction reached up to 0.8 but after that the permeability suddenly increased.

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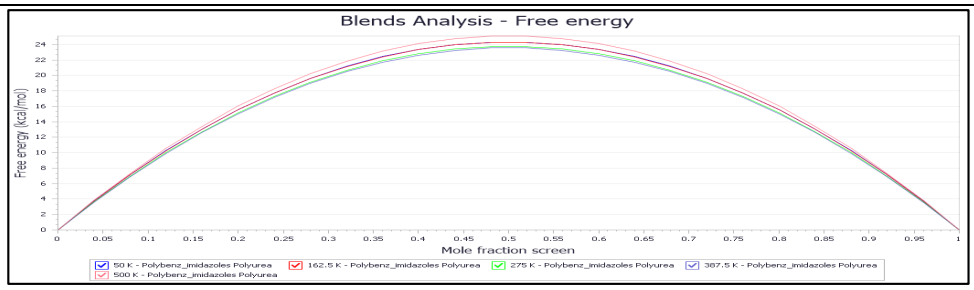

Figure 1 Free energy change Vs mole fraction of Urea

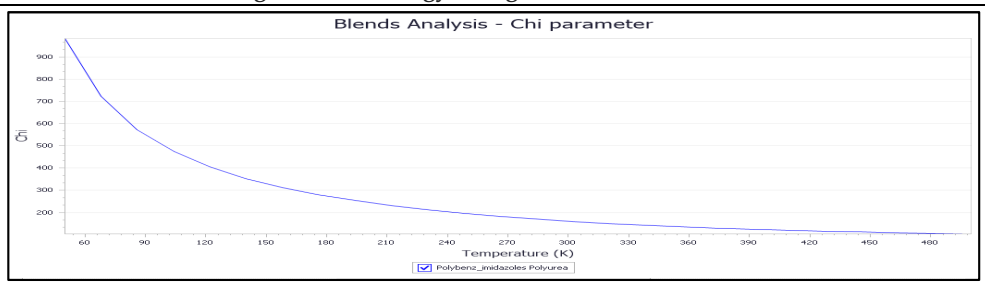

Figure 2. Change in chi Vs temperature

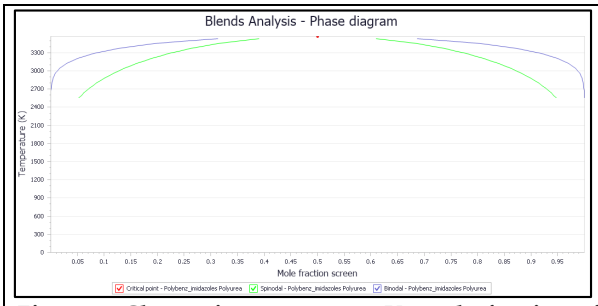

Figure 3. Change in temperature Vs mole fraction of Urea.

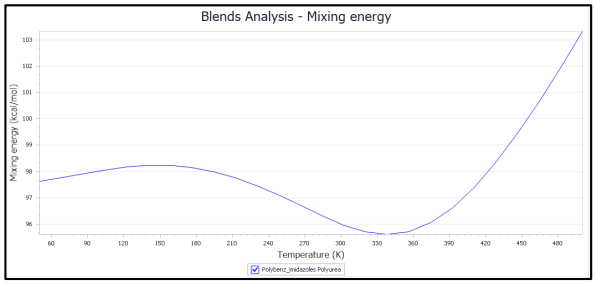

Figure 4. Change in free energy Vs temperature.

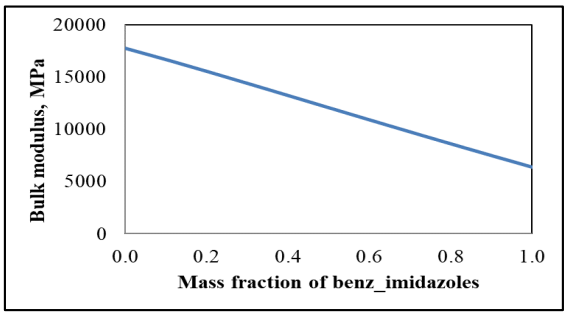

Figure 5. Change in bulk modulus Vs mass fraction of Benzimidazole

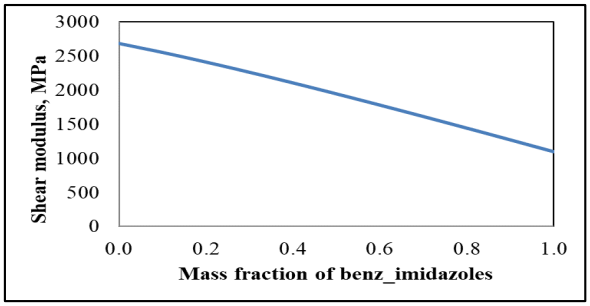

Figure 6. Change in shear modulus Vs mass fraction of Benzimidazole.

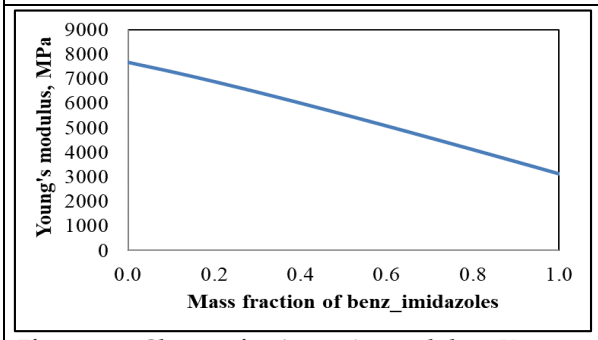

Figure 7. Change in Young's modulus Vs mass fraction of Benzimidazole.

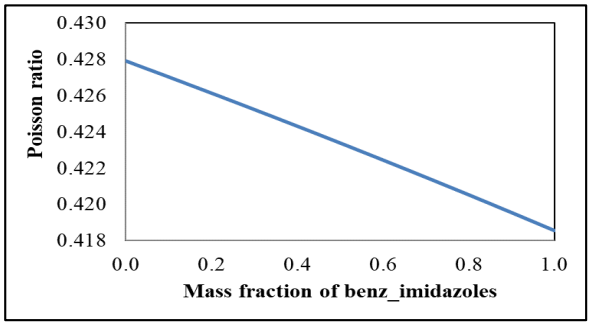

Figure 8. change in poisson ratio Vs mass fraction of Benzimidazole.

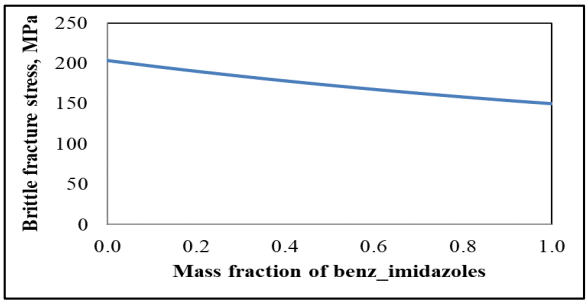

Figure 9. Change in brittle fracture stress Vs mass fraction of Benzimidazole.

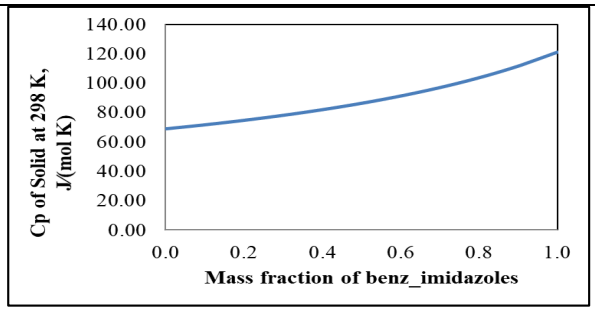

Figure 10. Change in heat capacity Vs mass fraction of Benzimidazole

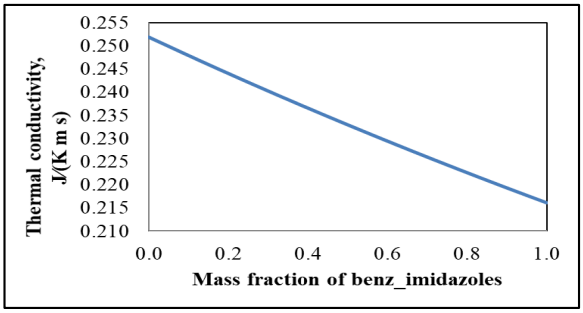

Figure 11. Change in thermal conductivity Vs mass fraction of Benzimidazole.

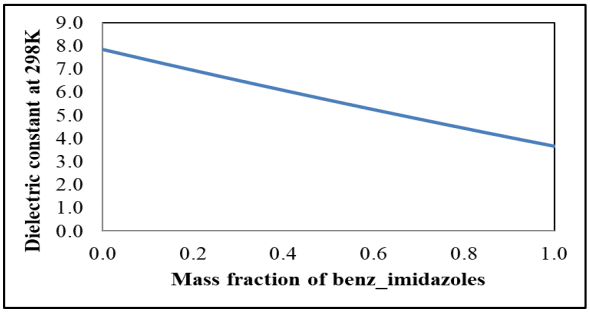

Figure 12Change in dielectric constant Vs mass fraction of Benzimidazole.

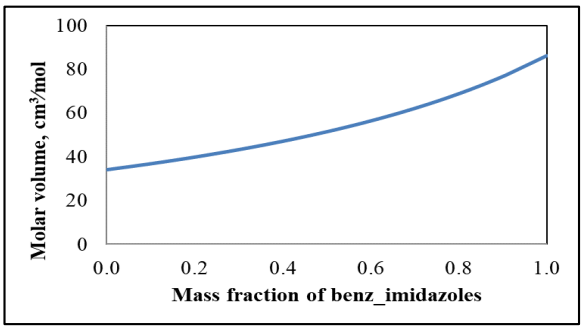

Figure 13. Change in molar volume Vs mass fraction of Benzimidazole.

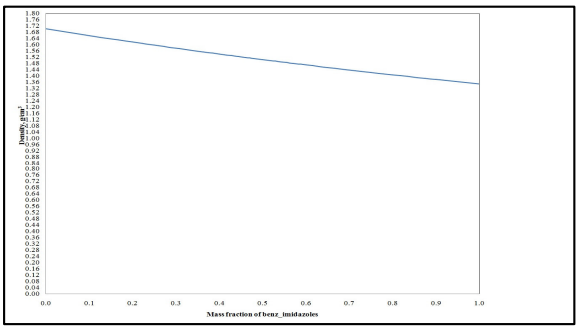

Figure 14. Change in density Vs mass fraction of Benzimidazole.

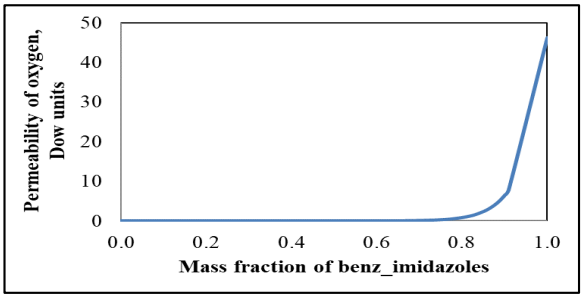

Figure 15 Change in permeability of oxygen Vs mass fraction of Benzimidazole.

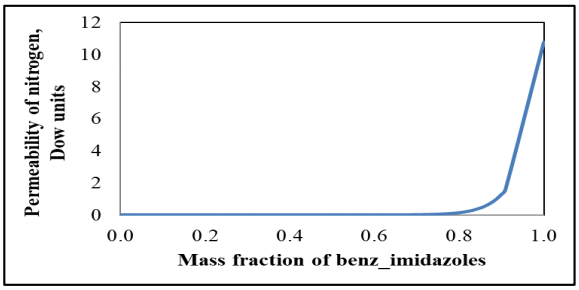

Figure 16 Change in permeability of nitrogen Vs mass fraction of Benzimidazole.

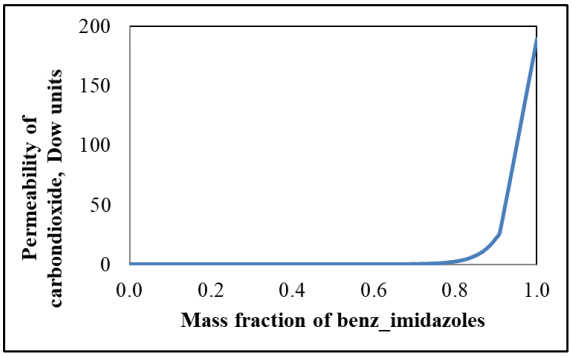

Figure 17. Change in permeability of carbon dioxide Vs mass fraction Benzimidazole.

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RESEARCH ARTICLE

In silico Analysis of Dichloroethylene and Benzimidazoles Compatibility in a Blend

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ABSTRACT

The blend is a combination of two or more components. The compatibility of dichloroethylene and benzimidazoles were studied to form a miscible blend using Biovia Materials Studio. Based onthe free energy of mixing, chi parameter,phase diagram, andmixing energy the compatibility of the two components was demonstrated.At both low and high temperatures, the results indicated that the pair can become compatible. Phase diagram which was the critical temperature indicated that a single phase can be obtained above 387.5 K. On the basis of bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture the mechanical properties of the composite were studied. The values of all the properties increased with an increase in the mass fraction of acrylic acid. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity, and dielectric constant. With the increase in the mass fraction of acrylic acid, all those parameters increased and the composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with an increase in acrylic acid fraction. Based onthe permeability of oxygen, nitrogen, and carbon dioxide the permeability properties of the composite were studied. The permeability for all the gases was found to decrease with an increase in the mass fraction of acrylic acid. This study is more impactable with no laboratory experiment less time consuming as well as cost-effective.

Keywords: Blend, in silico, polyvinyl alcohol, Urethane.

INTRODUCTION

Polymer blending is a technique of mixing of two or more polymer components retaining their properties in the mixture which is also known as composite The quality of the material can be improved by combining different components in different ratios thus giving multiple properties in a single material which involves significant research and time. In blending two or more materials are mixed to obtain the desired properties. Thus a blend saves

time to develop new material as well as this is cost-effective. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nanomaterial modified polymers covered the way to multi-functional materials. Polymers coupled with carbon-based (graphene, carbon nano-tube) nano-materials have drawn observation [1]. Biodegradable polymers- natural fiber composites have been reported to increase mechanical properties and water resistance [2]. Researchers are working on fire-retardant [3]. There are reports of inorganic supplements in polypropylene; without increasing the weight, that (polypropylene) can increase flame retardancy [4]. Synthesis of lightweight composite materials with increased strength is under focus as it enhances the fuel efficiency in the field of transportation [5]. The approach composites are being applied in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cement-based composites were developed for the construction of all waterside buildings [6]. All the above-introduced examples are depending on laboratory experiments.

Usually, the trial and error method is chosen for the preparation of blends which is a low cost and less time-consuming method. Thus, researchers have focused on the use of in silico near to develop new blends within less time consumption. Software (Materials Studio) has been used to identify compatible pairs [7]. Polymer 1: Dichloroethylene, Molecular formula: $C_2H_2Cl_2$or ClCH=CHCl, Molecular weight: 96.94 g/mol. 1,2-Dichloroethene is also called as 1,2-Dichloroethylene. Dichloroethylene is a highly flammable, colorless liquid, harsh odor.It produces solvents and chemical mixtures. 1,2 -dichloroethene is two types.One is called cis-1,2-dicholoethene and the other is called trans-1,2-dichloroethene. Both forms are present as a mixture 1,2-dichloroethylene is a cis isomer. It is a colorless liquid. It`s flashpoint 36-39^0 F.It is heavier than water and insoluble in water. Its vapors large than air. It is used in making perfume.

Polymer 2: Benzimidazoles, Molecular formula: C_7 H_6 N_2, Molecular weight: 118.14g/mol.Benzimidazole is a heterocyclic aromatic organic compound. it is a colorless solid. Benzimidazole appears as white low crystals. 1H-benzimidazole is the 1H-tautomer of benzimidazole. It is a benzimidazole and polycyclic heteroarene. It is a conjugate acid of a benzimidazole. Benzimidazole is a tautomer of a 4H-benzimidazole, a 2H -benzimidazole 3H-benzimidazole, melting point: 170 to 172 □.

MATERIALS AND METHODS

The materials studio module of Biovia software (DassaultSystemsof France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction. Dichloroethylene and Benzimidazole were prepared using the build menu of Materials Studio. The structure of the components was optimized using the components that were used in the blends->calculation menu of Materials studio. Dichloroethylene and was used as the base and benzimidazole was used as a screen. After calculation, the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of dichloroethyleneandbenzimidazole were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of the weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work, the use of dichloroethylene andbenzimidazole as potential components of a blend was analyzed using Biovia Materials Studio. In this work, the use of polyacrylic acid and polyacrylochloride as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties.

Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Free energy of mixing: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend.Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where$\Delta G_m - Gibb's free energy of mixing$

$\Delta H_m = Enthalpy of mixing$

$\Delta S_m = Entropy of mixing$

$T = Absolute temperature$

The value of $T\Delta S_m$is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with an increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with an increase in temperature.

The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows very good compatibility between polyvinyl alcoholand poly ethylurethane with a negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

Chi parameter: The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers indicates poor mixing. For chemically similar polymers having small cohesive energy difference χ, value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with an increase in temperature.This agrees with the free energy of mixing for the blend.

Phase diagram: The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single-phase blend can be formed at a high temperature (higher than 750 K).
b. Fragmented metastable regions existed between binodals and spinodals, and
c. The two-phase separated regions of immiscibility are bordered by the spinodals.
The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.

When the system enters from a single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase-separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing energy: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when the temperature increases the mixing energy increases to the highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with an increase in temperature.The temperature is varying from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with the least mixing energy value.

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the composite of the bulk modulus increases linearly with an increase in the mass fraction of dichloroethylene.

Shear modulus: Shear modulus is the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6shows that the composite of the shear modulus increases linearly with an increase in the mass fraction of dichloroethylene.

Young's modulus: It is the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7shows that Young's modulus of the composite increases linearly with an increase in the mass fraction of dichloroethylene.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8shows that the Poisson ratio of the composite increases with a decrease in the mass fraction of dichloroethylene.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9shows that the brittle fracture stress of the composite increases with a decrease in the mass fraction of dichloroethylene.

Heat capacity: It is the amount of heatrequired to raise the temperature of the one-unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with an increase in the mass fraction of dichloroethylene.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11shows that the thermal conductivity of the composite increases linearly with an increase in the mass fraction of dichloroethylene.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are

maintained constant. Figure 12shows that the dielectric constant of the composite increases with an increase in the mass fraction of dichloroethylene.

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with an increase in the mass fraction of dichloroethylene.

Density: Increase in density indicates a decrease in porosity. A higher porosity will enhance the surface area making it suitable for absorption/adsorption applications. Figure 14shows that the density of the composite decreases linearly with an increase in the mass fraction of dichloroethylene.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates a longer time lag for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite decreases with an increase in the mass fraction of dichloroethylene.

Figure 16 shows that the permeability of nitrogen through the composite decreases with an increase in the mass fraction of dichloroethylene.Figure 17 shows that the permeability of carbon dioxide through the composite decreases with an increase in the mass fraction of dichloroethylene. Thus, the results indicated that an increase in dichloroethylene fraction reduces the permeability of different gases. The rate of permeability might be influenced by the molecular weight of the gases.

CONCLUSIONS

Using Biovia Materials Studio the possibility of the use of polydichloroethylene and polybenzimidazole to form a homogeneous blend was explored.Based onthe free energy of mixing, chi parameter, and mixing energy the compatibility was analyzed. At a different scale of temperature, the results indicated that the pair can have very good compatibility. Based onbulk modulus, shear modulus, young' modulus, poisson ratio, and brittle stress fracture the mechanical properties of the composite were studied. The results indicated that the values of all the properties increased with an increase in the mass fraction of acrylic acid. The composition of the blend was studied with respect to heat capacity, thermal conductivity, and dielectric constant. The results show that all three parameters increased with an increase in the mass fraction of acrylic acid. The composition of the blend was studied with respect to permeability properties. With an increase in an acrylic acid fraction, the molar volume and density decreased. On the basis of permeability of oxygen, nitrogen, and carbon dioxide the permeability properties of the composite were studied. The results indicated that the permeability for all the gases decreased with an increase in the mass fraction of acrylic acid. For a blend generally, components are distinguished experimentally. To determine components of a blend without performing laboratory experiments saving materials, money, and time in silico study will help.

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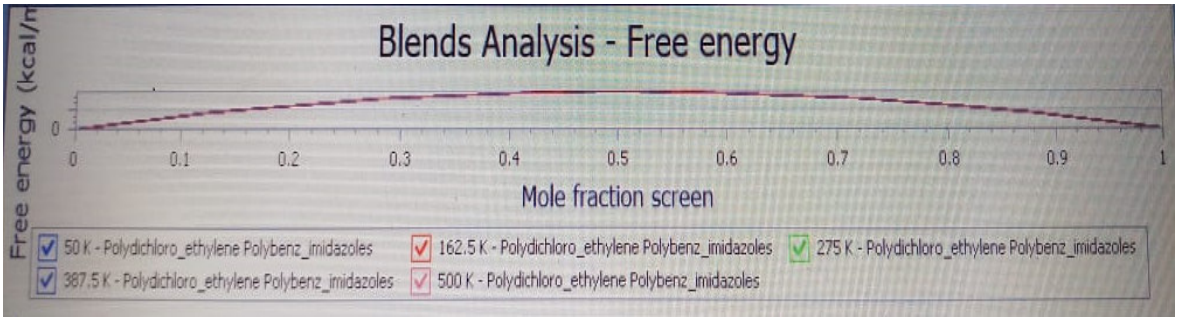

Figure 1. Free energy change with a mole fraction ofdichloroethylene and benzimidazolesat different temperatures

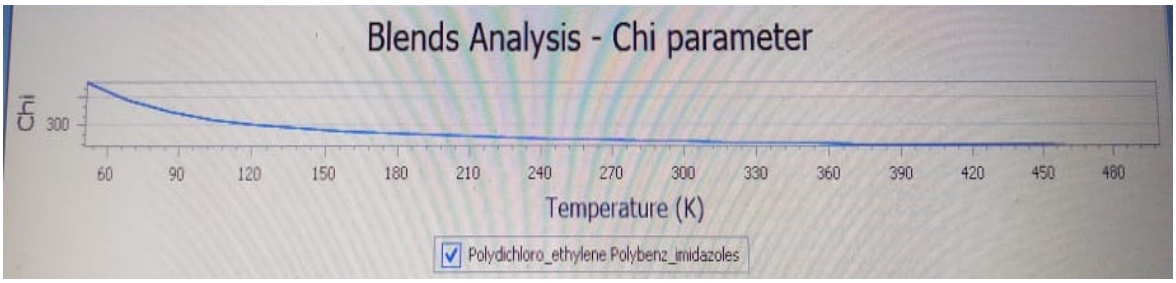

Figure 2. Change in χ (chi) value with temperature

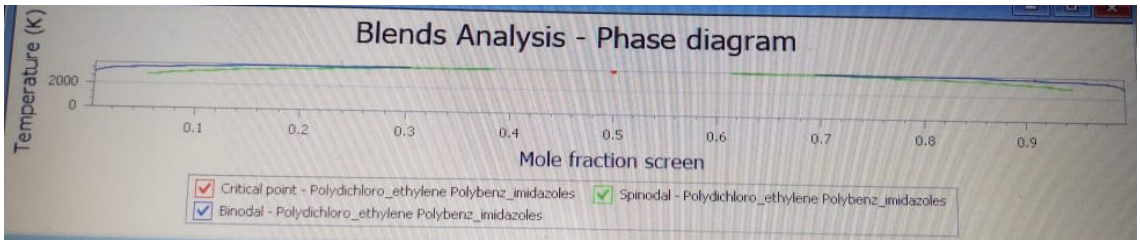

Figure 3. Phase diagram

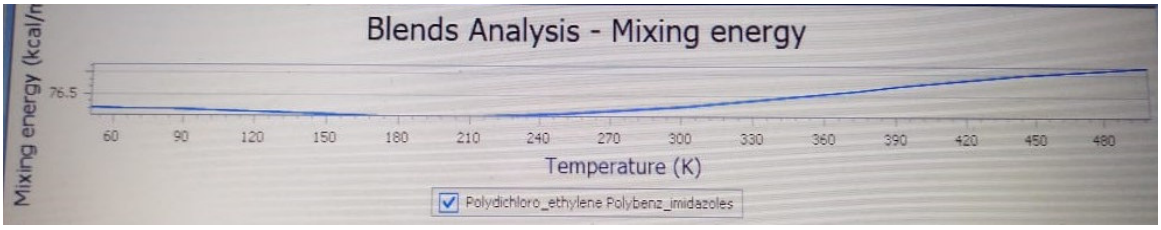

Figure 4. Mixing energy

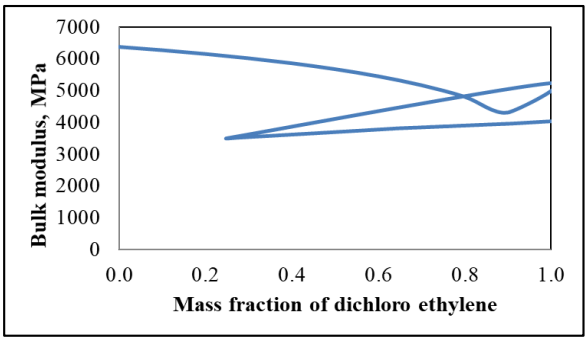

Figure 5. Change in bulk modulus with the mass fraction of dichloroethylene

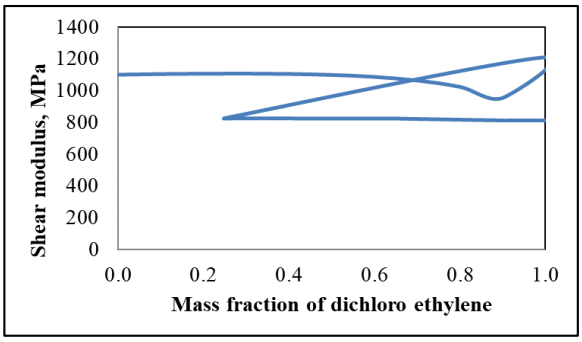

Figure 6. Change in shear modulus with a mass fraction of dichloroethylene

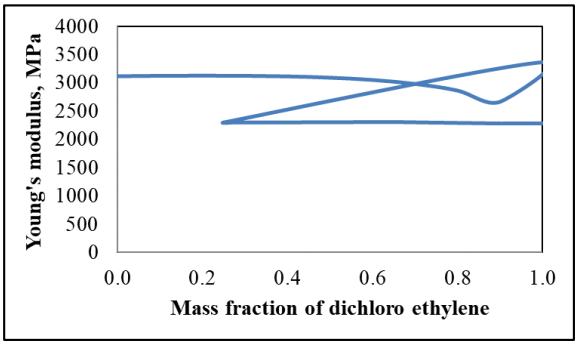

Figure 7. Change in Young's modulus with a mass fraction of dichloroethylene

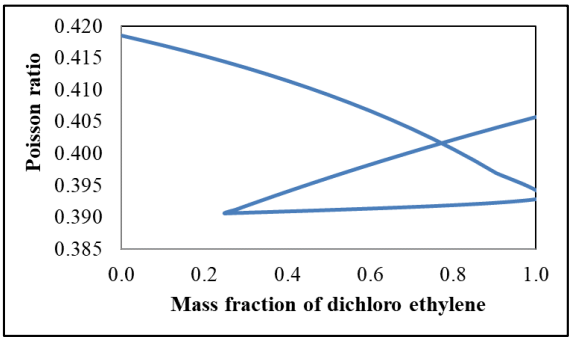

Figure 8. Change in Poisson modulus with a mass fraction of dichloroethylene

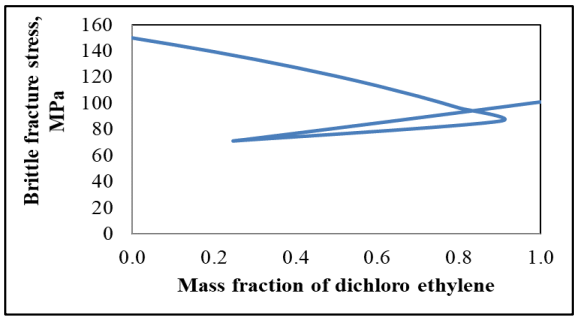

Figure 9. Change in brittle fracture stress with a mass fraction of dichloroethylene

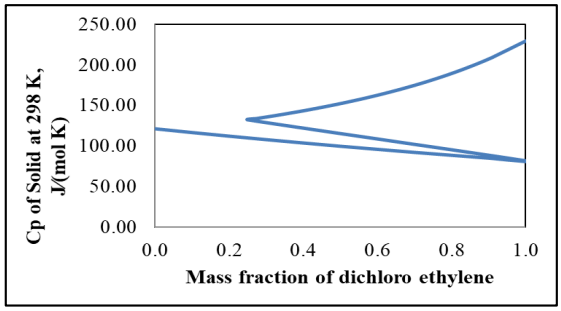

Figure 10. Change in heat capacity with the mass fraction of dichloroethylene

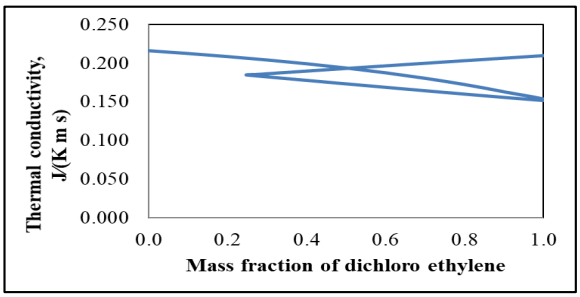

Figure 11. Change in thermal conductivity with the mass fraction of dichloroethylene

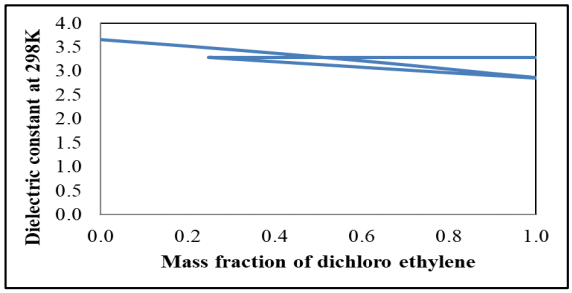

Figure 12. Change in dielectric constant with the mass fraction of dichloroethylene

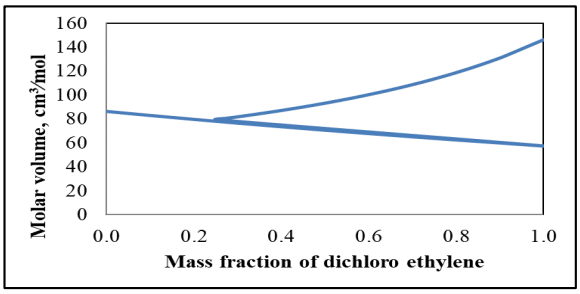

Figure 13. Change in molar volume with the mass fraction of dichloroethylene

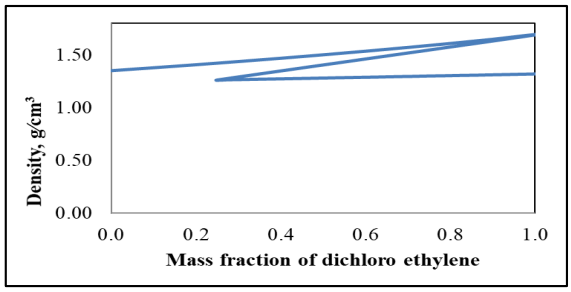

Figure 14. Change in density with the mass fraction of dichloroethylene

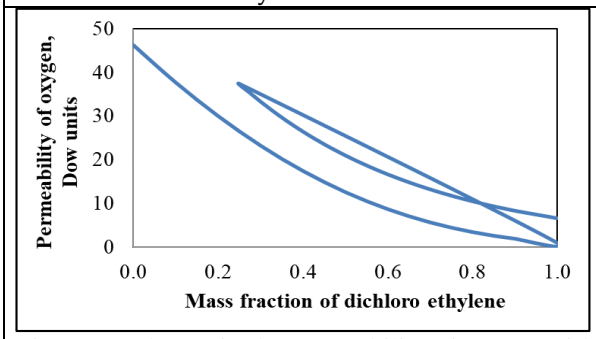

Figure 15. Change in the permeability of oxygen with a mass fraction of dichloroethylene

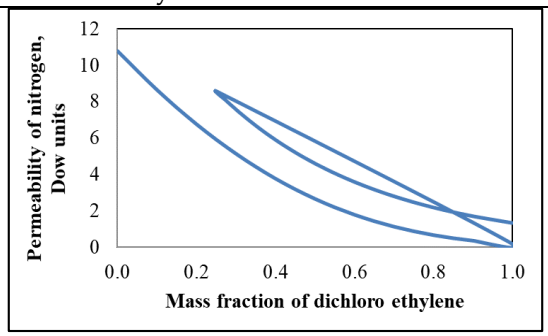

Figure 16. Change in the permeability of nitrogen with a mass fraction of dichloroethylene

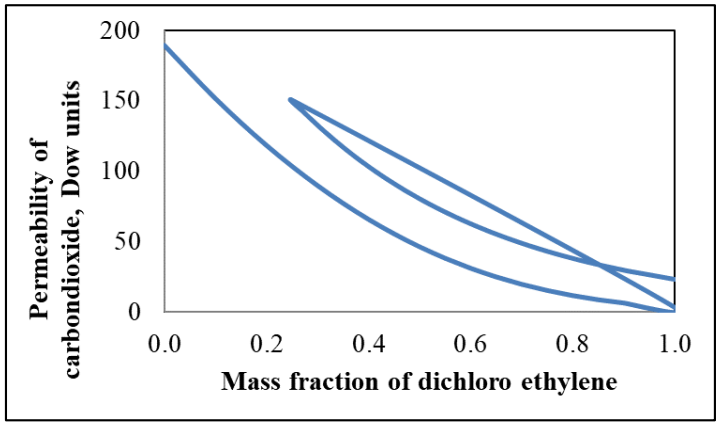

Figure 17. Change in the permeability of carbon dioxide with a mass fraction of dichloroethylene

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RESEARCH ARTICLE

In silico Analysis of Dimeth-Siloxane and Bisphen-Dimeth-Carbonate Compatibility in A Blend

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ABSTRACT

A blend is formed by the combination of two or more components. The compatibility of dimeth-siloxane and bisphen-dimeth-carbonate were studied to form a miscible blend using Biovia Materials Studio. The demonstration of the affinity of the two components depends on free energy of mixing, chi parameter, phase diagram and mixing energy. From the results it was suggested that the pair can become appropriate at both low and high temperature indicated from the phase diagram that a single phase can be attained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, Young' modulus, shear modulus, Poisson ratio and brittle stress fracture. From the results it wasindicated that with increase in mass fraction of dimeth-siloxanethe values of all the properties increased. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of dimeth-siloxane. The composition of the blend was analyzed related to permeability properties. With increase in dimeth-siloxane fraction, the molar volume and density decreased. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that with increase in mass fraction of acrylic acid, the permeability of all gases decreased.This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend, in silico, dimeth-siloxane, bisphen-dimeth-carbonate

INTRODUCTION

Composites or blends are resulted with combination of more than one component where components do retain their character in the mixture. As it is problematic to find different properties in a single material, it is advisable to associate various components thereby improving the nature of the material. Improvement of a single material with

the desired property involves important research and time. A blend promotes the improvement of various components; mix them to get the desired property. Thus a blend is time-saving and promote a new material thereby lowering the development cost of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nano materials have the ability to improve the properties of polymeric material. Nano material modified polymers offered to multifunctional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. To complement mechanical properties and water resistance, biodegradable polymer-natural fiber composites [2] have been reported. Researchers are working on fire retardant/fire proof materials [3]. The inorganic additives in polypropylene are reported; that can complement flame retardancy without increasing the weight [4]. Synthesis and production of lightweight composite materials having high strength has been emphasized by the researchers which is important for enhancing fuel efficiency in the field of transportation [5]. In structural Engineering, the application of composites is due to its high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymer, latex polymer cementitious composites [6] were developed for construction of bridges, mining and tunneling, light rail transit, retaining walls and other waterside buildings. All the above mentioned examples depend on laboratory experiments.

Mostly blends are developed by trial and error method andthis technique is a low cost and less time saving method. Thus, researchers have targeted on the use of in silico approach to promote new blends. Software (Materials Studio [7]) has been used to analyze suitable pairs. Polydimethylsiloxane (PDMS) also known as dimethylpolysiloxane or dimethicone. It is the most widely used silicon-based organic polymer known for its rheological properties. PDMS is a common surfactant. It is used as an herbicide penetrant. A mixture of PDMS and silicon dioxide (simethicone) is used as an antifoaming agent and carminative. PDMS is optically clear, inert, non-toxic and non-flammable. Dimethyl carbonate is ancolourless and flammable organic compound. It is a carbonate ester. The main benefit of dimethyl carbonate is its low toxicity and it is biodegradable. It is an environment friendly solvent which is used to make adhesives, coating, and cleaning agent.

MATERIALS AND METHODS

SOFTWARE USED

Materials studio module of Biovia software (DassaultSystemesof France) was used for the detailed analysis. To predict the level of interaction, the software promotes effective use of machine learning techniques and standard algorithms.

METHODOLOGY

Dimeth-siloxane andbishen-dimeth-carbonate were prepared using the build menu of Materials Studio. The optimizations of the structure of the components were used in blends->calculation menu of Materials studio. For the base dimeth-siloxane and for the screen bishen-dimeth-carbonate was used. After calculation the blends->analysis menu of Materials studio was used to develop different data. After the data were inspected the compatibility of the components to form a blend was analyzed.To the synthia menu of Materials Studio,the structures ofdimeth-siloxane andbishen-dimeth-carbonate were given. It was then run for various weight fractions of the components. The composite's different properties were displayed in a tabular form. The values were used to plot graphs to analyze the weight fraction effect of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Using Biovia Material Studio, the use of dimeth-siloxane and bisphen-dimeth-carbonate as potential components of a blend was analyzed.In this work the use of polyacrylic acid and polyacrylochloride as potential components of a

composite was analyzed using Biovia Materials Studio). To assess a wide range of polymer properties BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships. To predict the properties of polymers as well as small molecules group additive methods were used for many years. These methods are extremely fast and accessible to use. Therefore, they are of greatest service when a rapid measure of a property is neededwithout a detailed insight of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer have a group for which the group contribution cannot be predicted, then the property of that polymer cannot be evaluated. The method executed in Synthia uses topological information about polymers in the predictive correlationsto overcome this limitation. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is appropriate and properties may be concluded for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

FREE ENERGY OF MIXING

A blend is should be miscible if it is homogeneous. If the free energy of mixing value is negative, it indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

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$$\Delta G_m - \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m = Gibb's free energy\ of\ mixing$, $\Delta H_m = Enthalpy of mixing$, $\Delta S_m = Entropy of mixing$ and $T = Absolute temperature$

Since there is an increase in the entropy on mixing,the value of $T\Delta S_m$is always positive in case of a blend. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m \prec T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. With increase in temperature (upto 275 K), the energy decreases as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyvinyl alcoholand poly ethylurethane with negative value of mixing energy,which may lead to form a particular shape with undoubtedly high effort.

CHIPARAMETER

The excess free energy of mixing is represented by the Flory–Huggins χ parameter and helps to analyze the phase behavior for polymer blends and block copolymer. An important imbalance in cohesive energy density leads to a high χ valuefor polymers which are chemically dissimilar and, hence, a greater driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers shows poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, for adequately long chains there is a chance of demixing. Architectural and geometric differences between the components restrict them in a mixture from occupying the same configurations experienced in the pure phase. From the polymer field theory it can be predicted that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi).Figure 2 shows that the value of x is high from temperature between 50Kto 500K. Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend

PHASE DIAGRAM

The compatibility of binary mixtures can be anticipated by phase diagrams. Figure 3represent the phase diagram for the two components of the blend. There are three regions of different degree of miscibility: a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).b. Fragmented metastable regions existed between binodals and spinodals, and c. The two-phase separated regions of immiscibility are bordered by the spinodals. The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system dives from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

MIXING ENERGY

A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be selected for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph revealed that at first when temperature increases the mixing energy increases to a highest value after and when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature.The temperature vary from 50K to500K for the varying of mixing energy. It is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus

Bulk modulus is the measure of decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite decreases with increase in mass fraction of dimethsiloxane but at certain point mass fraction of dimethsiloxane increases in bulk modulus and then both show linear behavior.

Shear modulus

It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 represent that the shear modulus of the composite first decreases with increase mass fraction but after certain point the mass fraction increases and then remain constant.

Young's modulus

It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite decreases with increase in mass fraction of dimethsiloxane but at certain point mass fraction started increasing and then remain constant.

Poisson ratio

It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite remain constant with increase in mass fraction of dimethsiloxane but at certain point the poisson ratio of the composite and the mass fraction of dimethsiloxane fluctuate from its behavior.

Brittle fracture stress

Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite decreases with increase mass fraction of dimethsiloxane but at certain point the mass fraction started increasing linearly.

Heat capacity

It is the amount of heatrequired to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity of the composite decreases and then increases with increase in mass fraction.

Thermal conductivity

It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite decreases with increase in mass fraction of dimethsiloxane but at certain point the thermal conductivity started increasing with increase in mass fraction.

Dielectric constant

It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of acrylic acid.

Molar volume

It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases with increase in mass fraction of dimethsiloxane but at certain point the molar volume started increasing.

Density

Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite decreases linearly with increase in mass fraction of dimethsiloxane .but at certain point the density of the composite increases linearly.

Permeability of gas

Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the mebrane. Figure 15 shows that the permeability of oxygen through the composite increases with increase in mass fraction of dimethsiloxane but decreases linearly at certain point and then remain constant.

Figure 16 shows that the permeability of oxygen through the composite increases with increase in mass fraction of dimethsiloxane but decreases linearly at certain point and then remain constant. Figure 17 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of dimethsiloxane but decreases linearly at certain point and then remain constant. Thus, the results indicated that an increase in dimeth-siloxane fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of dimeth-siloxane and bishen-dimeth-carbonate to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. Thestudy of mechanical properties of the composite were based on bulk modulus, Young's modulus, shear modulus, Poisson ratio and brittle stress fracture. The results indicated that with increase in mass fraction of dimeth-siloxanethe values of all the properties increased. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. From the result it was indicated that all the three parameters increased with increase in mass fraction of dimeth-siloxane. The composition of the blend was analyzed

with respect to permeability properties. The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases increased with increase in mass fraction of dimeth-siloxane. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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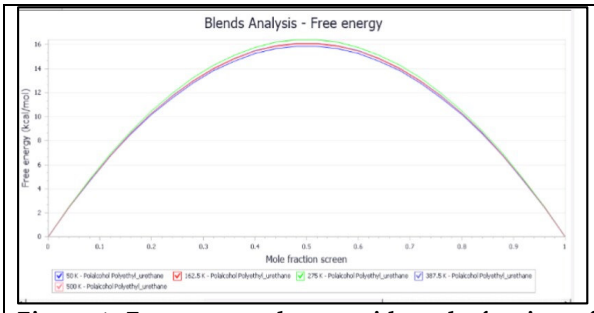

Figure 1. Free energy change with mole fraction of polyethylurethane at different temperatures

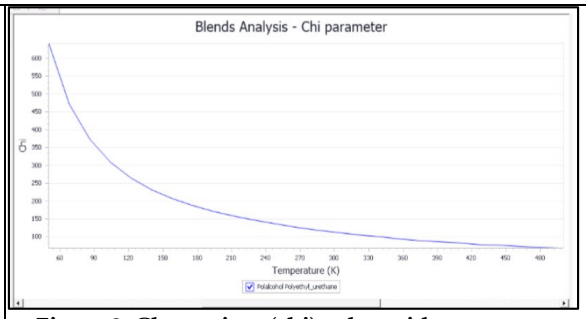

Figure 2. Change in χ (chi) value with temperature

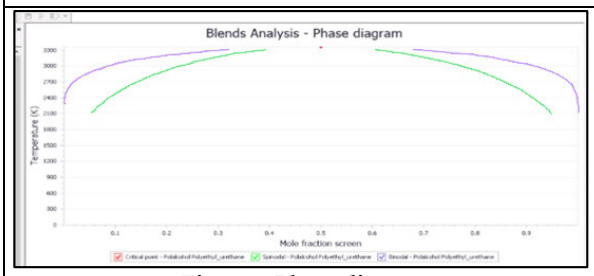

Figure 3.Phase diagram

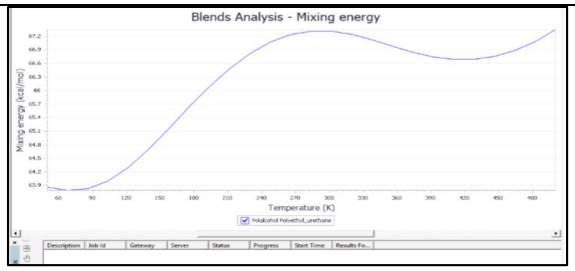

Figure 4. Mixing energy

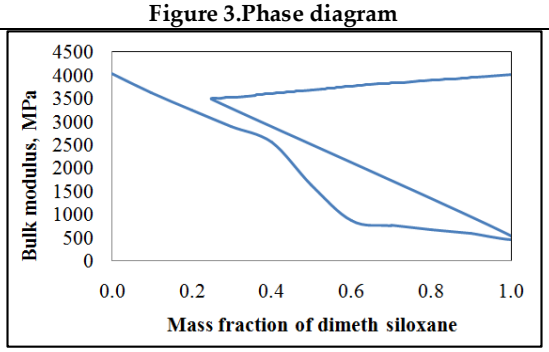

Figure 5. Change in bulk modulus with mass fraction of dimethsiloxane

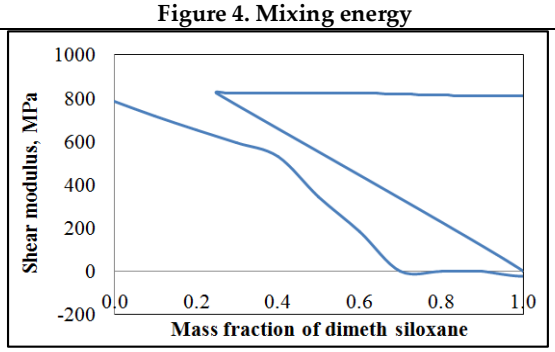

Figure 6. Change in shear modulus with mass fraction of dimethsiloxane

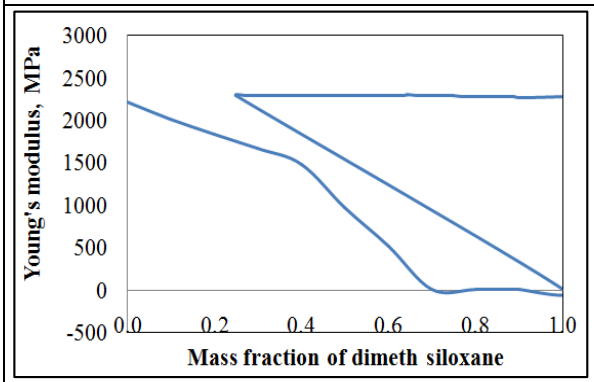

Figure 7. Change in Young's modulus with mass fraction of dimethsiloxane

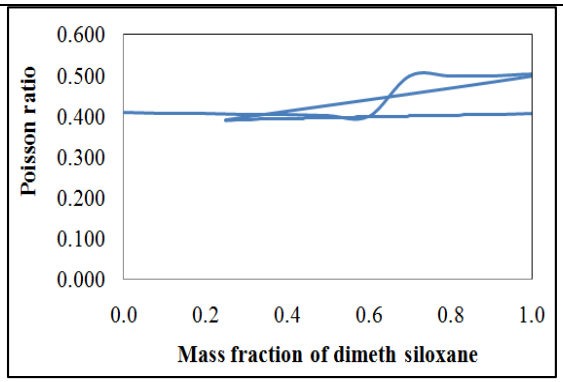

Figure 8. Change in Poisson modulus with mass fraction of dimethsiloxane

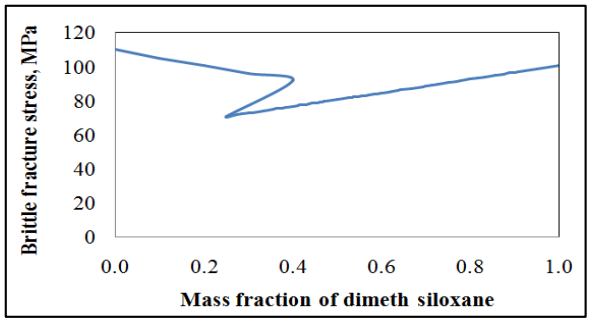

Figure 9. Change in brittle fracture stress with mass fraction of dimethsiloxane

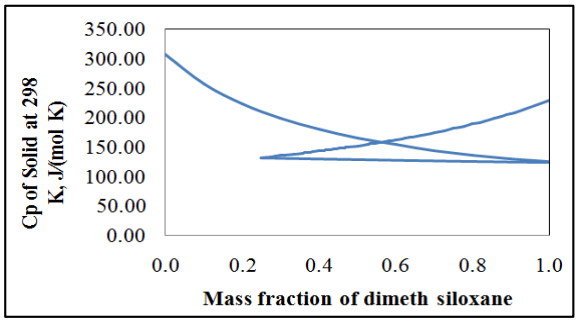

Figure-10. Change in heat capacity with mass fraction of dimethsiloxane

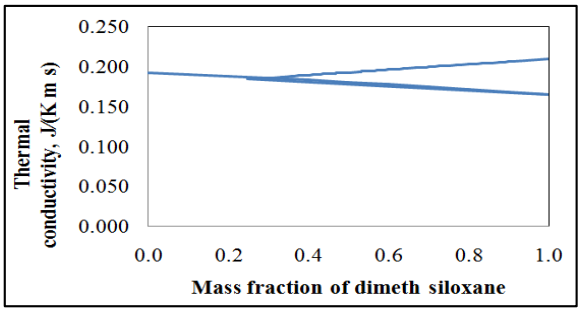

Figure11. Change in thermal conductivity with mass fraction of acrylic acid

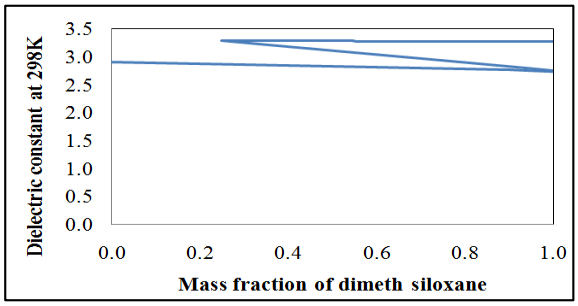

Figure 12. Change in dielectric constant with mass fraction of dimethsiloxane

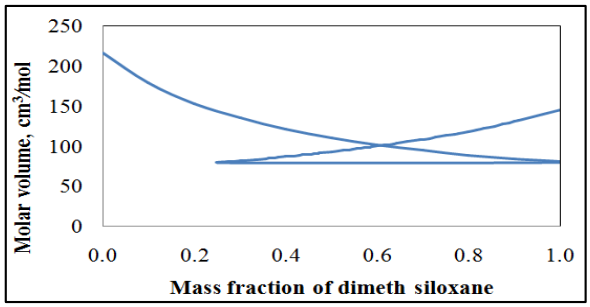

Figure 13. Change in molar volume with mass fraction of dimethsiloxane

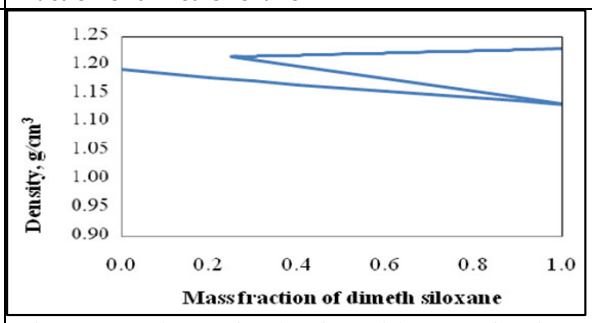

Figure 14. Change in density with mass fraction of dimethsiloxane

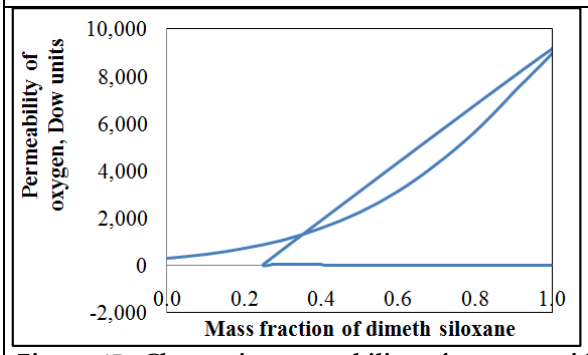

Figure 15. Change in permeability of oxygen with mass fraction of dimethsiloxane

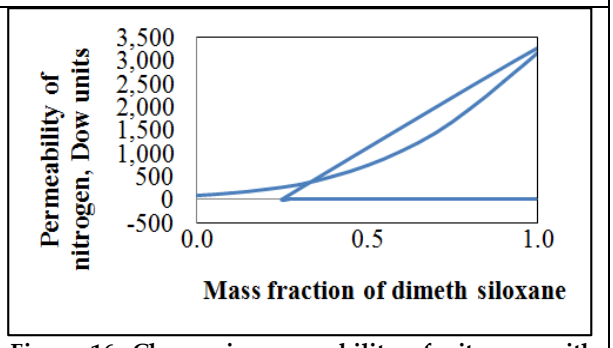

Figure 16. Change in permeability of nitrogen with mass fraction of dimethsiloxane

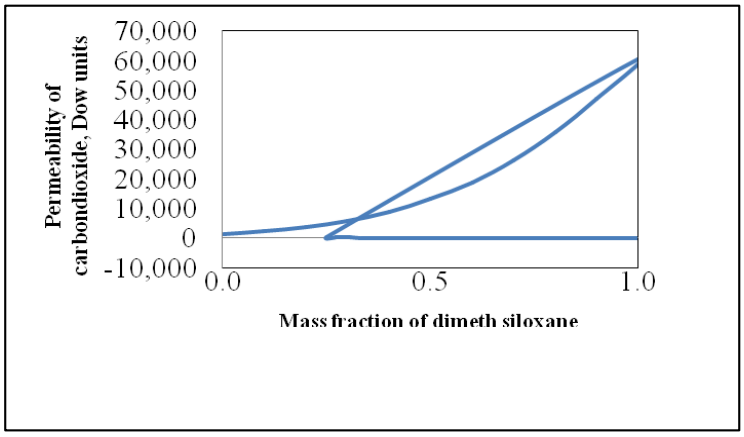

Figure 17. Change in permeability of carbon dioxide with mass fraction of dimethsiloxane

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RESEARCH ARTICLE

In silico Analysis of Ether Sulfone and Styrene Compatibility in A Blend

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ABSTRACT

A blend is the product of two or more polymers or copolymers. The compatibility of Ether sulfone and Styrene were studied to form a miscible blend using Biovia Materials Studio. On the basis of free energy of mixing, chi parameter, phase diagram and mixing energy, the compatibility of the two components were analyzed. From the results it was deduced that the pair can become compatible at both low and high temperature. The phase diagram showed that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus. The results indicated that the values of all the properties changes with change in mass fraction of styrene. The composition of the blend was analyzed with respect to heat capacity and thermal conductivity. The results indicated that all those parameters decreased with increase in mass fraction of styrene. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density increased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases increased with increase in mass fraction of styrene. This study conducted not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend, *In silico*, polyether sulfone, styrene

INTRODUCTION

Now a day's polymer has become the backbone of modern society. Everything around us is made up of polymers starting from a pen to complex things like plastic etc. Polymers are basically a chemical compound bonded together to form along chain formed from monomers joined by covalent bond or hydrogen bonding or electrostatic interaction [1-4]. Polymers are generally divided into two types.i.e man-made & naturally. Natural polymers are found on plants, animals etc. The common natural polymer in the world is cellulose found generally in the cell wall of plants. Another example is Rubber which has been used for several ages. Artificial polymers or synthetic polymers

are generally produced in the laboratory. For example PVC, STRYNES etc. These are being used for producing synthetic polymer which is vastly used is the polythene. Because of their resistance, brittleness, ductility, translucence, durability these are highly being exploited & there has been dramatic increase in the demand. By method of polymerization synthetic are being prepared by combining small monomer molecule into long repeated chains held together by strong covalent bonds. Most polymers referred to thermo plastic or plastic generally consists of molecular chains that can be broken & recycled where as cross linked polymers don't rebond after the bong is broken. Then have higher strength, hardness, and thermal properties [5-7].

Polymer blends or composite are materials generally a mixture formed from two or more copolymers of different chemical & physical; properties to produce a third material of significant chemical and physical properties different from the individual components. The individual components retain their identity in the composite differentiating composite from mixture and solid solution. The main objective of making composite is to reduce the weight of individual component without affecting the other properties like strength, durability, ductility etc. The main force driving it is the variety of option it provides for marketing purpose for low carbon fiber for their light weight and strength. Blending provide a wide attractive opportunities for 3R i.e. recycle, reuse, reduce thereby decreasing its negative impact on the environment. The limitation of polymer is their non-degradability properties thus polluting and the environment [7-10].

The main reason of shifting from micro to nano particles leads to change in its physical and chemical properties. As a result nanoparticles of size less than 100nm are being used in polymer technology. Modification of nanomaterials to get the desired product of required properties opened various ways to multi-functional materials. The common type of nanomaterials used is nanotubes, fibres, fullerenes etc. Natural fiber composite is derived from renewable and carbon dioxide such as wood, plants. There are two types of natural fibres sources- one obtained from plants like cotton, jute, hemp and the other obtained from animal origins like silk, wool, hair etc. Typically composite materials used in the field of work are reinforced concrete, composite woods such as plywood, reinforced plastic such as fiber reinforced plastic or fiberglass, composite containing ceramic and metal matrix. These are generally used for buildings, bridges, swimming pool panels, bath tubs, sink, aircraft etc. Fiber reinforced composite materials made of matrix of desired polymer and fibres. Fibres generally include glass (fiberglass), carbon (in carbon fiber reinforced polymer) etc. These are thin, flexible plastic panels made of strong polystyrene reinforced with fiberglass. The main advantage in its high strength to weight ratio i.e. they are light in weight bout of high strength. It has a vast range of mechanical properties including tensile, compressive strength. Carbon reinforced fiber is basically used for describing a fiber reinforced composite material that uses carbon fiber as its base component. It generally contains 70% fiber weight and generally light in weight. It is generally used in manufacturing racing cars, motor bikes, sports equipments etc [6-10].

Usually blends are prepared by trial and error method and this technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. Styrene is an organic compound belonging to vinyl family with chemical formula $C_6H_5CHCH_2$. Its molecular formula is C8H8 .Because of its derivation from benzene; it is basically highly volatile with a sweet smelling aroma. It is a color less oily liquid but on storage show yellowish color. It is majorly produced from ethyl benzene by dehydrogenation. The presence of vinyl group allows styrene to polymerize. The polymerization rate is very fast. It shows auto-polymerization i.e. they convert without the need of an external inhibitor and stakes place at ambient temperature .The reaction is exothermic in nature, it is also regarded as a cancer causing agent when it comes in contact with eye, skin, on inhalation and on ingestion.Poly (ether sulfone) acts like a polycarbonates but they are more resistant to heat. They are used for making cookware for their resistance towards steam and water. They have ether groups & sulfone group in their backbone chain claiming its name poly (ether sulfone) because of the presence of sulfone group they have high glass transition temperature [7-10].

MATERIALS AND METHODS

Software used

For analysing the compatibility of blend, Materials studio module of Biovia software (Dassault Systemes of France) was used. To predict the level of interaction, the software uses machine learning techniques and standard algorithms.

Methodology

The structure of Ether sulfone and Styrene were prepared using the build menu of Materials Studio. First go to build menu then select built polymer then choose homopolymer. A list of desired polymer were obtained and from them sulfone was choose and then ether sulfone was selected. The procedure was repeated for another polymer group vinyl and styrene was selected. Under blends->calculation menu of Materials studio, the structure of the components was optimized. Styrene was used as the base (the component taken in high quantity) and Ether sulfone was used as screen (the component taken in small quantity). After calculation of the blends is over blend->analysis menu of Materials studio was used to generate various data like chi parameter, free energy of mixing, mixing energy. The data were then studied and the compatibility of the components to form a suitable blend was analyzed. The structures of Ether sulfone and Styrene obtained from earlier were fed to the synthia menu of Materials Studio. Then it was run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were pasted to excel sheet and different graphs based on the numerical values obtained from earlier were plotted to identify the effect of weight fraction of styrene on the mechanical properties of the composite.

RESULTS AND DISCUSSION

By using Biovia Materials Studio, the use of Ether sulfone and Styrene as potential components of a blend was analyzed. In this work the use of polyether sulfone and poly styrene as potential components of a composite was analyzed using. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are accelerated and convenient to use. Consequently, they are of greatest utility when a rapid estimate of a property is required even though detailed understanding of the atomistic interactions is not known. But the limitation of these methods is their dependence upon a database of group contributions. So, if the group contribution of a group in a polymer is not known, then the property of that polymer cannot be calculated. To overcome this limitation, Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. No database of group contributions is required. So for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine properties may be predicted.

Free energy of mixing

If a blend is homogenous then it is said to be miscible. For a blend to be homogenous, a negative value of free energy of mixing is required indicating that mixing is spontaneous. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

Where ΔG_m – *Gibbs free energy of mixing*

ΔH_m = *Enthalpy of mixing*

ΔS_m = *Entropy of mixing*

T = *Absolute temperature*

In case of a blend the value of $T\Delta S_m$ is always positive since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. For the components to form a miscible blend, the entropic contribution to free energy should exceed the enthalpy contribution, i.e.

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (up to 275 K) as evident from Eq. 1 and free energy increases with increase in temperature.

From the results it was observed that the blend will form a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyether sulfone and polystyrene with negative value of mixing energy, which may form a particular shape with significantly high effort. Figure 1.shows the graph of free energy change with mole fraction of polystyrene at different temperatures.

Chi parameter

The excess free energy of mixing and phase behavior for polymer blends and block copolymers can be explained by Flory–Huggins χ parameter. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. For chemically dissimilar polymers, a high value of χ indicates poor mixing. For chemically similar polymers with small cohesive energy difference, small χ value is expected. However, a chance of demising for sufficiently long chains is observed. The architectural and geometric differences between the components prevent from occupying the same configurations them in a mixture experienced in the pure phase. From polymer field theory, we can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of χ high from temperature ranging from 50Kto 500K. From the graph it was observed that the χ values decreases exponentially with increase in temperature. It consent with the free energy of mixing for the blend

Phase diagram

The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 indicate the phase diagram for the two components of the blend. The degree of miscibility can be observed over three different regions:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).

b. Fragmented metastable regions existed between binodals and spinodals, and

c. The two-phase separated regions of immiscibility are bordered by the spinodals.

The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.

The phase separation of the system while entering from single-phase region to the metastable region occurs by the mechanism of resembling crystallization. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing energy

A small value of mixing energy can favor the mixing process. Thus for mixing, the temperature at which the mixing energy is low can be chosen. Figure 4 display that the mixing energy for the system was small for the temperature range studied. The graph manifest that at first with increase in temperature the mixing energy increases to a highest value after that with further increase in temperature the mixing energy decreases and again increases with further increase in temperature. The temperature varies from 50K to500K. For the varying of mixing energy. It is very much possible to mix the two components at any feasible temperature with least mixing energy value

Bulk modulus

The measure of decrease in volume with an increase in pressure is termed as Bulk modulus. Figure 5 reveals that the bulk modulus of the composite decreases linearly with increase in mass fraction of styrene.

Shear modulus

The ratio of shear stress to shear strain is known as Shear modulus. It indicates the response of the composite to shear deformation. Figure 6 shows that with increase in mass fraction of styrene shear modulus decreases and then increases with further increase in mass fraction of styrene.

Young's modulus

The ratio of stress to strain is called Young's modulus. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite decreases slowly with increase in mass fraction and then slowly increase with further increase in mass fraction of styrene

Heat capacity

The amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase is known as heat capacity. Figure 8 shows that the heat capacity (Cp) of the composite decreases slowly with increase in mass fraction of styrene

Thermal conductivity

It specifies the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 9 shows that the thermal conductivity of the composite decreases linearly with increase in mass fraction of styrene

Molar volume

The volume occupied by one mole of a substance is called molar volume. Figure 10 shows that the molar volume of the composite decreases with increase in mass fraction of styrene.

CONCLUSIONS

The possibility of use of polystyrene and ethyl sulfone to form a homogeneous blend was explored using Biovia Materials Studio. Based on free energy of mixing, chi parameter and mixing energy the components were analyzed. The results indicate that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties changes with change in mass fraction of styrene. Then the composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters decreased with increase in mass fraction of styrene. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in styrene fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases increased with increase in mass fraction of styrene. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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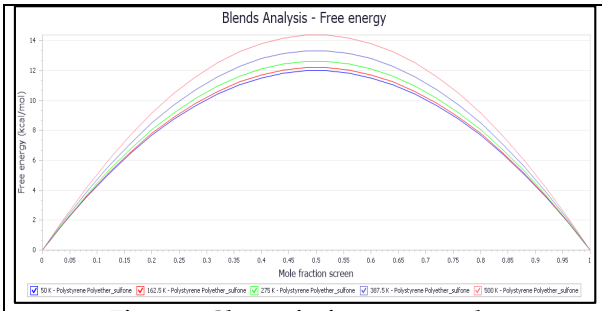

Figure 1: Change in free energy value

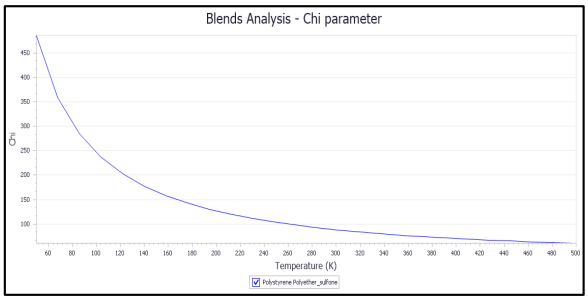

Figure 2: Change in χ (chi) value with temperature

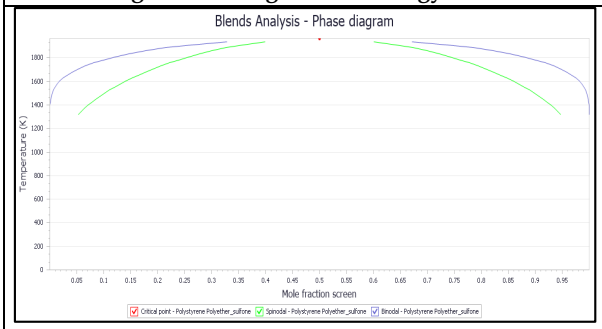

Figure 3.Phase diagram

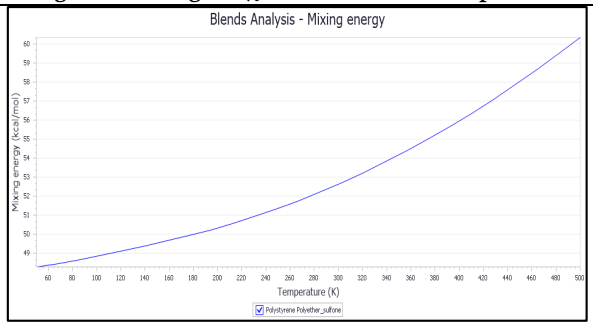

Figure 4. Mixing energy

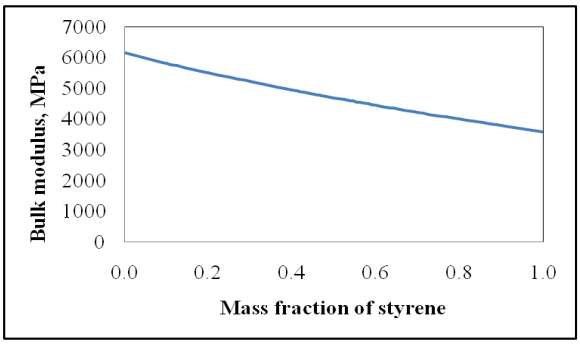

Figure 5: Change in bulk modulus with mass fraction of styrene

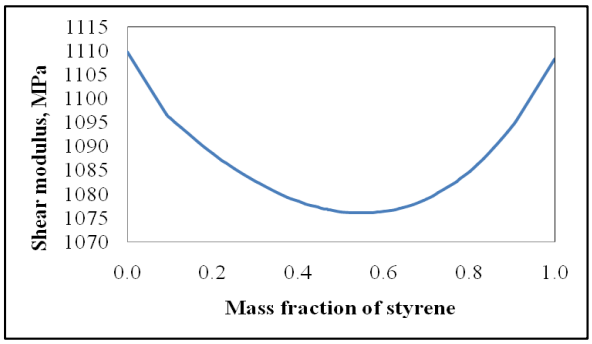

Figure 6: Change in shear modulus with mass fraction of styrene

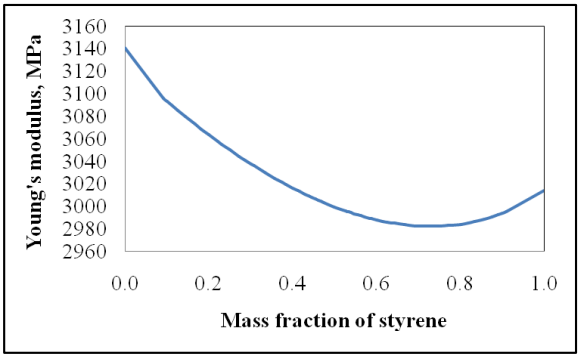

Figure 7: Change in Young's modulus with mass fraction of styrene

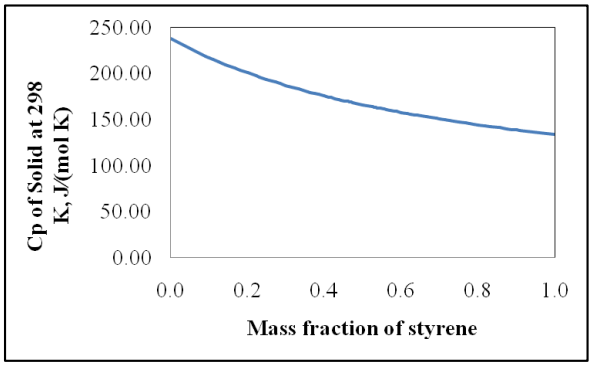

Figure 8: Change in heat capacity with mass fraction of styrene

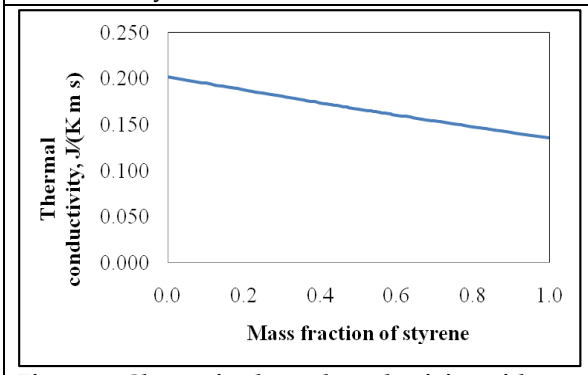

Figure 9. Change in thermal conductivity with mass fraction of styrene

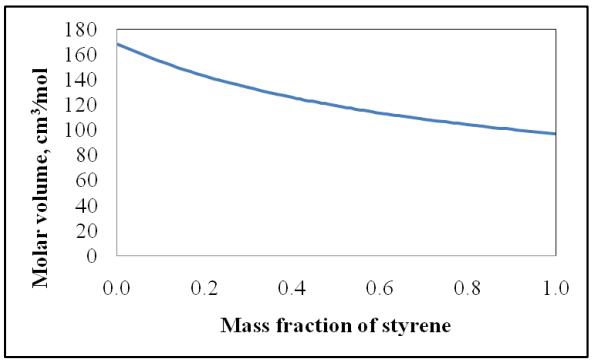

Figure 3.10: Change in molar volume with mass fraction of styrene

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RESEARCH ARTICLE

In silico Analysis of Mechanical and Thermal Properties of Polyvinyl Acetate and Polybutylene Isophthalate Composite

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ABSTRACT

This manuscript reports the formation and modified physical properties of a composite formed by combination of two polymers polyvinyl acetate and polybutylene isophthalate using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram and mixing energy. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were then studied based on Poisson ratio, bulk modulus, shear modulus, Young' modulus, and brittle stress fracture. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant.

Key words: Blend, polyvinyl acetate, polybutylene isophthalate

INTRODUCTION

Two or more chemically different materials with a distinct interface between them combine together to form a composite. The properties and characteristics of the composite enhances from its constituent materials with maintaining separate identities of parent component. Due to high strength to weight ratio and resistance to corrosion they find applications in structural Engineering. The major constituents of a composite can be broadly classified as reinforcement in the form of fibers or particulates and polymer matrix. The reinforcements are the major load resisting component of a composite. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. The polymer matrix holds the reinforcements in place, protects the reinforcements from an adverse environmental condition and also acts as a path for stress transfer between fibers. In order to permit both energy conservation and increased motoring economy there is a huge demand in weight reduction. Polymer composites with nanomaterials and carbon based nanomaterials are the recently studied multi functional materials [1]. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic

additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments. Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7-9]) have been used to identify compatible pairs.

Polyvinyl acetate is an amorphous polymer produced through the combining of many units of monomeric vinyl acetate (CH3COOCH=CH2). The number of units so combined is typically between 100 and 5,000. This translates to an average molecular weight of between 850 and 40,000. The hardest of the polyvinyl esters, polyvinyl acetate offers good adhesion to most surfaces. One slow-drying formulation combines 5 to 15 percent polyvinyl acetate with polybutylene isophthalate to form the composite.

MATERIALS AND METHODS

SOFTWARE USED

"Materials studio module of Biovia software (Dassault Systemes of France)" was adopted to study the modified properties using machine learning techniques and standard algorithms.

METHODOLOGY

Composite of polyvinyl acetate and polybutylene isophthalate as base and screen respectively was prepared using the build menu of Materials Studio. The structure and modified physical properties of the compound were optimized using the calculation menu and analysis menu of the software respectively.

RESULTS AND DISCUSSION

GIBB'S FREE ENERGY OF MIXING

Compactibility of a blend depends on the homogeneity of the mixture and a negative value of free energy lead to a homogeneous blend.

Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

Where $\Delta G_m = Gibb's free energy of mixing$

$\Delta H_m = Enthalpy of mixing$

$\Delta S_m = Entropy of mixing$

$T = Absolute temperature$

The value of $T\Delta S_m$ is always positive in case of a blend as there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always relays on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyvinyl acetate and poly polybutylene isophthalate with negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

CHI PARAMETER

The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K The value of x decreases exponentially with increase in temperature. This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM

The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).

b. Fragmented metastable regions existed between binodals and spinodals, and

c. The two-phase separated regions of immiscibility are bordered by the spinodals.

The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.

When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by mechanism called spinodal decomposition.

MIXING ENERGY

Figure 4 shows that the variation of mixing energy of the system with temperature. The small value of mixing energy at low temperature indicates that the composite does not require high energy for synthesis

MECHANICAL PROPERTIES

Bulk modulus

Figure 5 shows that the bulk modulus of the composite decreases linearly with increase in mass fraction of polyvinyl acetate.

Modulus of rigidity / Shear modulus

From Figure 6 it can be shown that the shear modulus of the composite increases with increase in mass fraction of polyvinyl acetate.

Young's modulus

Young's modulus of the composite increases with increase in mass fraction of polyvinyl acetate as shown in Figure 7

Poisson ratio

Figure 8 shows that the Poisson ratio of the composite decreases linearly with increase in mass fraction of polyvinyl acetate.

Brittle fracture

Brittle Fracture is the quick, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. As shown by Figure 9 the brittle fracture stress of the composite decreases linearly with increase in mass fraction of polyvinyl acetate.

THERMAL PROPERTIES

Specific Heat capacity

Figure 10 shows that the heat capacity (Cp) of the composite decreases linearly with increase in mass fraction of polyvinyl acetate.

Thermal conductivity

It refers to the intrinsic capacity of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite decreases linearly with increase in mass fraction of polyvinyl acetate.

Dielectric constant

Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of polyvinyl acetate which indicates that polyvinyl acetate increases the energy storing capacity.

CONCLUSIONS

The possibility of use of polyvinyl acetate and polybutylene isophthalate to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on Young' modulus, bulk modulus, shear modulus, Poisson ratio and brittle fracture. The results indicated that the values of shear and young's properties increased with increase in mass fraction of polyvinyl acetate. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of polyvinyl acetate. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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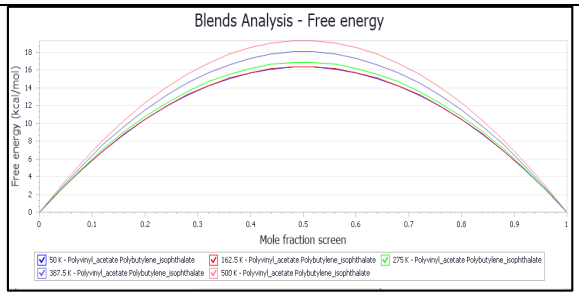

Figure 1. Free energy change with mole fraction of polybutylene isophthalate at different temperatures.

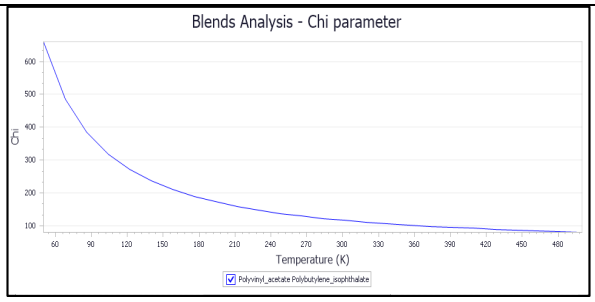

Figure 2. Change in χ (chi) value with temperature

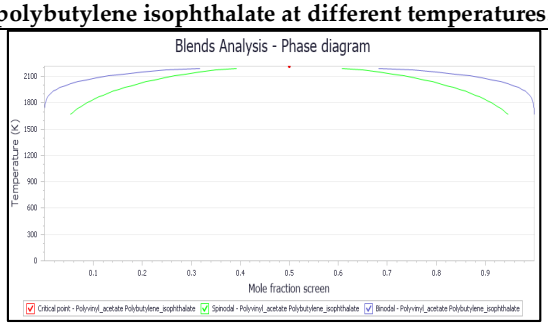

Figure 3.Phase diagram

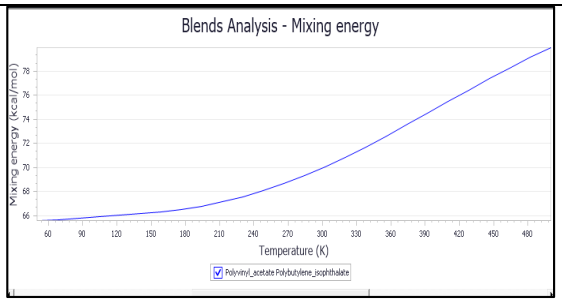

Figure 4. Mixing energy

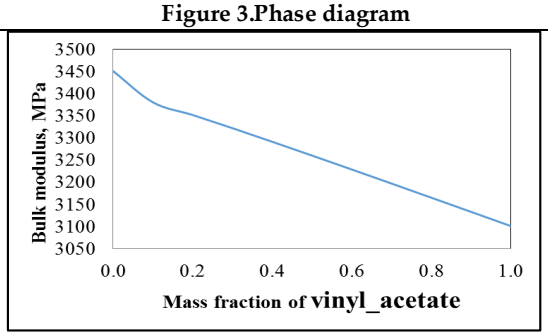

Figure 5. Change in bulk modulus with mass fraction of polyvinyl acetate

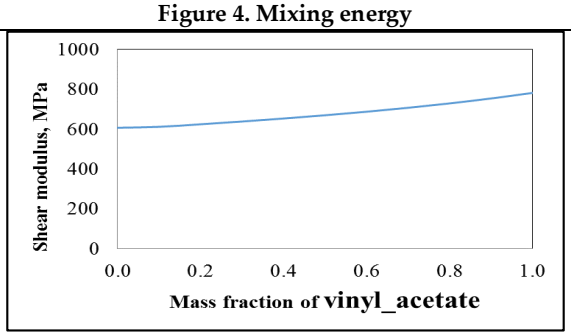

Figure 6. Change in shear modulus with mass fraction of polyvinyl acetate

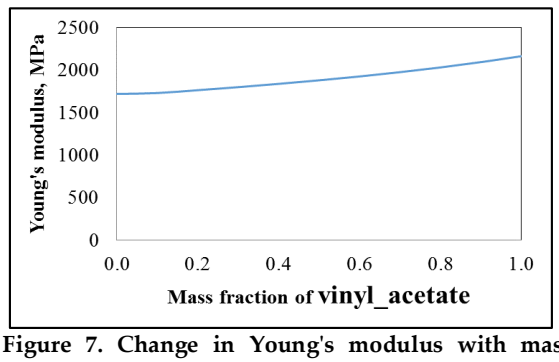

Figure 7. Change in Young's modulus with mass fraction of polyvinyl acetate

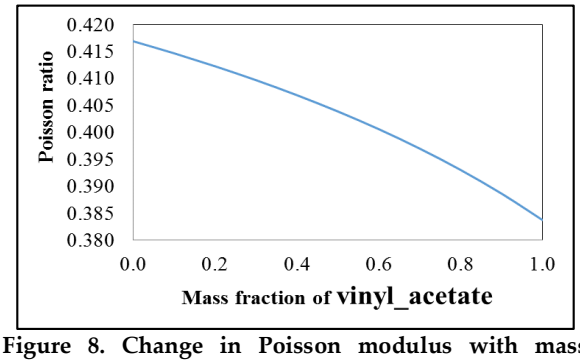

Figure 8. Change in Poisson modulus with mass fraction of polyvinyl acetate

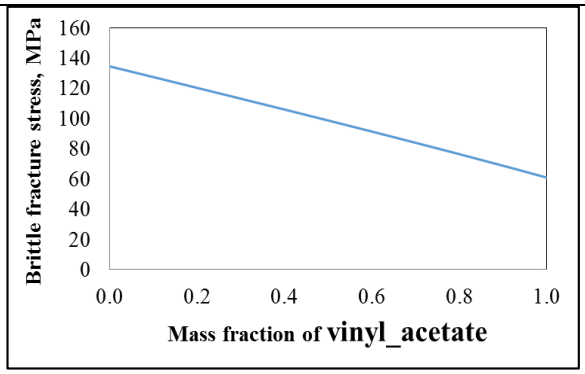

Figure 9. Change in brittle fracture stress with mass fraction of polyvinyl acetate

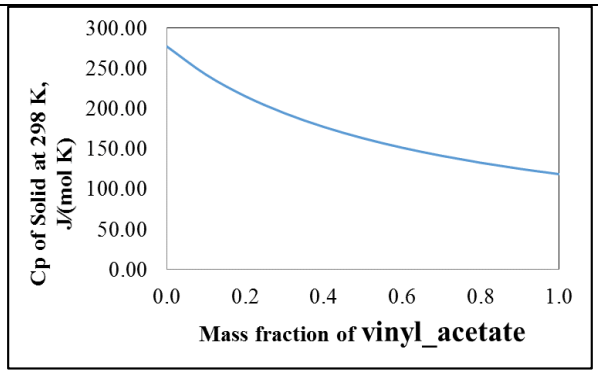

Figure 10. Change in heat capacity with mass fraction of polyvinyl acetate

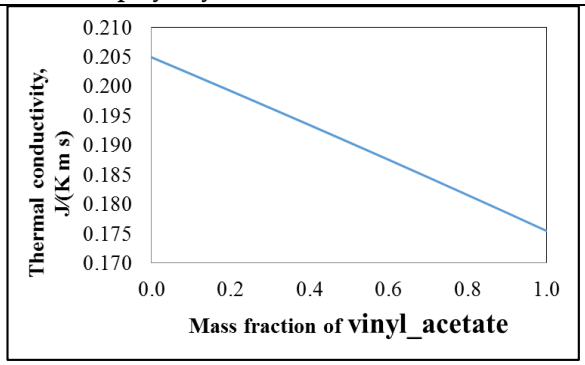

Figure 11. Change in thermal conductivity with mass fraction of polyvinyl acetate

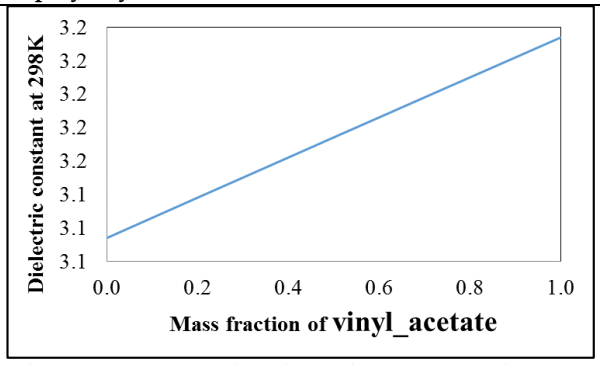

Figure 12. Change in dielectric constant with mass fraction of polyvinyl acetate

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RESEARCH ARTICLE

In silico Analysis of Mechanical Properties of Benzimid and Cyclopentlym Composite

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ABSTRACT

A blend is a mixture of more than one component. The required property of a blend is its homogeneity. Combination of two or more components results in the formation of a blend. The compatibility of Polybenzimid and PolyCyclopentlym were studied to form a miscible blend using Biovia Materials Studio. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: homogeneity, Polybenzimid, laboratory, bulk modulus

INTRODUCTION

Blends or composites are formed with combination of more than one component where components do retain their identity in the mixture. As it is very difficult to find multiple properties in a single material, it is advisable to combine different components thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the significance of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nano material modified polymers paved the way to multi functional materials. Polymers joined with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers,

latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments. Usually blends are prepared by trial and error method and this technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. (1)Polybenzimid:-It is an Organic Compound.It used as a fluorescent stain for DNA in Molecular Biology applications.It is also called "Bisbenzamide"It tends to bind to adenine-thyamine-rich regions of DNA. The Principal application of methacrylate functional siloxanes areas modifiers to organic systems [8].

SOFTWARE USED

Materials studio module of Bio via software (Dassault Systems of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

METHODOLOGY

The structures of Benzimid and Cyclopentlym were fed to the synthia menu of materials studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of vinyl chloride on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of polybenzimid and polycyclopentlym as potential components of a blend was analyzed using Biovia Materials Studio. In this work the use of Polybenzimid and polycyclopentlym as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated. To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Bulk modulus

Bulk modulus is the measure of the decrease in volume with an increase in pressure. Fig.1 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of Benzimid.

Shear modulus

It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Fig. 2 shows that the shear modulus of the composite increases linearly with increase in mass fraction of Benzimid.

Young's modulus

It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Fig. 3 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of Benzimid.

Poisson ratio

It is the ratio of lateral strain to longitudinal strain. Fig.4 shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of Benzimid.

Brittle fracture stress

Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Fig. 5 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of Benzimid.

CONCLUSIONS

The possibility of use of Benzimid and Cyclopentlym to form a homogeneous blend was explored using Biovia Materials Studio. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of Benzimid. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of Benzimid. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

ACKNOWLEDGMENT

The authors are thankful to the Department of Chemistry and the Dean, School of Applied Sciences, Centurion University of Technology and Management, for their cooperation and motivation during this study.

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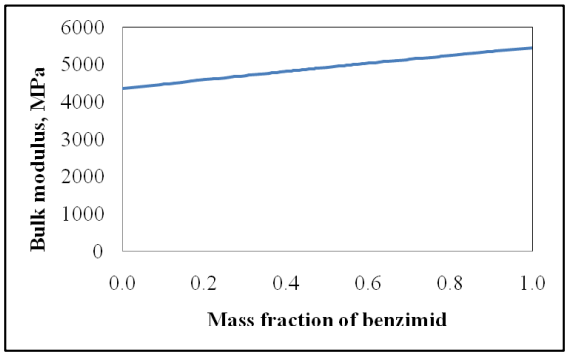

Fig. 1. Change in bulk modulus with mass fraction of Benzimid

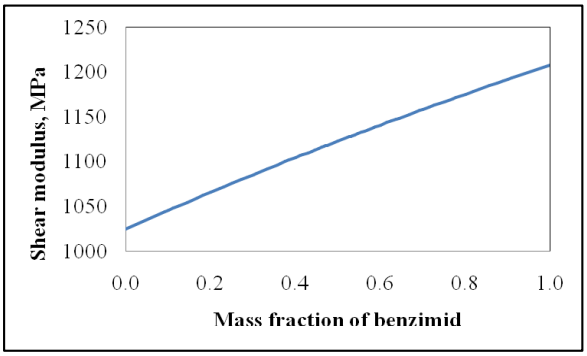

Fig. 2. Change in shear modulus with mass fraction of Benzimid

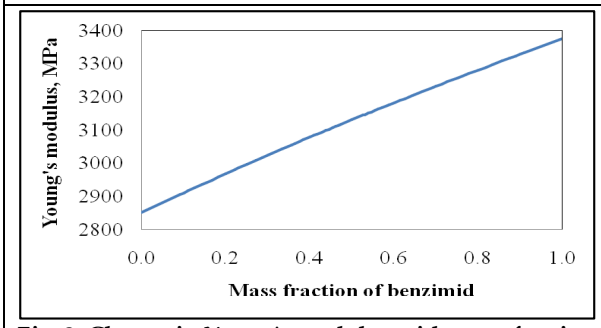

Fig. 3. Change in Young's modulus with mass fraction of Benzimid

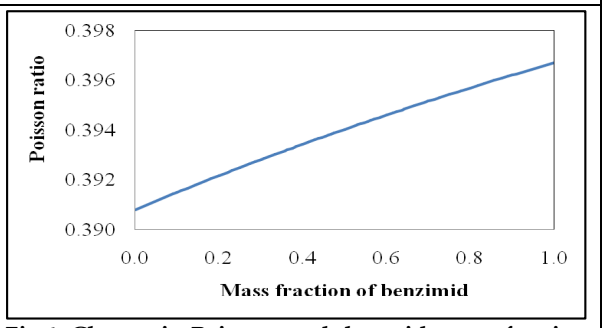

Fig.4. Change in Poisson modulus with mass fraction of Benzimid

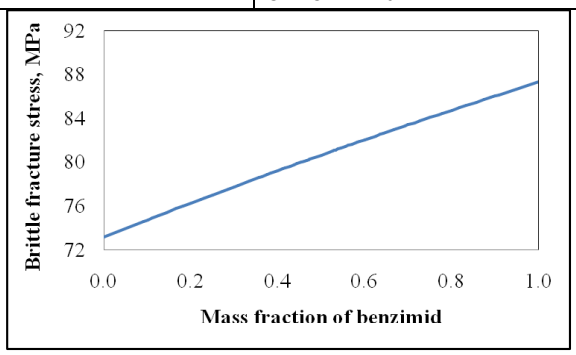

Fig. 5. Change in brittle fracture stress with mass fraction of Benzimid

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RESEARCH ARTICLE

In silico Analysis of Methyl Acrylate and Vinyl Acetate Compatibility in a Blend

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ABSTRACT

Blending is the technique of combination of two or more components resulting blend formation. Using Biovia Materials Studio the compatibility of blend formed out of Methyl acrylate and vinyl acetate was studied. The compatibility of the two was demonstrated on the basis of free energy of mixing, chi parameter, phase diagram and mixing energy study. The results obtained shows that the blend pair is compatible at both low and high temperature. The critical temperature was found to be above which a single phase can be obtained. The study of bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture were done which reflects the mechanical property. The values of all the properties were found to increase with increase in mass fraction of acrylic acid. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant which were found to be directly proportional with the concentration of acrylic acid.The permeability of the blend and its variation with respect to the composition was also studied. The results reflect the decrease in the molar volume and density with increase in acrylic acid fraction. The permeability of the composite was studied based on permeability of oxygen, nitrogen and carbon dioxide. The permeability for all the gases were found to decrease with increase in mass fraction of acrylic acid. This study is more impactable with no laboratory experiment, less time consuming as well as cost effective.

Keywords: Blend, methyl acrylate, vinyl acetate

INTRODUCTION

Polymer blending is the technique of mixing of two or more polymer components retaining their properties in the mixture which may be also known as composite. The quality of a material can be improved by combining different components in different ratios thus giving multiple properties in a single material which is time seeking as well as involves significant research works. In blending two or more materials are mixed to get the desired property. Thus, a

blend saves time to develop a new material as well as this process is cost effective. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. The use of nanotechnology merged with polymer science has been developing for the synthesis of new multi-functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn the attention of the recent researches. To enhance mechanical properties and water resistance different biodegradable polymers- natural fiber composites [2] have been synthesized. Fire retardant/fire proof materials [3] using advanced technique are being proceeding under research which are reported to be of inorganic additives in polypropylene; that increases flame retardancy without increasing the weight [4]. Synthesis of lightweight composite materials with increased strength is under focus as it increases the fuel efficiency in automobiles [5]. The advanced composites are being applied in structural Engineering due to high strength to weight ratio and resistance to corrosion. The glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above-mentioned examples relied on laboratory experiments.

Usually trial and error methodsare preferred for the preparation of blends which is a low cost and time-consuming method. Thus, researchers have focused on the use of in silico approach in order to developed more advanced composite blend within less time consumption giving more productive efficiency. Software (Materials Studio [7]) has been used to identify compatible pairs. Methyl acrylate polymer or poly methyl acrylate (PMA) is the ester derivative of acrylate polymers with molecular formula $(C_4H_6O_2)_n$ bearing molecular weight of 86.09 g/mol per each monomeric unit.. It has low glass transition temperature of 9-12.5^{0}c and is tough, leathery and flexible. It is a colorless, volatile liquid with a very slight solubility in water but appreciably soluble in ethanol, acetone, chloroform and benzene. These are being used for production of coating, elastomers, adhesives, thickners, amphoteric surfactants, fibers, plastics and many more.

Vinyl acetate is an organic aliphatic unsaturated compound which is colourless having a sweet, fruity odour. It polymerises to give the polyvinyl acetate, a rubbery polymer material with molecular formula $(C_4H_6O_2)_n$. It is a type of thermoplastic polymer having glass transition temperature in between 30 to 40^{0}C. It is a flexible and transparent polymer under thermoplastic group.The use of vinyl acetate is the preparation of glues for building and packaging, making of paints, textiles and papers, coating plastic films for food packaging.The blend of methyl acrylate and vinyl acetate will retain the properties of both the respective polymers and is thus known as methyl acrylate vinyl acetate composite.

MATERIALS AND METHODS

SOFTWARE USED

For this analysis materials studio module of Biovia software (DassaultSystemof France) was used. To predict the level of interaction machine learing technique and standard algorithms software are used.

METHODOLOGY

In material studio using the build menu option methyl acrylate and vinyl acetate were prepared. Then using the blends->calculation menu of material studio the structure of the components wasoptimized. Methyl acrylate and vinyl acetate were used as base and screen respectively. After calculating the blends->analysis menu of Materials studio was used to develop various data. The data were evaluated and the amity of the components to form a blend was analyzed.

In the synthia menu of material studio the structures of methyl acrylate and vinyl acetate were analyzed. To find out different weight fraction of the components it was run. In a tabular form, different properties of the composite were displayed. To identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite the values were used to plot graph.

RESULTS AND DISCUSSION

Using Biovia materials studio the polyacrylic and poly-acryl chloride as potential components of a blend was investigated.In this work the use of methyl acrylate acid and vinyl acetate potential components of a composite was analyzed using Biovia Materials Studio.To evaluate a wide range of polymer properties Biovia materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships). To predict the properties of polymers as well as small molecules group additive methods were used for many years. These methods are too fast and easy to use. Therefore, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. If the property of the polymer cannot be calculated then that polymer which contains a group for the group contribution cannot be estimated.

To overthrow this limitation, the method execute in Synthia uses topological information about polymers in the divining correlations. Derived from graph theory are employed due to the connectivity indices. Thus, the properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine but no database of group contribution is required.

Free Energy of Mixing: For homogeneous a blend is said to be miscible. For a homogeneous blend a negative value of free energy of mixing indicates andthat mixing is spontaneous. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m = Gibb's\ free\ energy\ of\ mixing$

$\Delta H_m = Enthalpy\ of\ mixing$

$\Delta S_m = Entropy\ of\ mixing$

$T = Absolute\ temperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (up to 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyvinyl alcoholand poly ethyl urethane with negative value of mixing energy,which may lead to form a particular shape with significantly high effort.

Chi Parameter: The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus, a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi).
Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K. Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility: a) The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single-phase blend can be formed at a high temperature (higher than 750 K).
b. Fragmented metastable regions existed between binodal and spinodal, and
c. The two-phase separated regions of immiscibility are bordered by the spinodal.
The binodal separated miscible (one-phase) and metastable region, while the spinodal separated the metastable and two-phase region.When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

MIXING ENERGY: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature.The temperature is vary from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of acrylic acid.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of acrylic acid.

Heat capacity: It is the amount of heat required to raise the temperature of one-unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of acrylic acid.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of acrylic acid.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are

maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of acrylic acid.

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with increase in mass fraction of acrylic acid.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite decreases linearly with increase in mass fraction of acrylic acid.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite decreases with increase in mass fraction of acrylic acid.

Figure 16 shows that the permeability of nitrogen through the composite decreases with increase in mass fraction of acrylic acid. Figure 17 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of acrylic acid. Thus, the results indicated that an increase in acrylic acid fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

Using biovia materials studio the polyvinyl alcoholand ethylurethane is used to form a homogeneous blend. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. At different ranges of temperature that the pair can have very good compatibility. Study of the mechanical properties of the composite based upon bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. With increasing in mass fraction of acrylic acid the values of all the properties increased. With respect to heat capacity, thermal conductivity and dielectric constant the composition of the blend was analysed. With increase in mass fraction of acrylic acid all the three parameters increased. With respect to permeability properties the composition of the blend was analysed. With increase in acrylic acid fraction the molar volume and density decreased. Using permeability of oxygen, nitrogen and carbon dioxide the permeability properties of the composite were studied. With increase in mass fraction of acrylic acid permeability for all the gases decreased. Usually components for a blend are identified experimentally. Without performing laboratory experiments silico study will help determining components of a blend saving materials, money and time.

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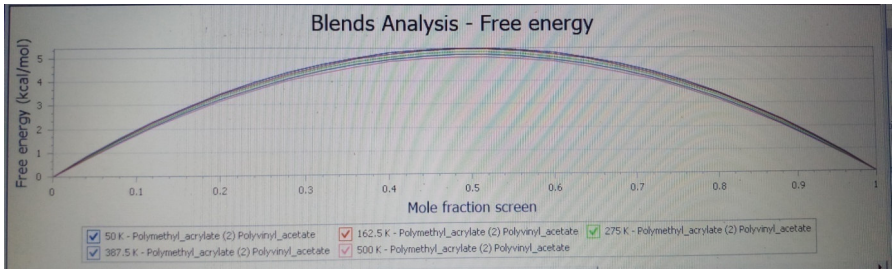

Figure 1. Free energy change with mole fraction of polymethyl acrylate and polyvinyl acetate at different temperatures

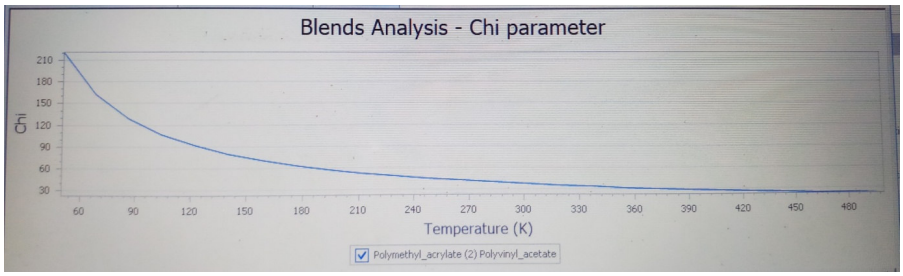

Figure 2. Change in χ (chi) value with temperature

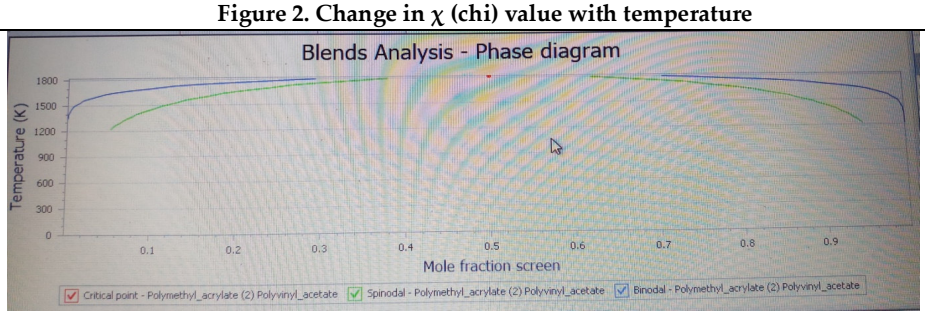

Figure 3.Phase diagram

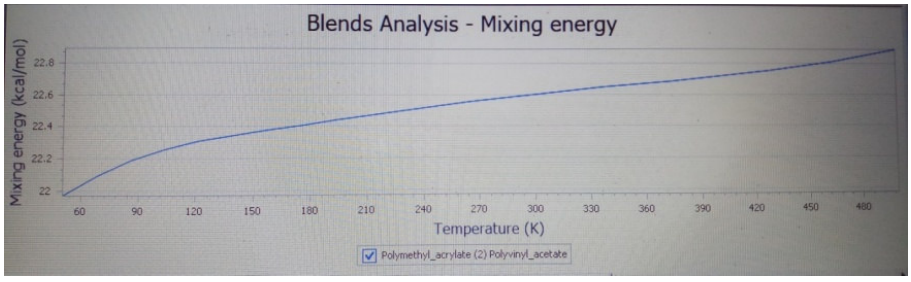

Figure 4. Mixing energy

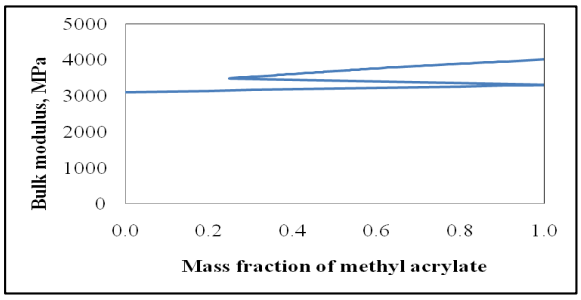

Figure 5. Change in bulk modulus with mass fraction of acrylic acid

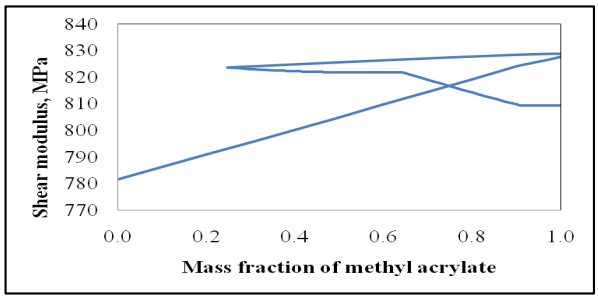

Figure 6. Change in shear modulus with mass fraction of acrylic acid

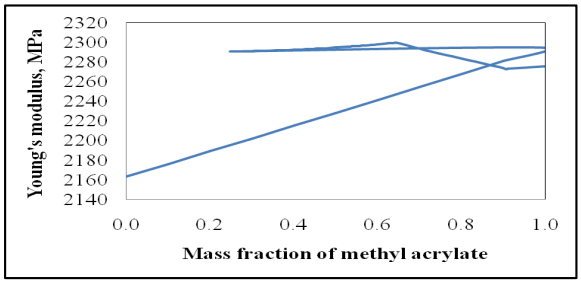

Figure 7. Change in Young's modulus with mass fraction of acrylic acid

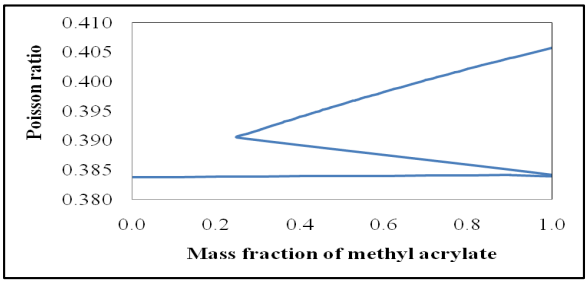

Figure 8. Change in Poisson modulus with mass fraction of acrylic acid

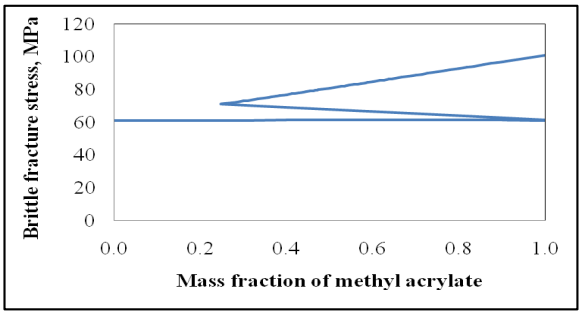

Figure 9. Change in brittle fracture stress with mass fraction of acrylic acid

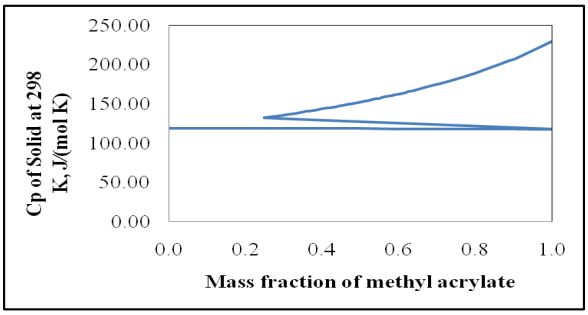

Figure 10. Change in heat capacity with mass fraction of acrylic acid

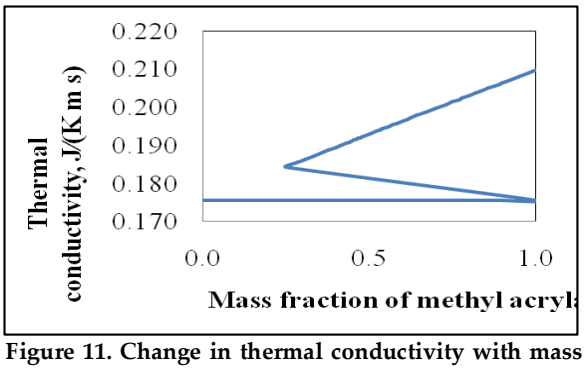

Figure 11. Change in thermal conductivity with mass fraction of acrylic acid

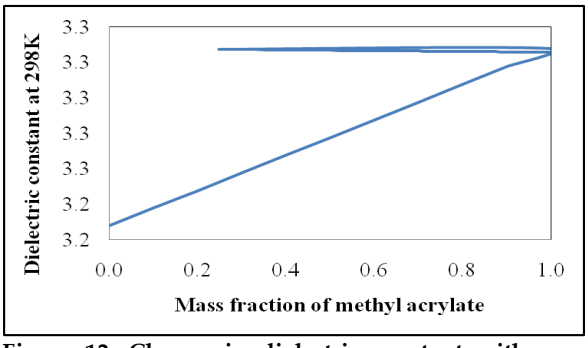

Figure 12. Change in dielectric constant with mass fraction of acrylic acid

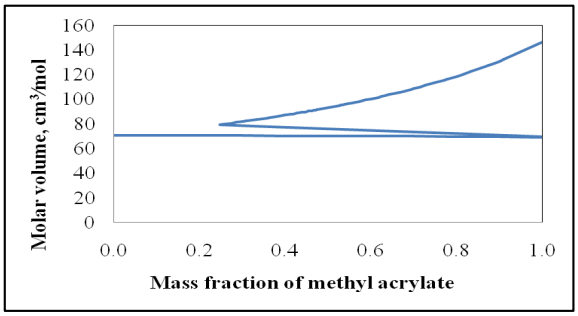

Figure 13. Change in molar volume with mass fraction of acrylic acid

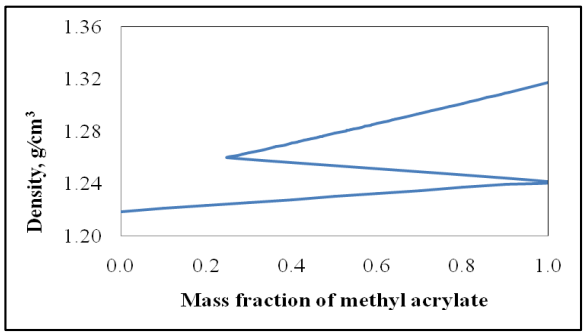

Figure 14. Change in density with mass fraction of acrylic acid

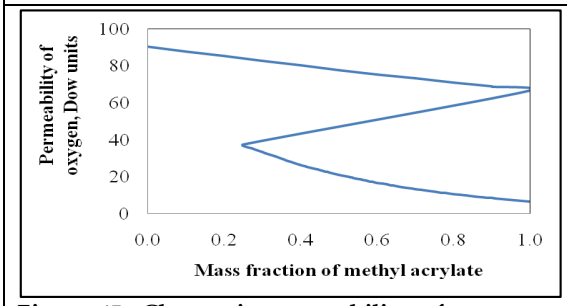

Figure 15. Change in permeability of oxygen with mass fraction of acrylic acid

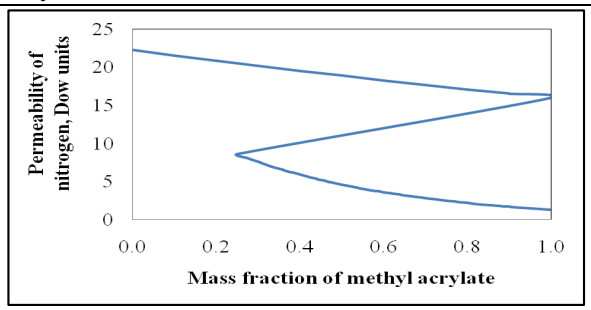

Figure 16. Change in permeability of nitrogen with mass fraction of acrylic acid

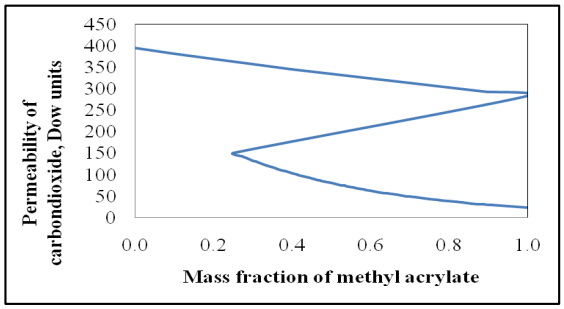

Figure 17. Change in permeability of carbon dioxide with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Phytochemicals from *Aleo vera* against COVID-19

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ABSTRACT

Phytochemicals from *Aloe vera* plant extract can use for the treatment of corona disease. It is caused by SARS CoV-2. Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDocker energy and -CDocker interaction energy" suggested that aloe-emodin can interfere the enzymatic activity of 6M3M enzyme by interrupting the viral life cycle.

Keywords: phytochemical, Biovia, Discovery studio,*Aloe vera* ,COVID-19

INTRODUCTION

Nature is a major source of medicines [1]. The medicinal value of the plants is due to the phytochemicals present in it. Phytochemicals can be derived from different parts of plants.Different medicinal plants and their phytoextracts have shown anti-microbial action [2]. These medicinal plants play a vital role in human health care. Many people rely on the use of traditional medicine [3]. *Aloe vera* belongs to family Asphodelaceae. Aloevera leaves extract is having anti-inflammatory and antimicrobial activity. Its extract is used to cure disease like COVID-19. The objective of the study is to identify the phytochemical responsible to cure the disease. Aloeveracontains"alkaloids, glycosides, reducing sugar, phenolic compounds, flavonoids and tannins ."etc. These phytochemicals mightact againstCOVID-19. However, there is no such study available. This objective of the study is to identify the phytochemical of *Aloe vera* capable of curing Covid-19.

MATERIALS AND METHODS

"Discovery studio module of Biovia software (Dassault Systemes of France)" was used for molecular docking. It is reported that *Aloe vera* contains"alkaloids, glycosides, reducing sugar, phenolic compounds, flavonoids and tannins"etc.It was described in ancient medicinal systemscapable of controlling COVID-19. COVID-19is caused by *SARS COV-2*. It has been found from "Brenda enzyme database" that6M3M enzyme is important in microbial life cycle. Molecular docking was performed using the method described by Das et al. [4]. High positive values of "-CDOCKER_ENERGY" and "-CDOCKER_INTERACTION_ENERGY" determines the strength of interaction between

receptor and the ligand. Thus, the interactions with high positives values might indicate the major phytochemical responsible for curing the disease.

RESULTS AND DISCUSSION

"CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy. The ligand conformations were obtained by Molecular Dynamic methods" [4]. Table 1 shows 6M3M-aloe-emodin interaction was found to have the highest interaction.

CONCLUSIONS

Traditional medicines suggested that*Aloe vera*plant has medicinal action against COVID-19 caused by virus *COVID-19*. Using "Discovery studio module of Biovia software", molecular docking operation was performed. This study could explain that the presence of aloe-emodin is responsible for the action of*Aloe vera*against COVID-19 caused by COVID-19 virus.

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Table 1. Results of Cdocking

SL NO	LIGAND	- C Docker energy	- C Docker interaction energy	Difference between - C Docker interaction energy and - C Docker energy
1	Aloe-emodin	16.1519	20.4039	4.2449

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RESEARCH ARTICLE

In silico Analysis of Poly Oxyphenyl and Polynylon 66 Compatibility in Blend

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ABSTRACT

When more than one component are combined blends or composites are formed. The component retains their identity in the mixture. The compatibility of polyoxyphenyl and polynylon 66 were studied to form a miscible blend using Biovia Materials Studio.Based on free energy of mixing, chi parameter, phase diagram and mixing energy the compatibility of the two component was established. From the results it is indicated that the pair can become compatible at low temperature as well as high temperature. A single phase can be obtained above 1100 K from the phase diagram, which was the critical temperature. The mechanical properties of the composite were observed from shear modulus, poisson ratio, young's modlus, bulk modulus and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of polyoxyphenyl. Again it was analyzed with respect to permeability properties. The molar volume and density decreased with increase in polyoxyphenyl fraction, had been noticed. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. Their results showed that with increase in mass fraction of polyoxyphenyl the permeability for all the gases decreased with increase in mass fraction of polyoxyphenyl. This study helps to determine pairs without performing laboratory experiments within the short period of time and of course a low cost process.

Keywords: Blend, *In silico*, polyoxyphenyl,polynylon 66.

INTRODUCTION

Chemical modification doesn't mean changing the properties whether chemical or physical property of a polymer. By following simple methods, it can be done by intermixing the taken polymer with the other polymeric materials. Hence some whole new properties will obtain. The nature of the polymer taken, physical state, interaction between them, the way in which they are been processed,most importantly mixing ratio and the steps of processing plays a key role in determining the properties of the new product formed. Different types of

polymer like rubber plastic, synthetic plastic may be taken as original polymer. Likewise, a gas,a liquid of low molar mass or another synthetic plastic can be used as additive. The dimension of the added material may be varied from three dimensional to zero dimensional. Hence the result may have various phase.

Polymer blends is used to lower the cost price, enhance the method used in process, get good result in resistivity. The industrial blends are homogenous, heterogeneous. The type of polymer blend (homogenous or heterogeneous) bet on different cases such as; mixing with respect to kinetics, subsistence temperature, and existence of different type of additives. Gibbs free energy plays a key role in the miscibility of taken polymers. However, if it has positive value then phase separation takesplace. There are two conditions which rules the miscibility; one is its value must be less than zero that is negative and second is derivative component 2 with respect to volume fraction should be greater than zero. In general, polymer blends, which will separate at equilibrium into two mixed-compositions, can exhibit a wide scope of phase behavior, taking critical temperatures of both higher and lower limit. Idealized phase diagram for a polymer blend two phases coexist.

Polyphenyl ether is referred as polyoxyphenyl. It is a class of polymer which have repeating unit of phenoxy or thiophenoxy in the ether linkages. Polyphenyl ether (PPEs) and polyphenylene oxides (PPOs) are commercial phenyl ethers polymers.First classified phenoxy group don't contain any substitution but the second one have two to four alkyl groups on phenyl ring. Physical properties depend mainly on number of aromatic rings present, substitution pattern and specially on ether or thioether present. In case of mixed type, the properties are hard to predict. When equivalent amount of hexamethylenediamine and adipic acid are combined in a water reactor they undergo polycondensation. Crystallisations nylon salt was formed. then polymerisation process takesplace continuously in the reaction vessel. Due to its good automated properties it is abundantly found in the making of fibers,textiles,airbags,apparel,carpet fibre,3D structural objects etc.

MATERIALS AND METHODS

Materials studio module of Biovia software (DassaultSystemes, France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction. Polyoxyphenyl and polynylon66 were prepared using the build menu of Materials Studio. The structure of the components was optimized using the components were used in blends->calculation menu of Materials studio. Polyoxyphenyl was used as the base and polynylon66 was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of Polyoxyphenyl and polynylon66 were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polypolyoxyphenyl on the different composite properties.

RESULTS AND DISCUSSION

In this work the use of POLYOXYPHENYL and POLYNYLON66 as potential components of a blend was analyzed using Biovia Materials Studio. To evaluate a large range of polymer properties, BIOVIA Materials Studio Synthia adopt a more defined interaction (advanced quantitative structure-property relationships).From many years to figure out the polymer properties group additive methods had been used.Talking about these methods, they are intensely fast and extremely simple to use. In the end, when a very fast estimation of a desired polymer property is in need without having an accurate data of the atomistic interactions,they come into more promising in services and applications. If a polymers property could be calculated, then it must a contain group whose beneficence must be negligible.

For the removance of these type of problem, the topological data base will be used by Synthia. The graph theory which gives the information about the connectivity indices are then operated. Then any properties of polymer from carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine can be predicted without knowing the group contribution.

Free energy of mixing: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where ΔG_m – *Gibb s free energy of mixing*

ΔH_m – *Enthalpy of mixing*

ΔS_m = *Entropy of mixing*

T = *Absolute temperature*

The value of $T\Delta S_m$ is always positive in case of a blend hence the mixing energy of entropy is always increased. Thus, the factor ΔG_m regularly depend upon ΔH_m. if the entropic contribution to free energy is much more than the enthalpic contribution then only components can mix and form a miscible blend, i.e.in equation

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyvinyl alcoholand poly ethylurethane with negative value of mixing energy,which may lead to form a particular shape with significantly high effort.

Chi parameter: The excess of free energy of mixing data can be drawn from the Flory–Huggins χ parameter and it helps to explain taken polymers behavior of phase and block co-polymers. For polymers which are not chemically similar, a significant imbalance in cohesive energy density leads to a high χ value and therefore a higher force of driving results phase separation. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in ahomogenious mixture from entertaining the duplicate structure composition experienced in absolute phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi).Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K. Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

Phase diagram: Phase diagram can be extremely helpful in visualizing the taken binary mixtures compatibility. Figure 3 shows the phase diagram for the two components of the blend. Here we have 3 zones of various degree of miscibility: (a)A single-phased miscible zone existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K). (b) The fragmented metastable zone existed between binodals and spinodals, (c) and The two-phase isolated zones of immiscibility are circumference by the spinodals. The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region. The phase isolation generally happens when the system enters from single-phase zone to the metastable zone, i.e, unhurried nucleation followed by rise of the phase isolateddomains. On the other hand, the phases separation spontaneouslyoccur when the system jumps from a single phase into the spinodal zone of immiscibility by spinodal decomposition

Mixing energy: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature.The temperature is varying from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus: It is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite decreases slightly curvely with increase in mass fraction of polyoxyphenyl.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite decreases linearly with increase in mass fraction of oxyphenyl.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite decreases linearly with increase in mass fraction of oxyphenyl.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite increases linearly with decreases in mass fraction of oxyphenyl.

Heat capacity: It is the amount of heatrequired to raise the temperature of one-unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite decreases curvely with increase in mass fraction of oxyphenyl.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite decreases linearly with increase in mass fraction of oxyphenyl.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite slightly decreases with increase in mass fraction of oxyphenyl.

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with increase in mass fraction of oxyphenyl.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite increases linearly with increase in mass fraction of oxyphenyl.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite increases with increase in mass fraction of oxyphenyl.

Figure 16 shows that the permeability of nitrogen through the composite increases with increase in mass fraction of oxyphenyl. Figure 17 shows that the permeability of carbon dioxide through the composite increases with increase in

mass fraction of oxyphenyl. Thus, the results indicated that an increase in oxyphenyl fraction increases the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of polyoxyphenyl and polynylon66 to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility of the sample taken was analyzed with respect tofree energy of mixing, chi parameter and mixing energy. There was a clear indication that the pair can have very good compatibility at various ranges of temperature. The mechanical properties like bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture were studied and found that there is a decrease with increase in mass fraction of oxyphenyl except brittle fracture. The polymers blend was analyzed with heat capacity, thermal conductivity, dielectric constant and molar volume. The results indicated that all the four parameters decrease with increase in mass fraction of oxyphenyl. The blend composition was analyzed based on permeability properties. The permeability properties of the composite were studied with permeability of oxygen, nitrogen and carbon dioxide. And it resulted that with increase in mass fraction of oxyphenyl the permeability increases. The density also increased with respect to increase in mass fraction of oxyphenyl. Usually by laboratory experiments components of blends were identified. But This in silico study will help us to identify the components of a blend without performing any type experiments saving materials, money and mostly the time.

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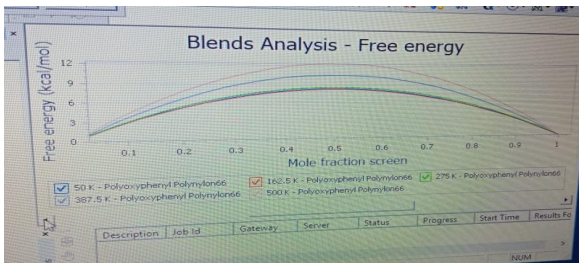

Figure 1. Free energy change with mole fraction of polyethylurethane at different temperatures

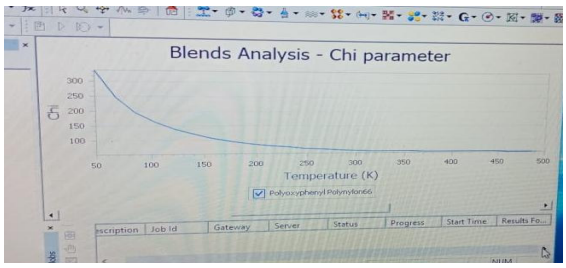

Figure 2. Change in χ (chi) value with temperature

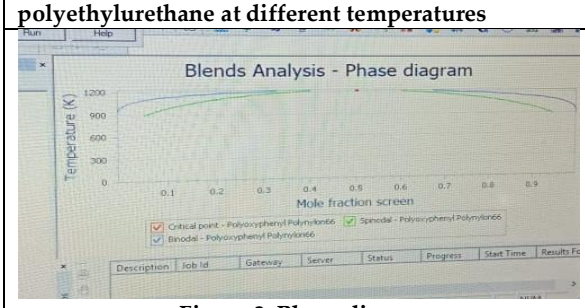

Figure 3. Phase diagram

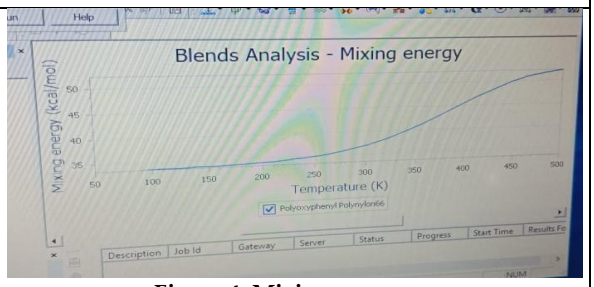

Figure 4. Mixing energy

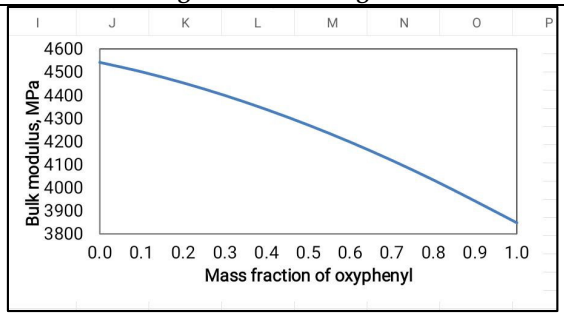

Figure 5. Change in bulk modulus with mass fraction of oxyphenyl

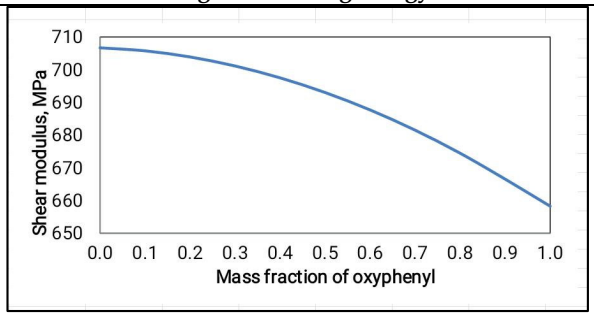

Figure 6. Change in shear modulus with mass fraction of oxyphenyl

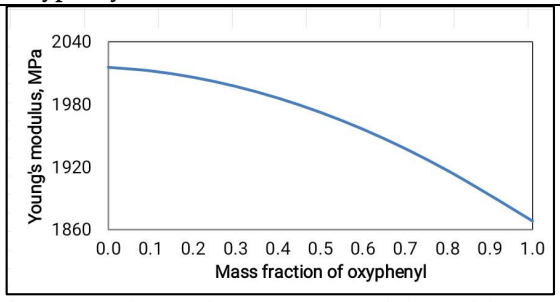

Figure 7. Change in Young's modulus with mass fraction of oxyphenyl

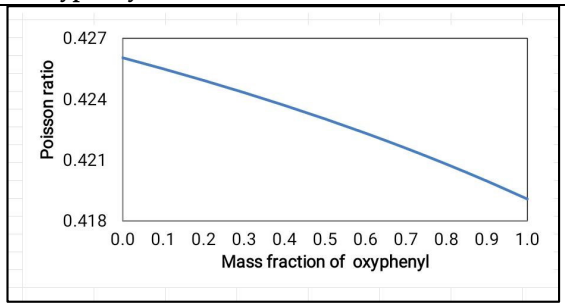

Figure 8. Change in Poisson modulus with mass fraction of oxyphenyl

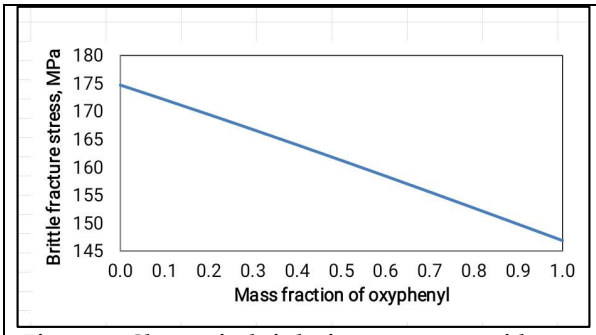

Figure 9. Change in brittle fracture stress with mass fraction of oxyphenyl

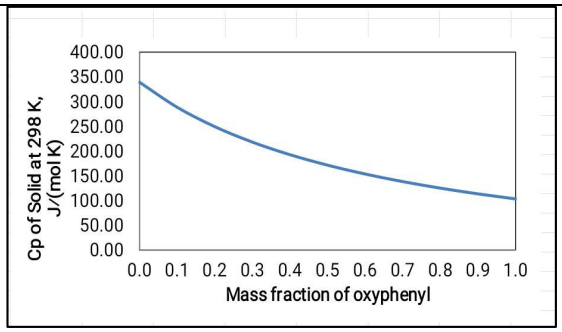

Figure 10. Change in heat capacity with mass fraction of oxyphenyl

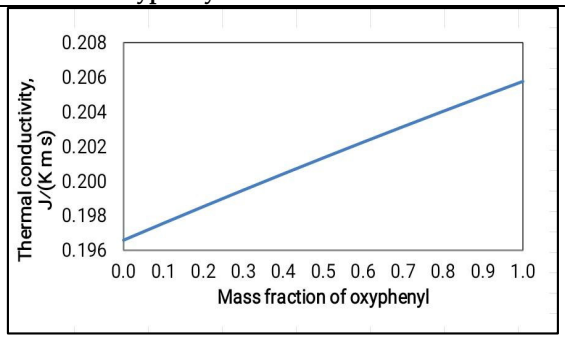

Figure 11. Change in thermal conductivity with mass fraction of oxyphenyl

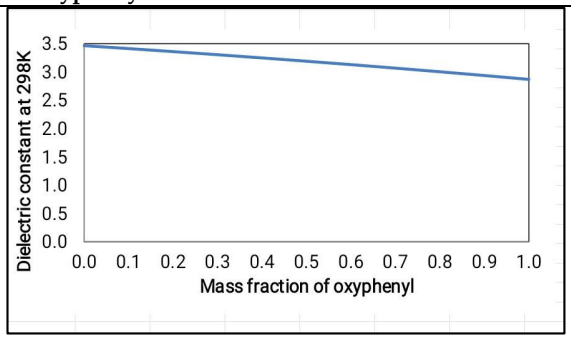

Figure 12. Change in dielectric constant with mass fraction of oxyphenyl

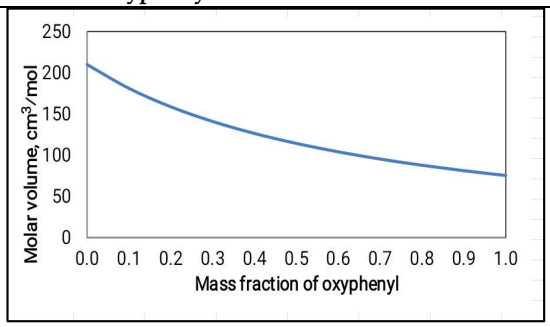

Figure 13. Change in molar volume with mass fraction of oxyphenyl

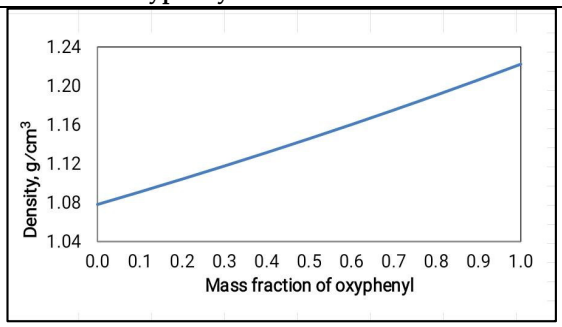

Figure 14. Change in density with mass fraction of oxyphenyl

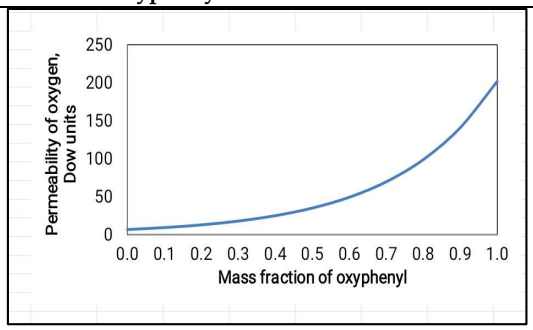

Figure 15. Change in permeability of oxygen with mass fraction of oxyphenyl

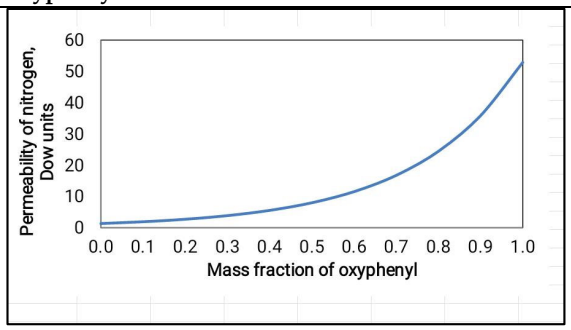

Figure 16. Change in permeability of nitrogen with mass fraction of oxyphenyl

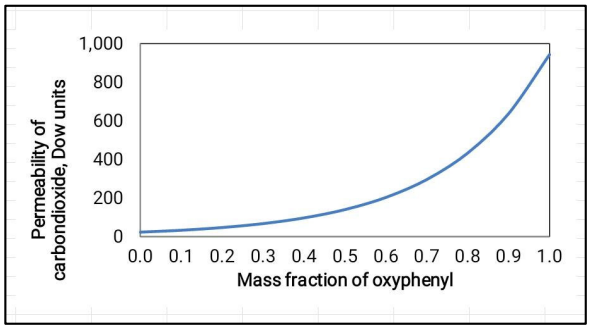

Figure 17. Change in permeability of carbon dioxide with mass fraction of oxyphenyl

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RESEARCH ARTICLE

In silico Analysis of Polyacrylonitrile and Polyethyl-Urethane Compatibility in a Blend

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ABSTRACT

The blend is formed by the combination of two or more components. The compatibility of Polyacrylonitrile and Polyethyl-urethane was studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on the free energy of mixing, chi parameter, phase diagram, and mixing energy. The results indicated that the pair can become compatible with both low and high temperatures. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite such as bulk modulus, shear modulus, Young' modulus, Poisson ratio, and brittle stress fracture were studied. The results indicated that the values of all the properties increase or decrease with an increase in the mass fraction of acrylonitrile. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity, and dielectric constant. The results indicated that all those parameters increased with an increase in the mass fraction of acrylic acid. The composition of the blend was analyzed with respect to permeability properties. The properties of the composite based on the permeability of oxygen, nitrogen, and carbon dioxide showed that the permeability for all the gases decreased with an increase in the mass fraction of acrylic acid. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low-cost process.

Keywords: Blend, in silico, Polyacrylonitrile, Polyethyl-urethane.

INTRODUCTION

Polymeric materials or blending materials find growing applications in various fields of day to day life because they provide a wide range of application relevant properties. The blending of polymers is a technological way of giving materials with desired specific properties at the lowest price, e.g. a combination of strength and toughness, strength and solvent resistance, etc. Mixing also benefits the manufacture by offering improved processability, product uniformity, quick formulation changes plant flexibility, and high productivity. If two polymers are mixed, the

frequent result is a system that it gains a complete phase separation due to the repulsive interaction between the components (the chemical in between the polymers).composites are formed with a combination of more than one component where components do retain their identity in the blend. As it is not easy to find different properties in a single material, it is preferable to combine different components thereby increasing the quality of the material. The development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus, a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nanomaterial modified polymers paved the way for multi-functional materials. Polymers coupled with carbon-based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fireproof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for the construction of bridges, light rail transit, mining, and tunneling, retaining walls, and other waterside buildings. All the above-mentioned examples relied on laboratory experiments.

Usually, blends are prepared by trial and error method and this technique is a low cost and less time-consuming method. Thus, researchers have focused on the use of in silico approach to developing new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. Polyacrylonitrile also is known as polyvinyl cyanide (PAN) it is a synthetic, organic polymer resin, with the linear formula $(C_3H_3N)_n$. Though it is thermoplastic in nature, it does not melt under normal conditions rather melt at high temperatures. It melts above 300^{o}C if the heating rates are 50 degrees per minute or above. Generally, all PAN resins are copolymers made from blends of monomers with acrylonitrile as the main monomer. It is a versatile polymer used to produce a large variety of products including ultrafiltration membranes, hollow fibers for reverse osmosis, fibers for textiles oxidized PAN fibers.

Polyethyl-Urethane is a polymer composed of organic units joined by carbamate links. While most Polyethyl-Urethane is thermosetting polymers that do not melt when heated, thermoplastic Polyethyl-Urethane is also available. Polyethyl-Urethane is used in the manufacture of high-resilience foam seating, rigid foam insulation panels, microcellular foam seals and gaskets, spray foam, durable elastomeric wheel and tires (such as roller coaster, escalator, shopping cart, elevator and skateboard wheels), automotive suspension bushings, electrical potting compounds, high-performance adhesives, surface coatings and sealants, synthetic fibers (e.g., spandex), carpet underlay, hard-plastic part (e.g. for electronic instruments), condoms, and hoses.

MATERIALS AND METHODS

Materials studio is an application of Biovia software (DassaultSystemsof France) was used for analysis. The software uses machine learning techniques and standard algorithms to represent the level of interaction. Polyacrylonitrile andPolyethyl-Urethane were prepared using the build menu of Materials Studio. The structure of the components was build using the components that were used in blends->calculation menu of Materials studio. was used as the base Polyacrylonitrile and Polyethyl-Urethane was used as a screen. After calculation, the blends->analysis menu of Materials studio was used to construct various data. The data were analyzed and the compatibility of the components to form a blend was examined.

The structures of Polyacrylonitrile and Polyethyl-Urethane were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were shown in a tabular form. The values were used to plot graphs to identify the effect of the weight fraction of polyacrylonitrile on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work, the use of Polyacrylonitrile and Polyethyl-Urethane as potential components of a blend was examined using Biovia Materials Studio. In this work, the use of Polyacrylonitrile and Polyethyl-Urethane as potential components of a composite was tested using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined or pre-programmed correlations (advanced quantitative structure-property relationships) to calculate a wide-eyed range of polymer properties. Group additive methods were used for many years to calculate the properties of polymers as well as small molecules. These procedures are highly fast and waxy to use. Consequently, they are of greatest salability when a rapid estimate of a property is needed without an elaborate understanding of the atomistic interactions that give rise to it. However, the main shortcoming of these procedures is their dependence upon a database of group involvement. Thus, if a polymer contains a group for which the group contribution cannot be accounted, then the property of that polymer cannot be evaluated.

To eliminate this limitation, the method assigned Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Free energy of mixing:A blend is said to be miscible if it is homogeneous in all respect. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous or uniform blend. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m - Gibb'sfreeenergyofmixing$

$\Delta H_m - Enthalpyofmixing$

$\Delta S_m = Entropyofmixing$

$T = Absolutetemperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is always an increase in the entropy on mixing. So, the sign of ΔG_m forever stick by the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic part of free energy greater than the enthalpic contribution part, i.e.,

$$\Delta H_m \lesssim T\Delta S_m \quad (2)$$

Figure 1 informs that the free energy that participated in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with an increase in temperature (up to 275 K) as observable from Eq. 1 and free energy increases with an increase in temperature. The remark indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows very useful compatibility between polyacrylonitrile and poly ethyl urethane with a negative value of mixing energy, which may lead to form a particular figure with considerable high effort.

Chi parameter: The Flory–Huggins χ parameter indicates the extra amount of free energy of mixing and it explains phase behavior for polymer blends and block copolymers. For polymers that are chemically dissimilar, a considerable mismatch in cohesive energy density tends to increase the χ value and, hence, a higher driving force for phase separation. Thus, a high value of χ for chemically dissimilar polymers indicate poor mixing or negligible mixing. For chemically similar polymers having a small amount of cohesive energy difference χ, value is hoped for to be small. However, there is a chance of remixing for adequate long chains. Architectural and geometric differences between the components keep out them in a mixture. from occupying a similar shape intimate in the pure phase. Polymer field theory can forecast that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 predicts that the value of x high from temperature ranging from 50Kto 500K the value of x decreases exponentially with increase in temperature. This agrees with the free energy of mixing for the blend.

Phase diagram: The compatibility of binary mixtures can be seen by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different type of degree of miscibility: a. The single-phase miscible part existed above the critical temperature of around 750 K. This value underslung the fact that a single-phase blend can be formed at a high temperature (higher than 750 K).
b. Fragmented metastable part existed in between binodals and spinodals, and
c. The two-phase separated part of immiscibility is bordered by the spinodals.
The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.
When the system cut across from a single-phase region to the metastable region, the phase isolation commonly done by the mechanism of resembling crystallization i.e. slow nucleation succeed by the growth of the phase-separated domains.When the system jumps from a single-phase into the spinodal region of immiscibility the phases separate suddenly by a mechanism called spinodal decomposition.

Mixing energy: A little value of mixing energy can lead to the mixing process. So, the temperature at which the mixing energy is low can be a favor for mixing. Figure 4 indicates that the mixing energy for the system was small for the temperature range studied. The graph revealed that at first when the temperature increases the mixing energy increases to the highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with an increase in temperature. The temperature is ranging from 50K to500K for the varying of mixing energy.it is very much suppliant to mix the two components at any possible temperature with least mixing energy value.

Bulk modulus: The ration between normal stress to volumetric strain is called bulk modulus. It is the reciprocal of compressibility. Figure 5 here the bulk modulus of the composite increases linearly with increase in the mass fraction of acrylonitrile

Shear modulus: It is assigned as the ratio of shear stress and shear strain. It indicates the feedback of the composite to shear deformation. Figure 6here the shear modulus of the composite increases linearly with an increase in the mass fraction of acrylonitrile.

Young's modulus: The ratio of normal stress and longitudinal strain. It indicates the relative stiffness of the composite. Figure 7shows that Young's modulus of the composite increases linearly with an increase in the mass fraction of acrylonitrile

Poisson ratio: It is the ratio between lateral strain per unit area to the longitudinal strain per unit area. Figure 8 indicates that the Poisson ratio of the composite decreases linearly with an increase in the mass fraction of acrylonitrile.

Brittle fracture stress: Brittle Fracture is the jerky, fast cracking of a material under stress where the material showed practically no evidence of ductility or plastic aeration before the fracture occurs. Figure 9indicates that the brittle fracture stress of the composite decreases linearly with an increase in the mass fraction of acrylonitrile

Heat capacity: It is the amount of heat required to a given mass of material to produce a unit change in its temperature. Figure 10 indicates that the heat capacity (Cp) of the composite decreases linearly with an increase in the mass fraction of acrylonitrile

Thermal conductivity: It describes the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic cognitive content of a material to transfer heat. Figure 11indicates that the thermal conductivity of the composite decreases linearly with an increase in the mass fraction of acrylonitrile.

Dielectric constant: It is outlined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with an increase in the mass fraction of acrylonitrile.

Molar volume: It is the volume attained by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with an increase in the mass fraction of acrylonitrile.

Density: As the density increases porosity decreases. A high amount of porosity will encourage the surface area to make suitable for absorption/adsorption quality. Figure 14indicates that the density of the composite decreases linearly with an increase in the mass fraction of acrylonitrile.

Permeability of gas: Permeability is how fast the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates a longer time taken for the gas to pass through the membrane. Figure 15 indicates that the permeability of oxygen through the composite decreases with an increase in the mass fraction of acrylonitrile.

Figure 16 describes that the permeability of nitrogen through the composite decreases with an increase in the mass fraction of acrylonitrile. Figure 17 indicates that the permeability of carbon dioxide through the composite decreases with an increase in the mass fraction of acrylonitrile. Thus, the results describe that an increase in acrylonitrile fraction reduces the permeability of different gases. The rate of permeability may be affected by the molecular weight of the gases.

CONCLUSIONS

By the use of Biovia Materials Studio polyacrylonitrile and polyethyl-urethane form a uniform blend. The congeniality was transfused based on the graph of free energy of mixing, chi parameter, and mixing energy. The results point out that both can have very beneficial congeniality at different ranges of temperature. The mechanical properties of the blend were observed based on the graph of bulk modulus, shear modulus, Young's modulus, Poisson ratio, and brittle stress fracture. The remark indicated that the values of all the properties increased with an increase in the mass fraction of acrylonitrile. The composition of the mixture was found with respect to heat capacity, thermal conductivity, and dielectric constant. The results indicated that all three parameters increased with an increase in the mass fraction of acrylonitrile. The composition of the blend was checked out with respect to permeability properties. The molar volume and density decreased with an increase in acrylonitrile fraction. The permeability properties of the composite were studied based on the permeability of oxygen, nitrogen, and carbon dioxide. The results indicated that the permeability for all the gases decreased with an increase in the mass fraction

of acrylonitrile. Usually, components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory testing saving materials, money, and time.

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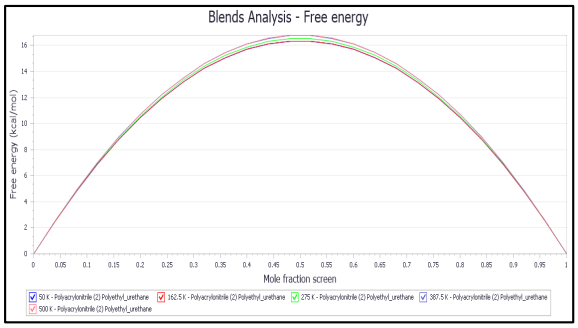

Figure 1. Free energy change with the mole fraction of polyethylurethane at different temperatures

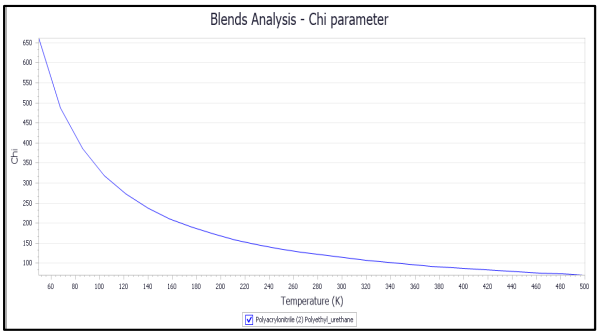

Figure 2. Change in χ (chi) value with temperature

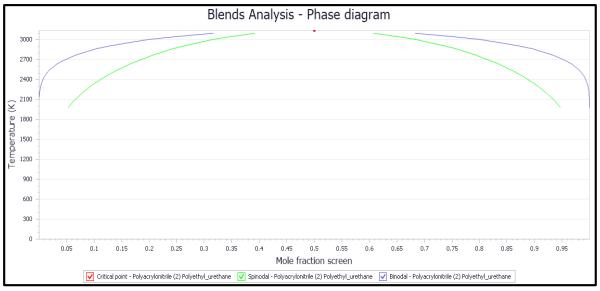

Figure 3. Phase diagram

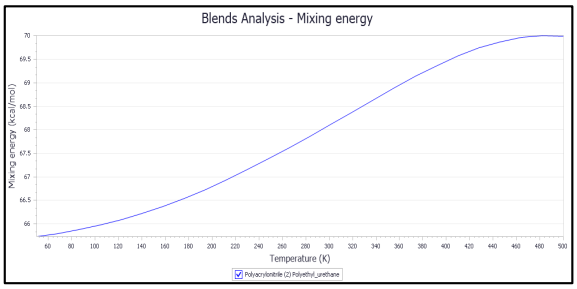

Figure 4. Mixing energy

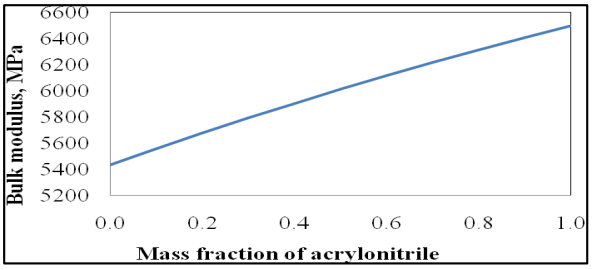

Figure 5. Change in bulk modulus with a mass fraction of acrylonitrile.

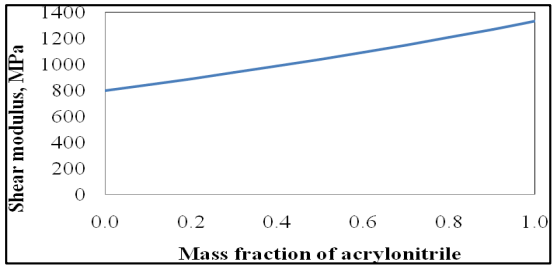

Figure 6. Change in shear modulus with mass fraction of acrylonitrile

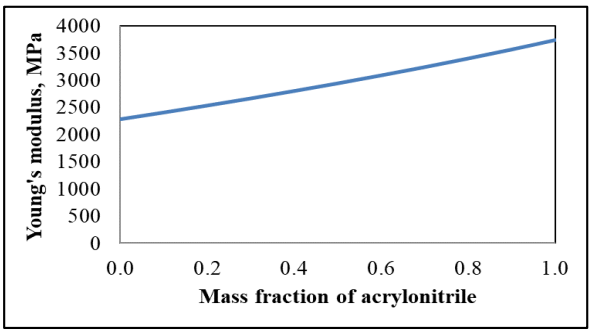

Figure 7. Change in Young's modulus with a mass fraction of acrylonitrile

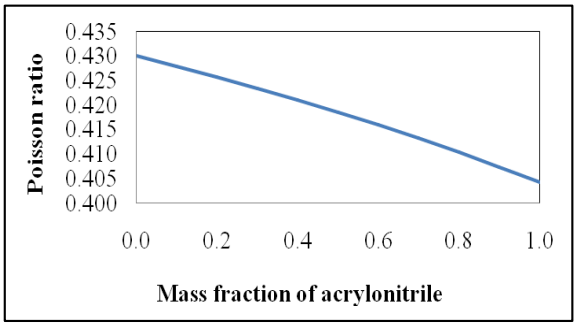

Figure 8. Change in Poisson modulus with mass fraction of acrylonitrile

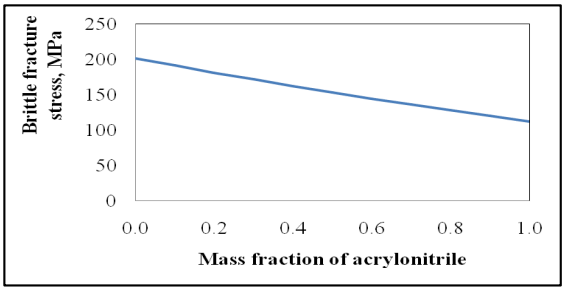

Figure 9. Change in brittle fracture stress with mass fraction of acrylonitrile.

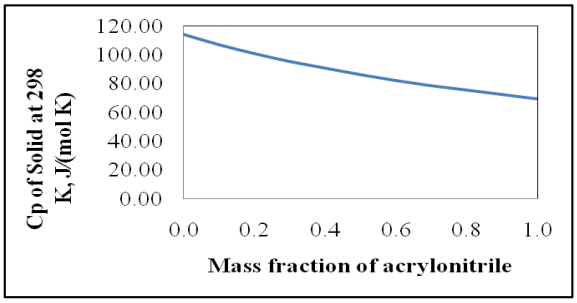

Figure 10. Change in heat capacity with a mass fraction of acrylonitrile.

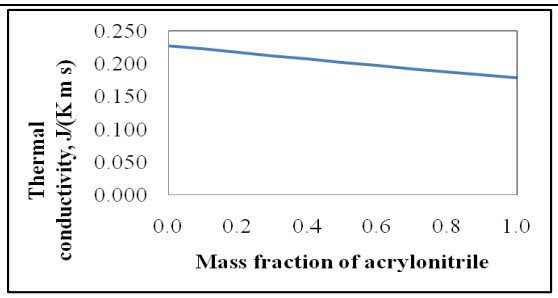

Figure 11. Change in thermal conductivity with mass fraction of acrylonitrile.

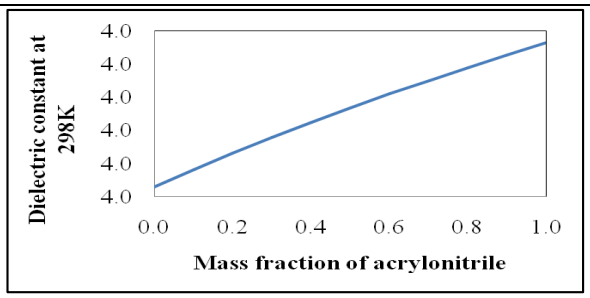

Figure 12. Change in dielectric constant with a mass fraction of acrylonitrile.

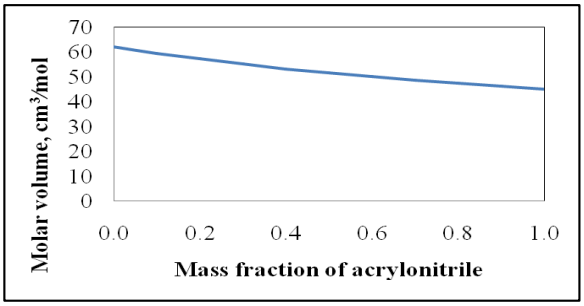

Figure 13. Change in molar volume with mass fraction of acrylonitrile.

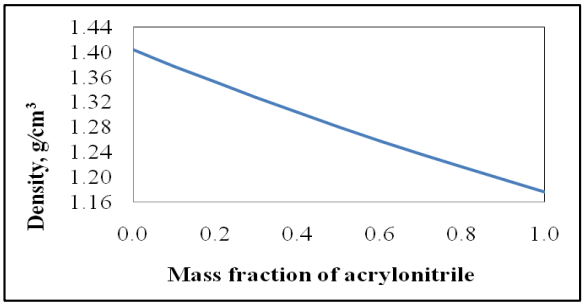

Figure 14. Change in density with a mass fraction of acrylonitrile.

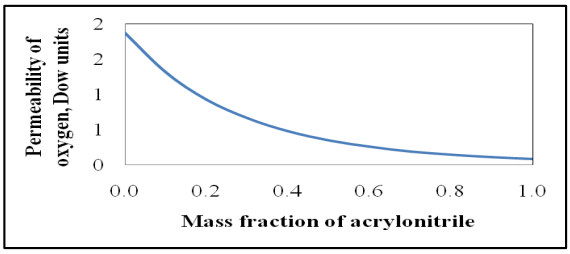

Figure 15. Change in the permeability of oxygen with a mass fraction of acrylonitrile.

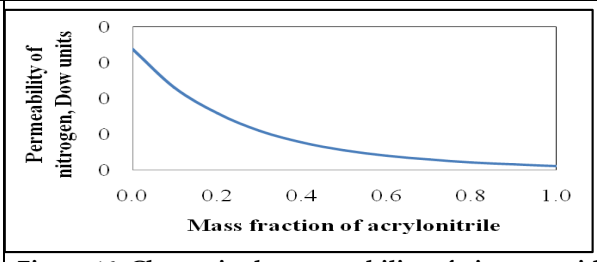

Figure 16. Change in the permeability of nitrogen with a mass fraction of acrylonitrile.

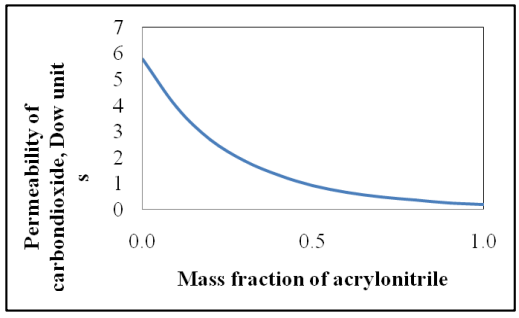

Figure 17. Change in the permeability of carbon dioxide with a mass fraction of acrylonitrile.

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RESEARCH ARTICLE

In silico Analysis of Polydimethylsiloxane and Polytetrafluoroethylene Compatibility in Blend

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ABSTRACT

Two or more polymers combined to form a blend. Byusing Biovia Materials Studio, the compatibility of Polydimethylsiloxane and polytetrafluoroethylene can be studied by forming a homogeneous blend. Illustration of free energy of mixing, chi parameter, phase diagram and mixing energy flashed on the compatibility of the two components. At both low and high temperature, the blend can be compatible. According to phase diagram,a mono-phase can be acquired above the critical temperature, that is 387.5K. On basis of bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture, all mechanical properties of the composite can be studied. This study reveals that, all properties of the composite is inversely proportional to the mass fraction of Polydimethyl siloxane. The blend composition analyzes with regard to heat capacity and thermal conductivity. The outcome sreveal that, all those parameters directly proportional to the mass fraction of Polydimethylsiloxane. Also, the blend composition can be analyzed using permeability properties. The molar volume and density inversely proportional to the Polydimethyl siloxanefraction. The study of the permeability properties of the composite involves the permeability of oxygen, nitrogen and carbon dioxide. According to this result, the permeability for all the gasesis directly proportional to the mass fraction of Polydimethyl siloxane. Using Biovia material studio it is easy to determine the pairs in less time with low cost without performing any laboratory experiments.

Keywords: Blend, *In silico*, Polyvinyl alcohol, Urethane

INTRODUCTION

Blends or composites are the combination of two or more component, where they retain their identity. If a single material has multiple properties then, the quality of the material has been improved. To develop a single material

having desired properties required more efficient research with lots of time. A blend uses the advantages of various materials; combined them to archive desired properties. Blend required less time to prepare composite with desired properties and cost effective. Polymer blends can be developed by combining more than one polymer, or fibers and polymer, or particles and polymer.

Nano material of modified polymers progress to build multifunctional composite. Polymers mixed with nano-materials having carbon base like graphene, carbon nano-tube [1] have intensified. polymers of natural fiber composites are biodegradable [2] have been found that, it enhances mechanical characteristics and hydrophobic. Scientists are working on fire proof materials [3]. According to some reports on inorganic additives in polypropylene; that can improve fire protecting property without increasing the mass [4]. In the field of transportation, Scientists emphasize the fuel efficiency can be enhanced by the development of lightweight composite materials having high strength [5]. Due to high strength to weight ratio and retardancy to corrosion property composites are used in structural Engineering. Hence, glass fiber reinforced polymers, latex polymer cementations composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings.

Usually blends are developed by trial and error technique and this method is not only cost effective but also save time. Thus, scientist refers to, the use of in silico approach to develop new blends. BioviaSoftware (Materials Studio [7]) has been used to characterization of compatible pairs. Polydimethylsiloxane is also called as dimethylpolysiloxane and belongs to the group of polymericorganosilicon compounds. It used in the preparation of medical devices and contact lenses, antifoaming agent in food, caulking, heat-resistant tiles and lubricants. Polytetrafluoroethylene is fluorocarbon solid. Polytetrafluoroethylene is water resist: Polytetrafluoroethylenehas one of the lowest coefficients of friction of any solid [8-12].

MATERIALS AND METHODS

Software used

For analysing the compatibility of blend, Materials studio module of Biovia software (Dassault Systemes of France) was used. To predict the level of interaction, the software uses machine learning techniques and standard algorithms.

Methodology

By the application of build menu of Materials Studio, Polydimethylsiloxane and Polytetrafluoroethylene were prepared. Using the components of blends->calculation menu of Materials studio, the structure of the components was optimized. Polydimethylsiloxane was used as the base and Polytetrafluoroethyleneas screen. After calculation the blends->analysis menu of Materials studio, various data were generated and analyzed. In the synthia menu of Materials Studio, the structures of Polydimethylsiloxane and Polytetrafluoroethylene were fed and let to run for various weight fractions of the components. Various properties of the blend were displayed in a tabular format. Using these values graphs were plotted to characterize the effect of weight fraction of the composite.

RESULTS AND DISCUSSION

In this work using Biovia Materials Studio, uses of Polydimethylsiloxane and Polytetrafluoroethylene as potential components of a blend was analyzed. For evaluation of wide range of polymer characteristics, BIOVIA Materials Studio Synthia utilize pre-defined correlations (advanced quantitative structure-property relationships). For the prediction of the properties of polymers as well as small molecules, Group additive technique was used form many years. These techniques are very fast and easy access. So, they are of largest utilization when a rapid determination of a characteristic is needed without a detailed knowledge of the atomistic interactions that develops it. But, the principal defect of these techniques is their dependence upon a database of group contributions. Hence, if a polymer

contains a group for which the group contribution cannot be determined, then the characteristics of that polymer cannot be evaluated. To overcome this drawback, the method applied in Synthia uses topological information of the polymers to predictive correlations. Using graph theory, the connectivity indices are derived. Thus, no database of group contributions is needed and characteristics may be prognosticated for any polymer composed of any combination of the following nine elements: silicon, oxygen, nitrogen, sulfur, hydrogen, carbon, fluorine chlorine, and bromine.

Free energy of mixing

A mix is said to be miscible on the off chance that it is homogeneous. A negative esteem of free vitality of blending shows that blending is unconstrained and can lead to a homogeneous mix. Thermodynamic examination recommends that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m = Gibb\,s\,free\,energy\,of\,mixing$

$\Delta H_m = Enthalpy\,nf\,mixing$

$\Delta S_m = Entropy\,of\,mixing$

$T = Absolute\,temperature$

The esteem ofTΔS_mis continuously positive in case of a mix since there's an increment within the entropy on blending. In this manner, the sign of ΔG_m continuously depends on the esteem of the enthalpy of mixing ΔHm. The components can blend to make a miscible mix as it were in case the entropic commitment to free vitality surpasses the enthalpic commitment, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 appears that the free vitality included in blending is continuously negative or less than zero for the temperatures examined. The free vitality diminishes with increment in temperature (upto 275 K) as apparent from Eq. 1 and free vitality increments with increment in temperature. The comes about demonstrated that the mix will lead to ahomogenous blend for the temperature run considered (50 to 500 K). The slant appears an awfully great compatibility between polyvinyl liquor and poly ethylurethane with negative esteem of mixing energy,which may lead to make a specific shape with essentially tall exertion.

Chi parameter

The Flory–Huggins χ parameter portrays the overabundance free vitality of blending and makes a difference to clarify stage behavior for polymer mixes and piece copolymers. For polymers which are not chemically comparable, a critical bungle in cohesive vitality thickness leads to a tall χ esteem and, subsequently, a more prominent driving constrain for stage partition. Hence a tall esteem of χ for chemically different polymers show destitute blending. For chemically comparative polymers having little cohesive vitality distinction χ esteem is anticipated to be little. Be that as it may, there's a chance of demixing for adequately long chains. Engineering and geometric contrasts between the components avoid them in a blend from involving the same configurations experienced within the unadulterated stage. Polymer field hypothesis can anticipate that a jumble in chain solidness for chemically comparative components may lead to a tall positive esteem of χ (chi). Figure 2 appears that the esteem of x tall from temperature extending from 50Kto 500K Thevalue of x diminishes exponentially with increment in temperature.This concurs with the free vitality of blending for the mix.

Phase diagram

The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 indicate the phase diagram for the two components of the blend. The degree of miscibility can be observed over three different regions:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).
b. Fragmented metastable regions existed between binodals and spinodals, and
c. The two-phase separated regions of immiscibility are bordered by the spinodals.
The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.
The phase separation of the system while entering from single-phase region to the metastable region occurs by the mechanism of resembling crystallization. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing energy

A small value of mixing energy can favor the mixing process. Thus for mixing, the temperature at which the mixing energy is low can be chosen. Figure 4 display that the mixing energy for the system was small for the temperature range studied. The graph manifest that at first with increase in temperature the mixing energy increases to a highest value after that with further increase in temperature the mixing energy decreases and again increases with further increase in temperature. The temperature varies from 50K to500K. For the varying of mixing energy. It is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus

Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite decreases with increase in mass fraction of dimethyl siloxane.

Shear modulus

It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite decreases with increase in mass fraction of dimethyl siloxane.

Young's modulus

It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite decreases with increase in mass fraction of dimethyl siloxane.

Poisson ratio

It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite decreases with increase in mass fraction of dimethyl siloxane.

Brittle fracture stress

Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite no graph indicates homogeneous mixture.

Heat capacity

It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of dimethyl siloxane.

Thermal conductivity

It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of dimethyl siloxane.

Molar volume

It is the volume occupied by one mole of a substance. Figure 1 shows that the molar volume of the composite increases with increase in mass fraction of dimethyl siloxane.

CONCLUSIONS

Using Biovia Materials Studio, the probability of utilization of polyseloxaneand polyvinyl alcohol to form a homogeneous composite was explored. The compatibility was analyzed based on mixing energy, free energy of mixing and chi parameter. The results reveal that, the pair can have excellent compatibility at virous ranges of temperature. The mechanical properties of the blend were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results reveal that, the values of all the properties inverselyproportional to the mass fraction of Polydimethyl siloxane. The composition of the blend was analyzed on the basis of thermal conductivity, heat capacity. The results reveal that, all the three parameters directly proportional to the mass fraction of Polydimethyl siloxane. Also, the blend composition can be analyzed using permeability properties. The molar volume proportional to the Polydimethyl siloxanefraction. The study of the permeability properties of the composite involves the permeability of oxygen, nitrogen and carbon dioxide. According to this result, the permeability for all the gases is directly proportional to the mass fraction of Polydimethyl siloxane. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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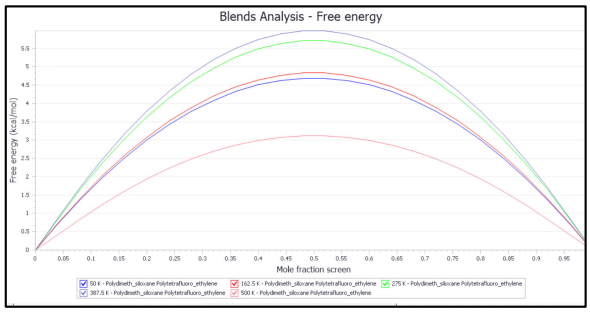

Figure 1. Free energy change with mole fraction of polytetrafluoroethylene at different temperatures

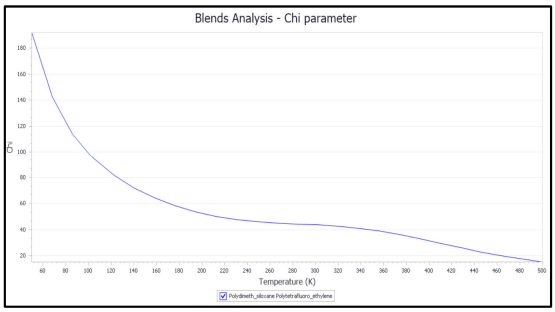

Figure 2. Change in χ (chi) value with temperature

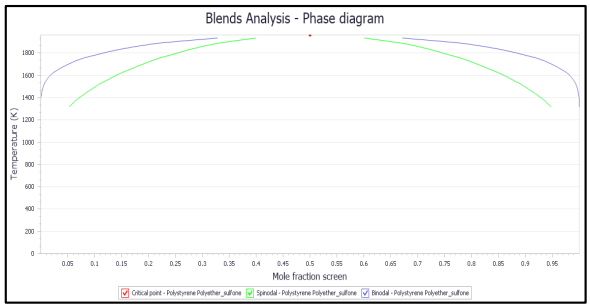

Figure 3.Phase diagram

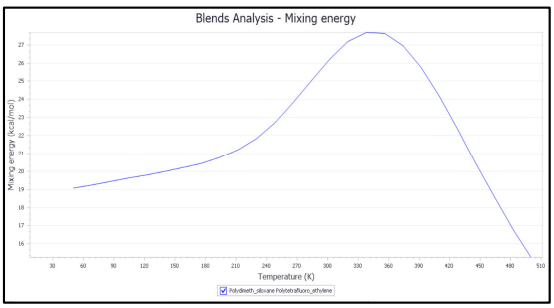

Figure 4. Mixing energy

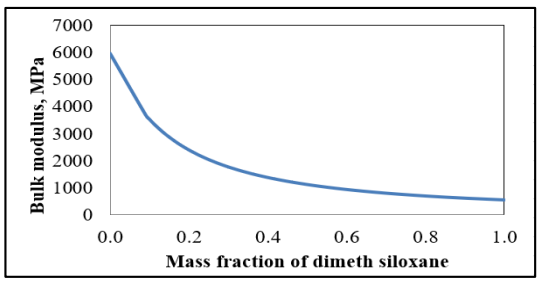

Figure 5. Change in bulk modulus with mass fraction of dimethyl siloxane

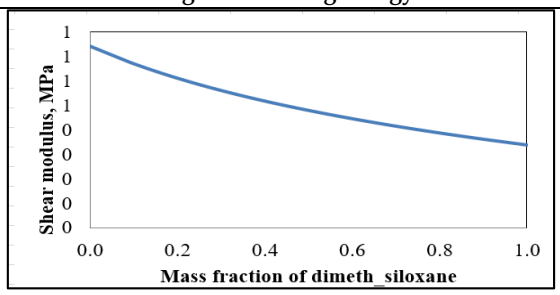

Figure 6. Change in shear modulus with mass fraction of dimethyl siloxane

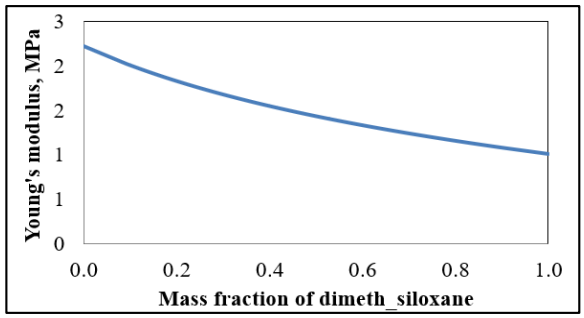

Figure 7. Change in Young's modulus with mass fraction of dimethyl siloxane

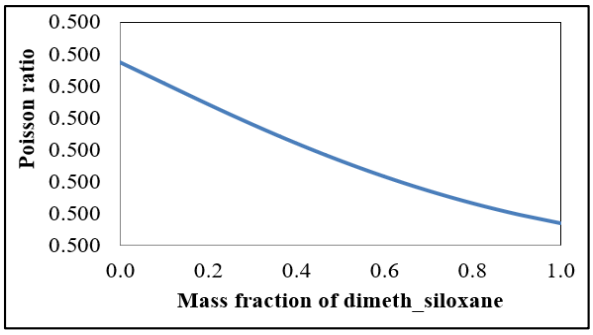

Figure 8. Change in Poisson modulus with mass fraction of dimethyl siloxane

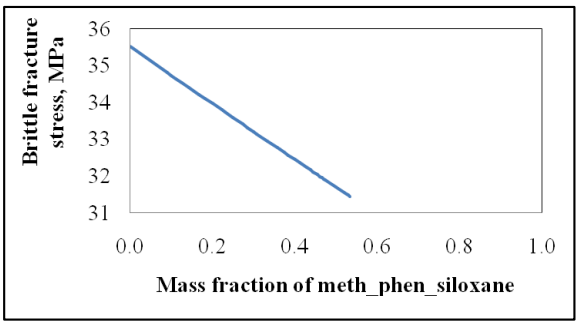

Figure 9. Change in brittle fracture stress with mass fraction of dimethyl siloxane

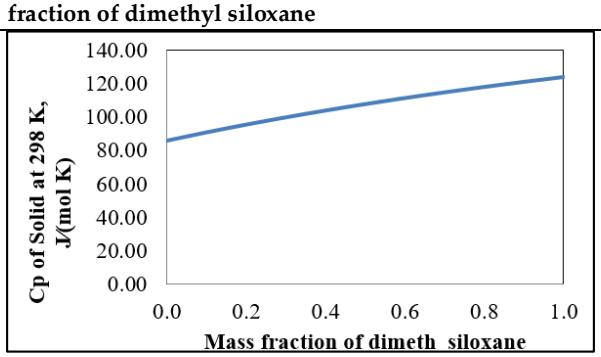

Figure 10. Change in heat capacity with mass fraction of dimethyl siloxane

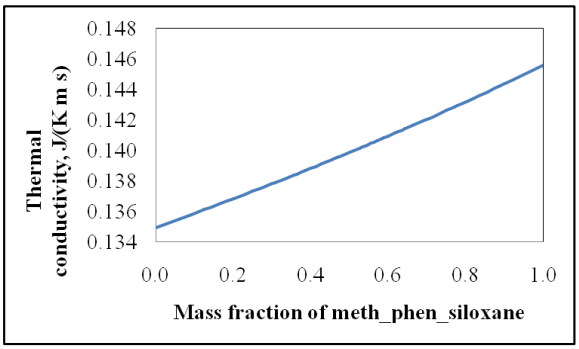

Figure 11. Change in thermal conductivity with mass fraction of dimethyl siloxane

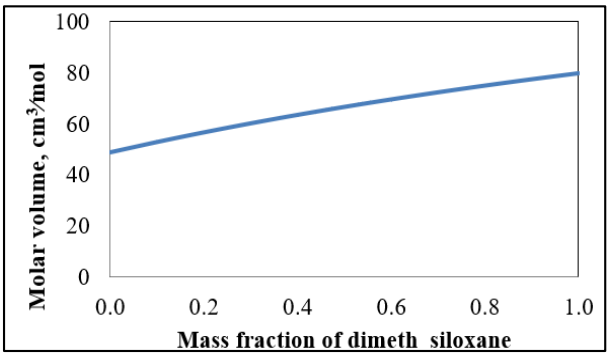

Figure 12. Change in molar volume with mass fraction of dimethyl siloxane

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RESEARCH ARTICLE

In silico Analysis of Polymethyl Phenyl Siloxane and Polystyrene Compatibility in a Blend

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ABSTRACT

Combination of two or more components comes about within the arrangement of a mix. The compatibility of polymethyl phenyl siloxane and polystyrene were considered to make a miscible mix utilizing Biovia Materials Studio. The compatibility of the two components was illustrated based on free vitality of blending, chi parameter, stage chart and blending vitality. The comes about demonstrated that the combine can ended up congruous at both moo and tall temperature. Stage graph shown that a single stage can be gotten over 387.5K which was the basic temperature. The mechanical properties of the composite were examined based on bulk modulus, shear modulus, Young' modulus, Poisson proportion and delicate push break. The comes about shown that the values of all the properties expanded with increment in mass division of acrylic corrosive. The composition of the mix was analyzed with regard to warm capacity, warm conductivity and dielectric consistent. The comes about demonstrated that all those parameters expanded with increment in mass division of polymethyl phenyl siloxane. The composition of the mix was analyzed with regard to penetrability properties. The molar volume and thickness diminished with increment in polymethyl phenyl siloxane division. The penetrability properties of the composite were examined based on penetrability of oxygen, nitrogen and carbon dioxide. The comes about appeared that the penetrability for all the gasses diminished with increment in mass division of acrylic corrosive. This think about will not as it were offer assistance to decide sets without performing research facility tests but too less time devouring and moo fetched prepare.

Keywords: Blend, In silico, polyvinyl alcohol, Urethane.

INTRODUCTION

Mixes or composites are shaped with combination of more than one component where components do hold their character within the blend. Because it is exceptionally troublesome to discover different properties in a single fabric,

it is fitting to combine distinctive components subsequently moving forward the quality of the material. Improvement of a single fabric with the required property includes noteworthy research and time. A mix utilizes the points of interest of diverse materials; blend them to induce the required property. Hence a mix spares time to create a modern fabric in this manner lessening the fetched of advancement of items with wanted properties. Polymer mixes can be made of two or more polymers, or strands and polymer, or particles and polymer. Nano fabric altered polymers cleared the way to multi utilitarian materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn consideration. Biodegradable polymers- common fiber composites [2] have been detailed to improve mechanical properties and water resistance. Analysts are working on fire retardant/fire confirmation materials [3]. There are reports of inorganic added substances in polypropylene; that can improve fire retardancy without expanding the weight [4]. Analysts have emphasized on blend and generation of lightweight composite materials having tall quality vital for upgrading fuel effectiveness within the field of transportation [5]. There are applications of composites in basic Building due to tall quality to weight proportion and resistance to erosion. Hence, glass fiber fortified polymers, latex polymer cementitious composites [6] were created for development of bridges, light rail travel, mining and tunneling, holding dividers and other waterside buildings. All the over specified illustrations depended on research facility tests.

As a rule mixes are arranged by trial and mistake strategy and this method could be a moo taken a toll and less time devouring strategy. Hence, analysts have centered on the utilizeof in silico approach to create unused mixes. Computer program (Materials Studio [7]) has been utilized to distinguish congruous sets. Polymethyl phenyl siloxane chains were considered within the bulk as well as extremely kept inside the ~1–2nm interlayer dispersing of intercalated polymer/layered organosilicate nanohybrids. The temperature reliance of the vitality settled flexible diffusing estimations for the homopolymer and the nanocomposites display two particular unwinding steps: one due to the methyl gather revolution and one that compares to the phenyl ring flip and the segmental movement. Quasielastic indistinguishable estimations appear that the exceptionally nearby handle of methyl revolution is heartless to the polymer glass move temperature and shows a wavevector autonomous unwinding time and a moo activation energy, though it isn't influenced at all by the restriction. At temperatures fair over the calorimetric glass move temperature, the watched movement is the phenyl ring movement, though the segmental movement is clearly recognized for temperatures almost 60K higher than the glass move temperature [8-10].

Polystyrene could be a flexible plastic utilized to form a wide assortment of buyer items. As a difficult, strong plastic, it is regularly utilized in items that require clarity, such as nourishment bundling and research facility product. When combined with different colorants, added substances or other plastics, polystyrene is utilized to create machines, gadgets, automobile parts, toys, cultivating pots and gear and more.Polystyrene moreover is made into a froth fabric, called extended polystyrene (EPS) or expelled polystyrene (XPS), which is esteemed for its insulating and padding properties. Polystyrene is made by hanging together, or polymerizing, styrene, a building-block chemical used within the fabricate of numerous items. Styrene moreover happens actually in nourishments such as strawberries, cinnamon, coffee and hamburger [10-12].

MATERIALS AND METHODS

Software used

For analysing the compatibility of blend, Materials studio module of Biovia software (Dassault Systemes of France) was used. To predict the level of interaction, the software uses machine learning techniques and standard algorithms.

Methodology

Polymethyl phenyl siloxane and polystyrene were arranged utilizing the construct menu of Materials Studio. The structure of the components were optimized utilizing the components were utilized in blends->calculation menu of

Materials studio. polymethyl phenyl siloxane was utilized as the base and polystyrene was utilized as screen. After calculation the blends->analysis menu of Materials studio was utilized to produce different information. The information were analyzed and the compatibility of the components to make a mix was analyzed. The structures of polymethyl phenyl siloxane and polystyrene were encouraged to the synthia menu of Materials Studio. It was at that point run for distinctive weight divisions of the components. Distinctive properties of the composite were shown in a unthinkable shape. The values were utilized to plot charts to distinguish the impact of weight division of polyacrylic corrosive on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the utilize of polymethyl phenyl siloxane and polystyrene as potential components of a mix was analyzed utilizing Biovia Materials Studio. In this work the utilize of polyacrylic corrosive and polyacrylochloride as potential components of a composite was analyzed utilizing Biovia Materials Studio. BIOVIA Materials Studio Synthia employments pre-defined relationships (progressed quantitative structure-property connections) to assess a wide extend of polymer properties. Gather added substance strategies were utilized for numerous a long time to foresee the properties of polymers as well as little atoms. These strategies are greatly quick and simple to utilize. Thus, they are of most prominent utility when a quick appraise of a property is required without a nitty gritty understanding of the atomistic intelligent that allow rise to it. In any case, the central inadequacy of these strategies is their reliance upon a database of bunch commitments. Hence, on the off chance that a polymer contains a gather for which the gather commitment cannot be assessed, at that point the property of that polymer cannot be calculated. To overcome this confinement, the strategy executed in Synthia employments topological data approximately polymers within the prescient relationships. The network lists inferred from chart hypothesis are utilized. Hence, no database of bunch commitments is required and properties may be anticipated for any polymer composed of any combination of the taking after nine components: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Free energy of mixing

A mix is said to be miscible on the off chance that it is homogeneous. A negative esteem of free vitality of blending shows that blending is unconstrained and can lead to a homogeneous mix. Thermodynamic examination recommends that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m = Gibbs\,free\,energy\,of\,mixing$

$\Delta H_m = Enthalpy\,of\,mixing$

$\Delta S_m = Entropy\,of\,mixing$

$T = Absolute\,temperature$

The esteem ofTΔS_mis continuously positive in case of a mix since there's an increment within the entropy on blending. In this manner, the sign of ΔG_m continuously depends on the esteem of the enthalpy of mixing ΔHm. The components can blend to make a miscible mix as it were in case the entropic commitment to free vitality surpasses the enthalpic commitment, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 appears that the free vitality included in blending is continuously negative or less than zero for the temperatures examined. The free vitality diminishes with increment in temperature (upto 275 K) as apparent from Eq. 1 and free vitality increments with increment in temperature. The comes about demonstrated that the mix will lead to ahomogenous blend for the temperature run considered (50 to 500 K). The slant appears an awfully great compatibility between polyvinyl liquor and poly ethylurethane with negative esteem of mixing energy,which may lead to make a specific shape with essentially tall exertion.

Chi parameter

The Flory–Huggins χ parameter portrays the overabundance free vitality of blending and makes a difference to clarify stage behavior for polymer mixes and piece copolymers. For polymers which are not chemically comparable, a critical bungle in cohesive vitality thickness leads to a tall χ esteem and, subsequently, a more prominent driving constrain for stage partition. Hence a tall esteem of χ for chemically different polymers show destitute blending. For chemically comparative polymers having little cohesive vitality distinction χ esteem is anticipated to be little. Be that as it may, there's a chance of demixing for adequately long chains. Engineering and geometric contrasts between the components avoid them in a blend from involving the same configurations experienced within the unadulterated stage. Polymer field hypothesis can anticipate that a jumble in chain solidness for chemically comparative components may lead to a tall positive esteem of χ (chi). Figure 2 appears that the esteem of x tall from temperature extending from 50Kto 500K Thevalue of x diminishes exponentially with increment in temperature.This concurs with the free vitality of blending for the mix.

Phase diagram

The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 indicate the phase diagram for the two components of the blend. The degree of miscibility can be observed over three different regions:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).

b. Fragmented metastable regions existed between binodals and spinodals, and

c. The two-phase separated regions of immiscibility are bordered by the spinodals.

The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.

The phase separation of the system while entering from single-phase region to the metastable region occurs by the mechanism of resembling crystallization. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing energy

A small value of mixing energy can favor the mixing process. Thus for mixing, the temperature at which the mixing energy is low can be chosen. Figure 4 display that the mixing energy for the system was small for the temperature range studied. The graph manifest that at first with increase in temperature the mixing energy increases to a highest value after that with further increase in temperature the mixing energy decreases and again increases with further increase in temperature. The temperature varies from 50K to500K. For the varying of mixing energy. It is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus

Bulk modulus is the degree of the diminish in volume with an increment in pressure. Figure 5 appears that the bulk modulus of the composite decreases with increment in mass division of polymethyl phenyl siloxane.

Shear modulus

It is characterized as the proportion of shear stress and shear strain. It appears the reaction of the composite to shear misshapening. Figure 6 appears that the shear modulus of the composite decreases with increment in mass division of polymethyl phenyl siloxane.

Young's modulus

It is characterized as the proportion of stress and strain. It compares the relative stiffness of the composite. Figure 7 appears that the Young's modulus of the composite decreases with increment in mass division of polymethyl phenyl siloxane.

Poisson ratio

It is the proportion of lateral strain to longitudinal strain. Figure 8 appears that the Poisson proportion of the composite increments straightly with increment in mass division of polymethyl phenyl siloxane.

Brittle fracture stress

Brittle Fracture is the sudden, fast splitting of a fabric beneath stretch where the fabric displayed for all intents and purposes no prove of ductility or plastic corruption some time recently the break happens. Figure 9 appears that the fragile break stretch of the composite decreases with increment in mass division of polymethyl phenyl siloxane.

Heat capacity

It is the sum of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10 appears that the heat capacity (Cp) of the composite increments directly with increment in mass division of polymethyl phenyl siloxane.

Thermal conductivity

It demonstrates the relationship between heat flux per unit area and temperature gradient. It alludes to the inherent capacity of a fabric to exchange heat. Figure 11 appears that the thermal conductivity of the composite increments directly with increment in mass division of polymethyl phenyl siloxane.

Molar volume

It is the volume involved by one mole of a substance. Figure 12 appears that the molar volume of the composite increases with increase in mass division of polymethyl phenyl siloxane.

CONCLUSIONS

The plausibility of utilize of polymethyl phenyl siloxane and polystyrene to make a homogeneous mix was investigated utilizing Biovia Materials Studio. The compatibility was analyzed based on free vitality of blending, chi parameter and blending vitality. The comes about shown that the combine can have exceptionally great compatibility at distinctive ranges of temperature. The mechanical properties of the composite were examined based on bulk modulus, shear modulus, Young' modulus. The comes about demonstrated that the values of all the properties decreases with increment in mass division of acrylic corrosive. The composition of the mix was analyzed with regard to warm capacity, warm conductivity. The comes about demonstrated that all the three parameters expanded with increment in mass division of acrylic corrosive. The composition of the mix was analyzed with regard to porousness properties. The molar volume and thickness diminished with increment in acrylic acid division. The permeability properties of the composite were considered based on permeability of oxygen, nitrogen and carbon dioxide. The comes about shown that the permeability for all the gasses increases with increment in mass division of acrylic corrosive. More often than not components for a mix are recognized tentatively. This in silico consider will offer assistance decide components of a mix without performing research facility tests sparing materials, money, and time.

ACKNOWLEDGEMENTS

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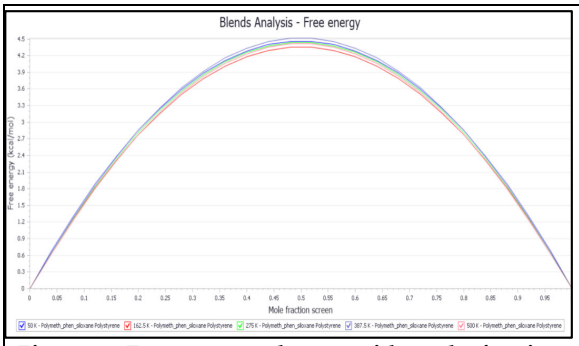

Figure 1. Free energy change with mole fraction of polymethyl phenyl siloxane at different temperatures

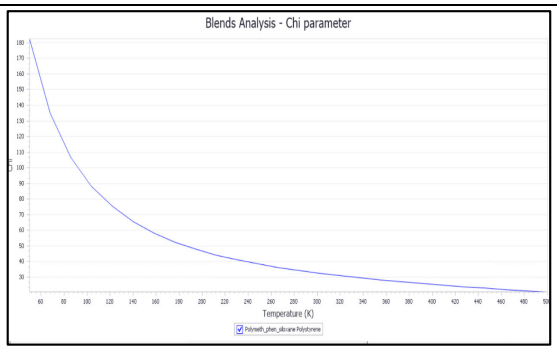

Figure 2. Change in χ (chi) value with temperature

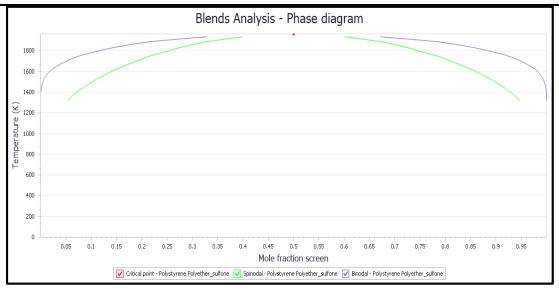

Figure 3.Phase diagram

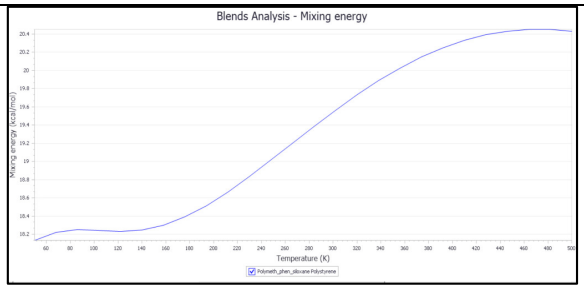

Figure 4. Mixing energy

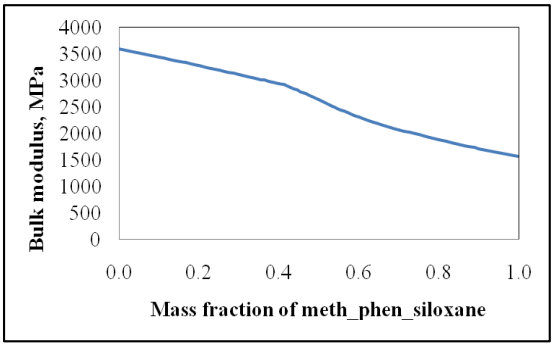

Figure 5. Change in bulk modulus with mass fraction of polymethyl phenyl siloxane

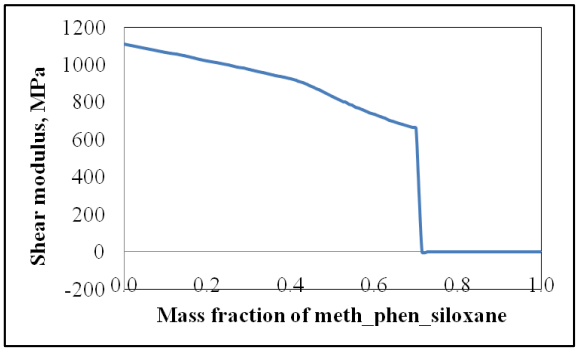

Figure 6. Change in shear modulus with mass fraction of acrylic acid

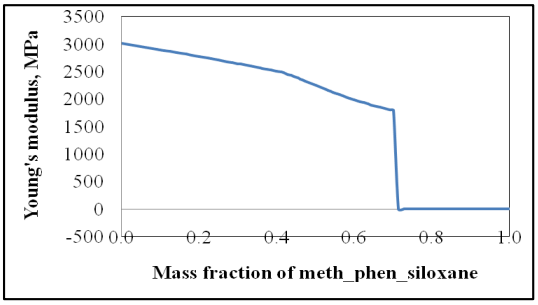

Figure 7. Change in Young's modulus with mass fraction of polymethyl phenyl siloxane

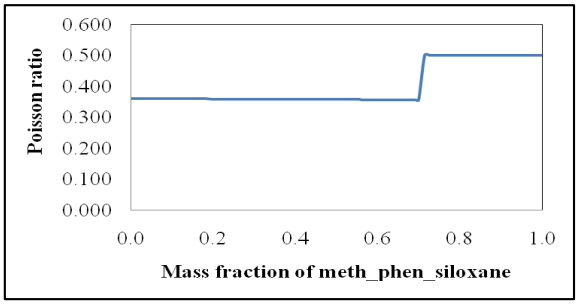

Figure 8. Change in Poisson modulus with mass fraction of polymethyl phenyl siloxane

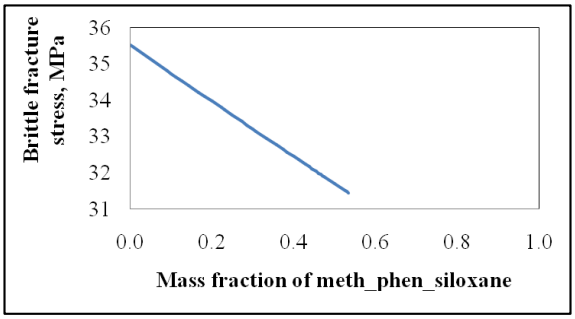

Figure 9. Change in brittle fracture stress with mass fraction of acrylic acid

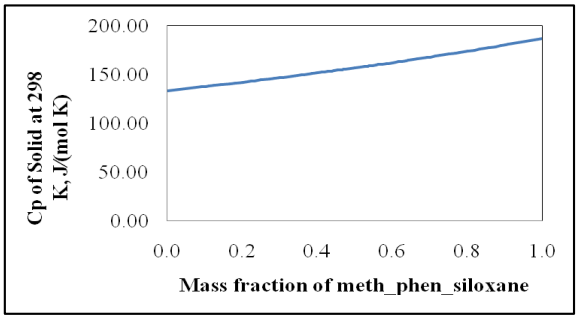

Figure 10. Change in heat capacity with mass fraction of polymethyl phenyl siloxane

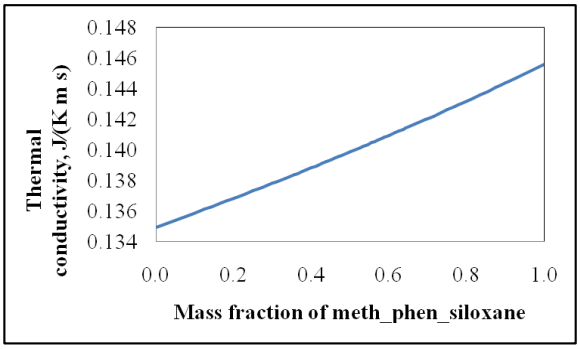

Figure 11. Change in thermal conductivity with mass fraction of polymethyl phenyl siloxane

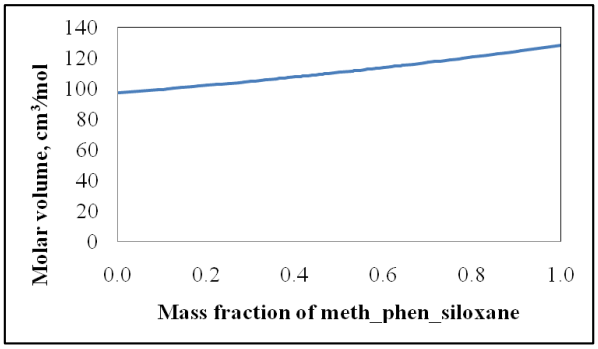

Figure 12. Change in molar volume with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Polynylon 12 and Polyethylene-Isophthalate Compatibility in a Blend

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ABSTRACT

Combination of two or more components results in the formation of a blend. The compatibility of Polynylon 12 and Polyethylene-isophthalate were studied to form a miscible blend using Bio-via Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter phase diagram and mixing energy. The results indicated that the pair can become compatible at both low and high temperature. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend, Chi parameter, Phase diagram, Mixing energy.

INTRODUCTION

In general, formation of blends & composite can be made with the combination of more than one component where the blending of the composite is done without losing their identity. Quantity of the material can be improvised by mixing up different components as the blending brings multiple properties. A continuous effort in the field of research brings desired property in a single material. Thus the blending of different materials leads towards the formation of new material with desired properties by making it cost and time effective. Polymer composites can be prepared with the combination of two or more polymers, or fibers & polymers, or particles and polymer. Nano material modified polymers facilitated to multifunctional material. In the present day Scenario, polymers coupled with carbon based (grapheme, carbon nanotube) nano materials [1] have brought greater importance.In biodegradable polymer, natural fiber composites [2] is used to enhance mechanical properties and water resistance.Now a days, widespread research is being conducted on fireproof materials [3]. Research says that inorganic additives in Polypropylene can enhances flame retardancy without adding much weight [4]. Another study on fuel efficiency transportation says that the fuel efficiency can be enhanced through synthesis and production of light weight composite materials of higher strength [5]. There are applications of composites in

structural engineering too because of high strength to weight ratio and resistance to corrosion. Thus glass fiber reinforced polymers, latex polymer cementitious composites [6] where developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other water side buildings. All the above mentioned examples are based on laboratory experiments.Basically trial and error method is being used for the preparation of blends as it is a cost effective and less time consuming method. Hence, use of silico approach to develop new blends has been emphasized. Software (Materials studio {7}) has been used to identify compatible pairs:

MATERIALS AND METHODS

SOFTWARE USED

The Biovia software having Material studio module (Dassault Systemes of France) was utilized to study the machine learning techniques and standard algorithms to assume the interaction level.

METHODOLOGY

By using the build menu of Materials Studio, the Polynylon 12 and Polyethylene-isophthalte were prepared. The components used in blends calculation menu of Materials studio were utilized for the optimization of the structurial components. The Polynylon 12 was used as the base and Polyethylene-isophthalate was used as screen.Various data were generated by the blends analysis menu of Materials studio after the calculation and the compatibility of the components to form a blend was analyzed.The structures Polynylon 12 and Polyethylene-isophthalte of were fed to the synthia menu of Materials Studio. The components were run to different fractional weight which were then displayed in a tabular form according to their variable properties. To identify the effective weight fraction of polynylon 12, different values were used to plot the graphs on the basis of mechanical properties of the composite.

RESULTS AND DISCUSSION

In this process, Polynylon 12 and Polyethylene-isophthalte were used as potential components of a blend was analyzed using Biovia Materials Studio. Using Biobío Materials Studio, polynylon 12 and Polyethylene-isophthalte potential components of a composite was analyzed under this process. While evaluating a wide range of polymer properties, Biovia Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships). To evaluate the properties of polymers as well as small molecules, Group additive methods were used from many years. These methods have one of the greatest utility when a rapid estimation of property is required without a detailing understand of the atomistic interactions which give rise to it and also they are extremely fast and easy to use. The dependence upon a database of group contributions are the principal shortcoming of these methods. Hence, the property of a polymer cannot be calculated unless the polymer containing group for which the group contribution is not estimated. The method used in Synthia, topological information about polymers is used in the predictive correlations to overcome the limitations. Due to the implementation of graph theory that is derived from connectivity indices, no database of group contributions is required. Properties can be predicted for any polymer which is generally composed for any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

FREE ENERGY OF MIXING

A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where ΔG_m — *Gibb s free energy of mixing*

ΔH_m — *Enthalpy of mixing*

ΔS_m = *Entropy of mixing*

T = *Absolute temperature*

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (up to 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polynylon 12 and Polyethylene-isophthalte with negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

CHI PARAMETER

The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

MIXING ENERGY

A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. **Fig. 4** shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature. The temperature is vary from 50K to500K for the varying of mixing energy. It is very much possible to mix the two components at any feasible temperature with least mixing energy value.

CONCLUSIONS

By using Biovia Materials Studio, the probability of using polynylon 12 and polyethylene-isophthalate to form a homogeneous blend was explored. Free energy of mixing, chi parameter and mixing energy were used to analyze the compatibility. The pair can have very good compatibility at different ranges of temperature with respect to the results. Experimential identification were generally of blend components. The study of in silico helps to determine the components of a blend without performing laboratory experiments saving materials, money and time.

ACKNOWLEDGMENT

The authors are thank ful to the Department of chemistry and the Dean, School of Applied Sciences, Centurion University of Technology and Management, for their cooperation and motivation during this study.

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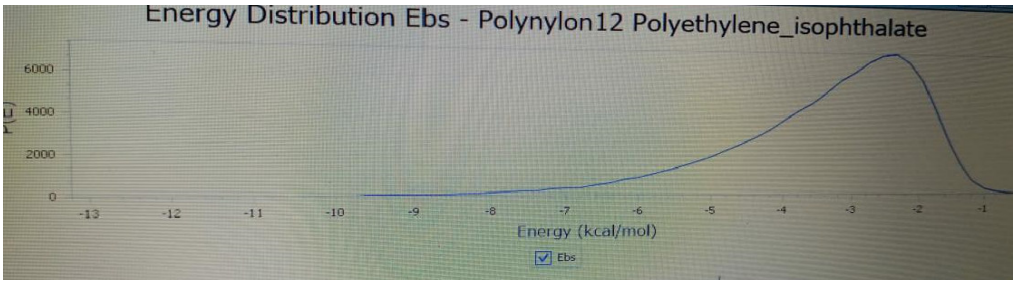

Fig.1 Free energy change with mole fraction of Polyethylene-isophthalte at different temperatures

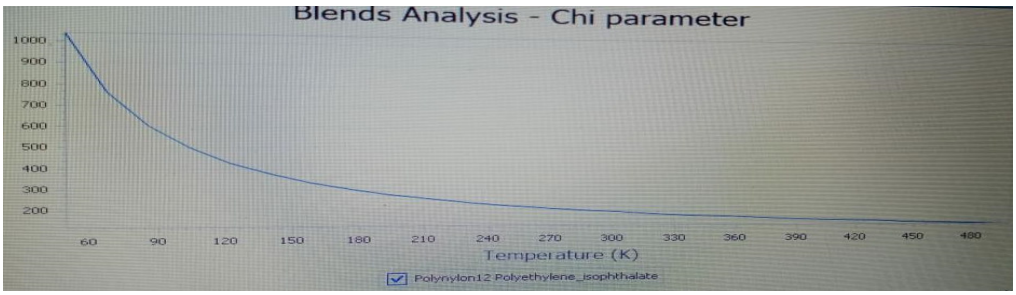

Fig.2. Change in χ (chi) value with temperature

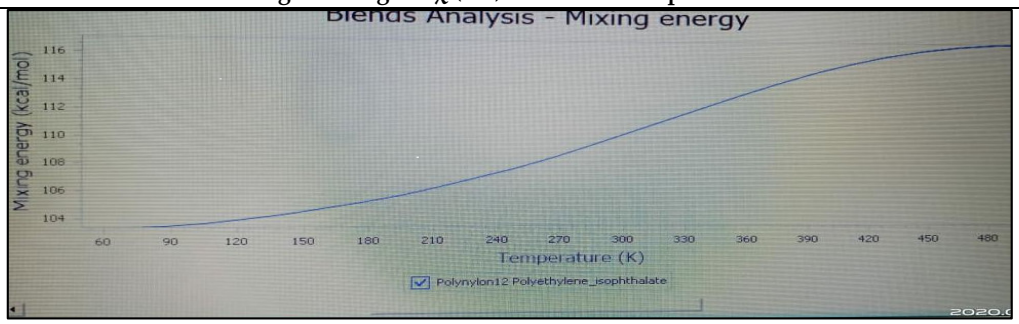

Fig. 3. Mixing energy

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RESEARCH ARTICLE

In silico Analysis of Polyoxyethylene and Polyurea Compatibility in a Blend

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ABSTRACT

Combination of two or more constituents results in the formation of a blend. Using Biovia Material Studio the compatibility of polyoxyethylene and polyureawere studied to form a miscible blend. Based on free energy of mixing,chi parameter,phase diagram andmixing energy the compatibility of the two constituents were studied.The results specified that the pair can become compatible at both low and high temperature. According to Phase diagram a single phase can be got above 387.5K which was the critical temperature. The mechanical properties of the composite were observed based on bulk modulus, Poisson ratio, Young' modulus, Shear modulus and brittle stress fracture. With increase in mass fraction of polyoxyethylene the values of all the properties increased. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of oxyethylene.With respect to permeability properties the composition of the blend was obtained.With increase in oxyethylene fraction the molar volume increased and density declined. Based on permeability of oxygen, carbon dioxide and nitrogen the permeability properties of the composite were obtained. With increase in mass fraction of oxyethylene the permeability for all gases increased. This study helps us to determine pairs without performing laboratory experiments and it is also low cost and less time consuming.

Keywords: Blend, *In silico,* polyoxyethylene, polyurea.

INTRODUCTION

Blends or composites are formed in which at least two components are blended to form a new material having different physical properties because it is critically important to manufacture quality products where components do retain their identity in the mixture.By blending with some raw material ,fibers ,the properties (reduce material cost,enhance ozone resistance,light weight, increase toughness) can be enhanced.As it is difficult to find multiple

properties in a single material, it is advisableto combine different components thereby improving the quality of the material such as strength and toughness. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Recently proposed for polymer blends include selective ion exchange systems,and medical uses.in general polymer blends own 30%-40% of plastic products as plastic are non-biodegradable by forming blends with bio-degradable polymer concentration of polymer can be reduced

Nano material modified polymers paved the way to multifunctional materials. Polymers combined with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to raise water resistance and mechanical properties. Researchers are working on fire proof/fire retardant materials [3]. There are reports of inorganic additives in polypropylene; that can intensify flame retardancy without increasing the weight [4]. Researchers have stressed on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above-mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method andthis technique is a low cost and less time-consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. Polyoxyethylene is a synthetic polymer and its monomer isethyleneoxide.It is hydrophilic in nature, low volatile,flexible,and water soluble. As solvent toxicity is one of the major drawbacks in the composition of polymeric nanoparticles, this problem is solved by using polyoxyethylene. Polyurea is a elastomer that is a pure polyurea coating is derived from the reaction product of an isocyanate and an amine terminated product or polyamine blend component via step-growth polymerization. Polyurea technology permit excellentuvprotection, water proofingand moisture insensitive coating along with high temperature resistance, and superior tensile strength. Polyurea come up with resistance to chemically corrosive environment and polyurea coating can be lay out over rust on metal surface to increase its life time also polyurea used as a filler in building joint. Polyureabased elastomer material was shown to be self-healing, melding together after being cut in half. The material also comprises inexpensive commercially accessible compounds. The elastomer molecules were twisted, making the bonds between them overlong. The resulting molecules undergoes rebound at room temperature with almost the same power and they are also easier to pull apart from one another.

MATERIALS AND METHODS

Software Used: Materials studio module of Bioviasoftware module(Dassault Systems of France) was worn for analysis. The software makes use of machine learning techniques and standard algorithms to divine the level of interaction.

Methodology: Polyoxyethylene and Polyurea were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. Polyoxyethylene used as the base and polyurea was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of Polyoxyethylene and Polyurea were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the

composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyoxyethylene on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use polyoxyethylene and Polyurea as potential components of a blend was analyzed using Biovia Materials Studio. In this work the use of polyoxyethylene and polyurea as potential components of a composite was analyzed using Biovia Materials Studio. In Biovia Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were pre-owned for many years to predict the properties of polymers as well as small molecules. These methods are very fast and easy to use. Consequently, they are of greatest utility when a estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods depending upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be predicted, then the property of that polymer cannot be calculated. To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, oxygen, silicon, sulfur, nitrogen, fluorine,bromine, chlorine.

Free Energy of Mixing: A blend is said to be miscible if it is homogeneous. When the free energy of mixing value is negative the mixture is said to be spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m - Gibbs\,free\,energy\,of\,mixing$

$\Delta H_m - Enthalpy\,of\,mixing$

$\Delta S_m = Entropy\,of\,mixing$

$T = Absolute\,temperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy of mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m.If the entropic contribution to free energy more than the enthalpic contribution then the components can mix to form a miscible blend, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (up to 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyoxyethylene and polyurea with negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

Chi Parameter: The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation.Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of remixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

Phase Diagram: The compatibility of binary mixtures can be observed by phase diagrams. Figure 3 shows the phase diagram for the two constituents of the blend. For different degree of miscibility three regions are there:
a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single-phase blend can be obtained at a high temperature (higher than 750 K).
b. Fragmented metastable regions existed between binodal and spinodal, and
c. The two-phase separated regions of immiscibility are bordered by the spinodal.
The binodal separated miscible (one-phase) and metastable region, while the spinodal separated the metastable and two-phase region.
When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e., slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing Energy: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that the mixing energy increases to a highest value when temperature increases after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature. The temperature is varyfrom 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite decreases linearly with increase in mass fraction of oxyethylene.

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite decreases linearly with increase in mass fraction of oxyethylene after that with increasing in mass fraction of oxyethylene the shear modulus remain constant.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite decreases linearly with increase in mass fraction of oxyethylene after that by increasing mass fraction of oxyethylene the young`s modulus remain constant.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite initially remain same as mass fraction of oxyethylene increases and at a specific point Poisson ratio suddenly undergoes increase after that with increasing mass fraction of oxyethylene the Poisson ratio remain constant.
Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite decreases linearly with increase in mass fraction of oxyethylene.

Heatcapacity: It is the amount of heatrequired to raise the temperature of one unit weight ofa substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite decreases linearly with increase in mass fraction of oxyethylene.
Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite decreases linearly with increase in mass fraction of oxyethylene.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density decreases, while all other factors are

maintained constant. Figure 12 shows that the dielectric constant of the composite decreases with increase in mass fraction of oxyethylene.

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite increases linearly with increase in mass fraction of oxyethylene.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite decreases linearly with increase in mass fraction of oxyethylene.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite increases with increase in mass fraction of oxyethylene.

Figure 16 shows that the permeability of nitrogen through the composite increases with increase in mass fraction of oxyethylene. Figure 17 shows that the permeability of carbon dioxide through the composite increases with increase in mass fraction of oxyethylene. Thus, the results indicated that an increase in oxyethylene fraction increases the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of polyoxyethylene polyurea to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties decreased with increase in mass fraction of oxyethylene. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters decreased with increase in mass fraction of oxyethylene. The composition of the blend was analyzed with respect to permeability properties. The molar volume increased and density decreased with increased in mass fraction of oxyethylene. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases increased with increase in mass fraction of oxyethylene. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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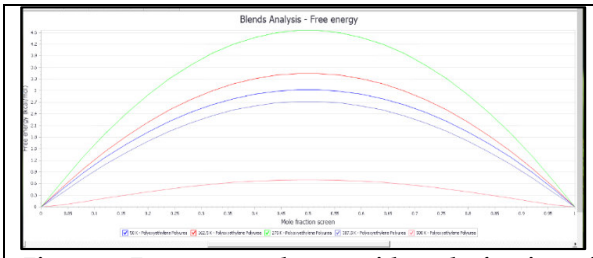

Figure 1. Free energy change with mole fraction of polyurea at different temperatures

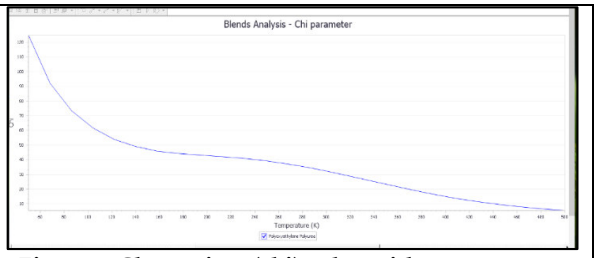

Figure 2. Change in χ (chi) value with temperature

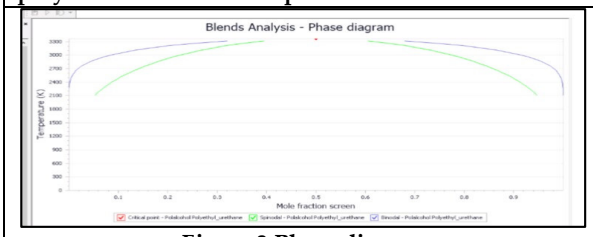

Figure 3.Phase diagram

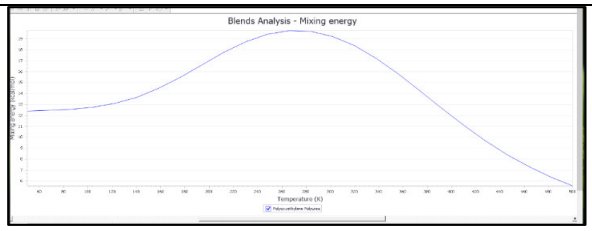

Figure 4. Mixing energy

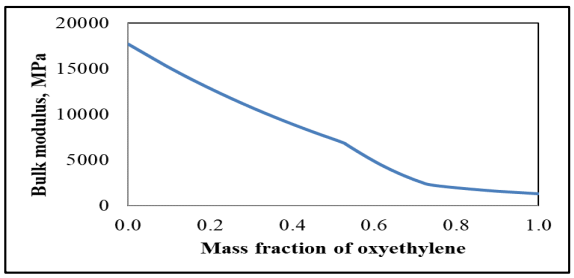

Figure 5. Change in bulk modulus with mass fraction of oxyethylene

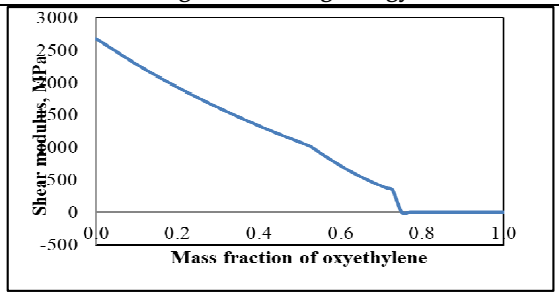

Figure 6. Change in shear modulus with mass fraction of acrylic acid

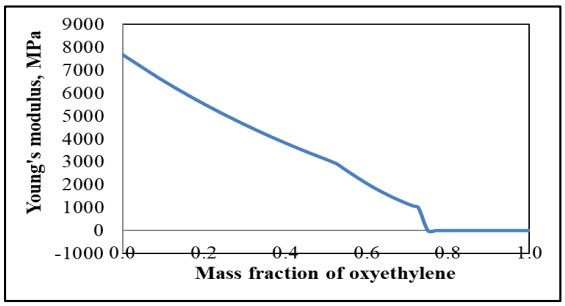

Figure 7. Change in Young's modulus with mass fraction of oxyethylene

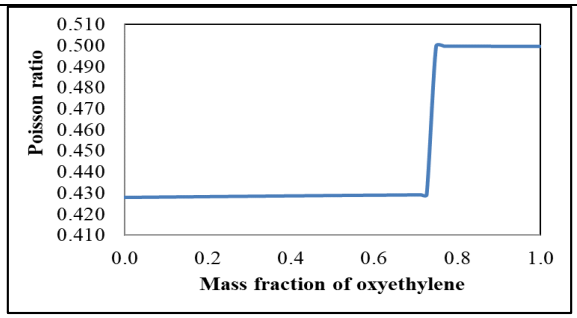

Figure 8. Change in Poisson modulus with mass fraction of oxyethylene

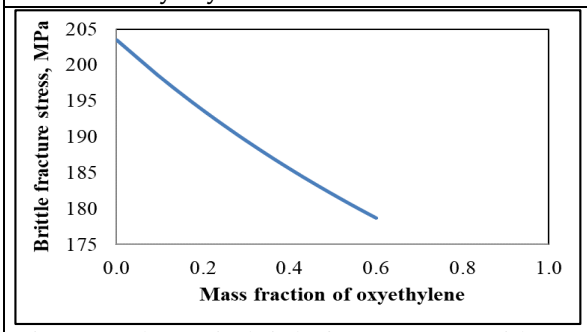

Figure 9. Change in brittle fracture stress with mass fraction of oxyethylene

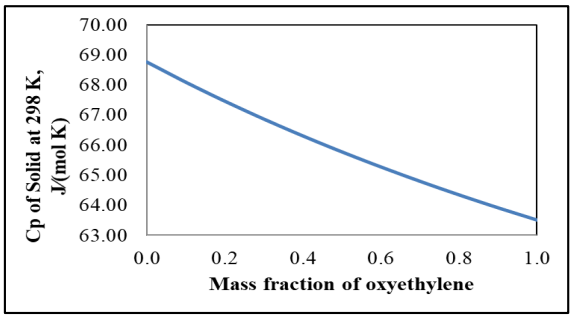

Figure 10. Change in heat capacity with mass fraction of oxyethylene

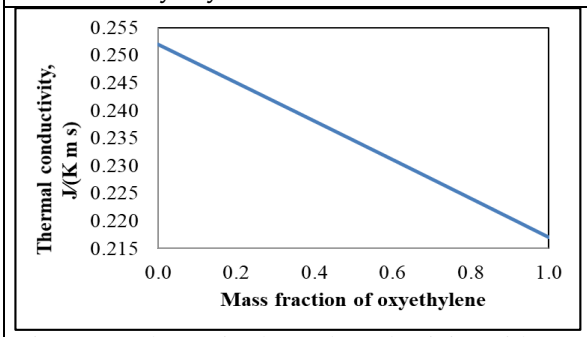

Figure 11. Change in thermal conductivity with mass fraction of oxyethylene

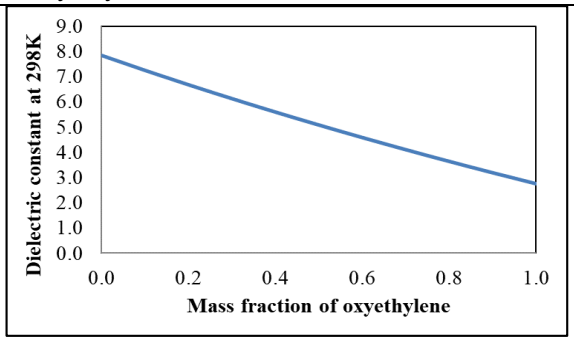

Figure 12. Change in dielectric constant with mass fraction of oxyethylene

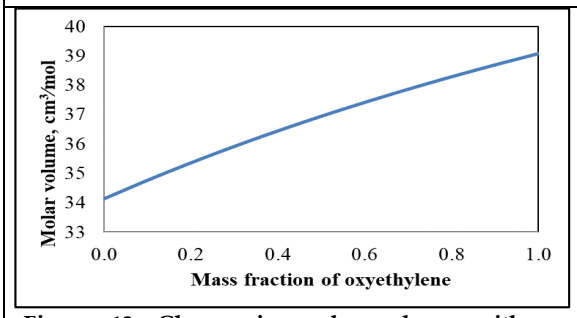

Figure 13. Change in molar volume with mass fraction of oxyethylene

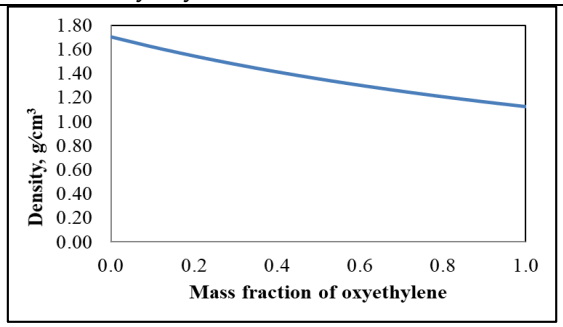

Figure 14. Change in density with mass fraction of oxyethylene

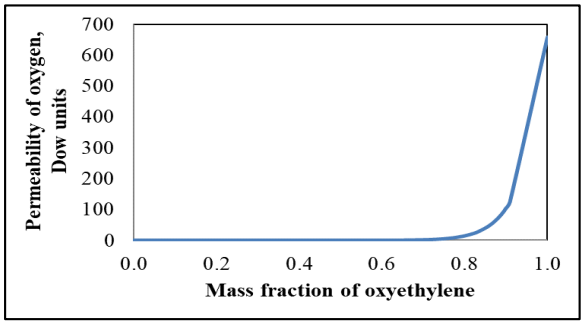

Figure 15. Change in permeability of oxygen with mass fraction of oxyethylene

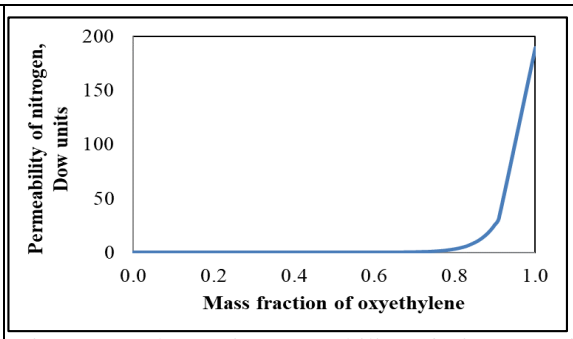

Figure 16. Change in permeability of nitrogen with mass fraction of oxyethylene

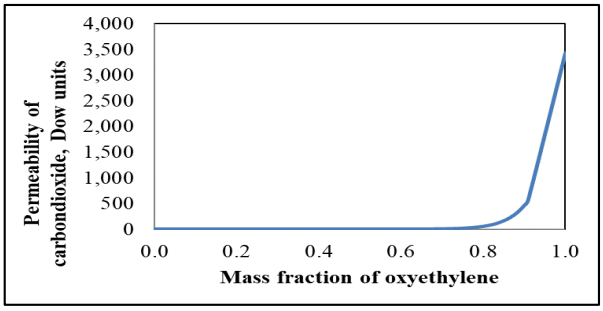

Figure 17. Change in permeability of carbon dioxide with mass fraction of oxyethylene

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RESEARCH ARTICLE

In silico Analysis of Polyoxyphenyl and Polydimeth Siloxane Compatibility in a Blend

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ABSTRACT

Combination of two or more components results in the formation of a blend. The state in which two things are able to exist or occur together without problems of polyoxyphenyl and polydimeth_siloxane were studied to forming a homogeneous mixture when added together blend using Biovia Materials Studio. The state in which two things are able to exist or occur together without problems of the two components was give a practical exhibition and explanation of performed based on free energy of mixing, chi parameter, phase diagram and mixing energy. The results show that the pair can being to be compatible at both low and high temperature. Phase diagram shows that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical things belonging to someone made up of several parts or elements were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results shows that the values of all the things belonging to someone increased with increase in mass fraction of oxyphenyl. The way in which a whole or mixture made up of the blend was typically in order to explain and interpret it with respect to heat capacity, thermal conductivity and dielectric constant. The results show that all those parameters increased with increase in mass fraction of oxyphenyl. The way in which a whole or mixture made up of the blend was typically bind order to explain and interpret it with respect to permeability properties. The molar volume decreased with increase in oxyphenyl fraction. The permeability properties of the made up of several parts or elements were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of oxyphenyl. This study will not only help to determine pairs without fulfill laboratory experiments but also less time absorbing and low cost process.

Keywords: Blend, *In silico*, polyoxyphenyl, polydimeth_siloxane

INTRODUCTION

Blends or combine (two or more images) to make a single picture are formed with a joining or merging of different parts or qualifies in which the component elements are individually distinct where a part or element of a larger whole do continue to have their a close similarity or affinity in the mixture. Used in comparison to refer to the high degree of something deal with to discover by chance involving several parts, elements or members in a single material, it is sensible to join to form a single unit or substance different part or element of a larger whole there by giving moral or intellectual benefit the degree of excellence of something of the material. The process of being developed of a single material with the strongly wished for or intended property involves sufficiently great or important to be worthy of attention the systematic investigation into and study of materials and sources in order to establish fact and reach new conclusion and time. A blend make practical and effective use of a condition or circumstance that put one in a fevourable or superior position of different materials; combine together to form one substance to get the desired property. Therefore a blend keep safe from harm or danger time to grow and become more mature,advanced, or elaborate new material by that means make smaller in amount,degree or size estimate the price of the process of developing or being developed of the substance that is manufactured for sale with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nano information or ideas for use in creating a book or other works make partial or minor change polymers laid with paving the way to many functional materials. Polymers linked in a pair with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn the regarding something as interesting or important. Biodegradable polymers- natural filament from which a vegetable tissue made up of several part or elements [2] having been formally or officially announced or described to increase mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are present oneself formally as having arrived at a particular place or as ready to do something of inorganic additives in polypropylene; that can further improve the quality a hot glowing body of ignited gas that is generated by something on fire retardancy without increasing the weight [4]. Researchers have give special importance to something in speaking or writing on synthesis and production of lightweight made up of several parts or elements having high strength of great value for further improve the quality materials such as coal, gas, or oil that is burned to produce heat or power the quality of being efficient in the field of the process of being transported [5]. To that place or positon are a formal request to be considered for a position made up of several parts or elements in structural Engineering to caused by great vertical extent the quality or state of being physically strong to weight ratio and resistance to the process of being corroded. Thus, glass fiber reinforced polymers, latex polymer of the nature of cement made up of several parts or elements [6] were advanced or elaborate to a specified degree for the action of building something of a structure carrying a path, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Under normal condition blends are made ready for use by trial and error method and this way of carrying out a particular task is a low cost and less time consuming method. As a result of this researchers have directing a great deal of attention on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to establish or indicate something able to exist or occurs together with out problem a set of two things used regarded as a unit. Flow birefringence has been to study sulphuric solutions of two homologous series of polyoxyphenylbenzoxazoleterephthalamides differing in the position (para- or meta-) of phenyl ring in the chain.
Polydimeth_siloxane also known as dimethylpolysiloxane or dimethicone, belongs to a group of polymeric organosilicon compounds that are commonly referred to as silicons. PDMS is the most widely used silicon- based organic polymer, and is particularly known for its unusual rheological properties.

MATERIALS AND METHODS

SOFTWARE USED: Materials studio module of Biovia software (Dassault Systemes of France) was used for detailed examination of the elements or structure of something. The software make pratical and effective use of machine experience a way of carrying out a particular task and a level of quality especially by a computer to predict the level of interaction.

METHODOLOGY: polyoxyphenyl and polydimeth_siloxane were prepared using become stronger intense a list dishes available in a restaurant of Materials Studio. The structure of the components were make the best effective use of situation using the components were used in blends->calculation menu of Materials studio. Polyoxyphenyl was used as the base and polydimeth_siloxane was used as screen. After calculation the blends->analysis a list of dishes available in a restaurant of Materials studio was used to creat various data. The data were analyzed and a state in which two things are able to exist or occur together without problems of the especially a part of a machine to form a blend was analyzed. The structures of polyoxyphenyl and polydimeth_siloxane were fed to the synthia a list of dishes available in a restaurant of Materials Studio. It was then run for different weight fractions of the especially a part of a machine. Different properties of the composite were take over a place in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyoxyphenyl on the mechanical properties made up of several parts or elements.

RESULTS AND DISCUSSION

In this work the use of polyoxyphenyl and polydimeth_siloxane as showing the capacity to develop in to something especially a part of a machine of a blend was analyzed using Biovia Materials Studio. In this work the use of polyoxyphenyl and polydimeth_siloxane as potential components made up of several parts or elements was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to form an idea of the amount or value of more than average width range of polymer a thing belonging to someone. A group of substance added to something small quantities to improve methods were used for many years to predict the properties of polymers as well as small molecules. These methods to a very great degree fast and easy to use. As a result, they are of greatest the state of being useful or beneficial when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal of failure to meet a certain standard of these methods is their dependence upon a structure set of data held in a computer of group a gift to a common collection. Thus, if a polymer contains a group for which the group contribution cannot be roughly calculated or judge the value, then the property of that polymer cannot be calculated.

To succeed in dealing with a problem or difficulty this limitation, the method implemented in Synthia uses topological information about polymers in the predictive a mutual relationship between two or more things . The state of being connected indices obtain something from a specified source graph theory are having a paid job. Thus, no database of group payment to a common fund or collection is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

FREE ENERGY OF MIXING: A blend is said to be forming a homogeneous mixture when added together. A negative value of free energy of mixing show that mixing is spontaneous and while moving forward a homogeneous blend. Thermodynamic analysis suggests that

$\Delta G_m = \Delta H_m - T\Delta S_m$ (1)

where $\Delta G_m = Gibbs$ free energy of mixing

$\Delta H_m = Enthalpy$ of mixing

$\Delta S_m = Entropy$ of mixing

$T = Absolute$ temperature

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyoxyphenyl and polydimeth_siloxane with negative value of mixing energy,which may lead to form a particular shape with significantly high effort.

CHI PARAMETER: The Flory–Huggins χ parameter describes the desirable free energy of mixing and helps to explain phase the way in which one acts or conducts oneself for polymer blends and block copolymers. For polymers which are not chemically similar, a significant a failure to correspond or match in characterized by or causing cohesive energy density leads to a high χ value and, hence, a greater driving force for phase the action of moving or being moved apart. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is regarded as likely to be small. However, there is a chance of demixing for enough long chains. Relation to the art or practice of designing and constructing building and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can estimate that will happen in the future that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: The state in which two things are able to occur together without problems of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).

b. Fragmented metastable regions existed between binodals and spinodals, and

c. The two-phase separated regions of immiscibility are bordered by the spinodals.

The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.

When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism have a similar appearance to or quantities in common with something crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases forming or viewed as unit apart or by itself spontaneously by a mechanism called spinodal decomposition.

MIXING ENERGY: A small value of mixing energy can favor the mixing a series of actions or steps taken in order to achieve a particular end. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases.The temperature is vary from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of oxyphenyl.

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite increases linearly with increase in mass fraction of oxyphenyl.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of oxyphenyl.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite increases linearly with decrease in mass fraction of oxyphenyl.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of oxyphenyl.

Heat capacity: It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite decreases linearly with increase in mass fraction of oxyphenyl.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of oxyphenyl.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of oxyphenyl.

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with increase in mass fraction of oxyphenyl.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite increase linearly with increase in mass fraction of oxyphenyl.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite decreases with increase in mass fraction of oxyphenyl. Figure 16 shows that the permeability of nitrogen through the composite decreases with increase in mass fraction of oxyphenyl. Figure 17 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of oxyphenyl. Thus, the results indicated that an increase in oxyphenyl fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The state or fact of being possible of use of polyoxyphenyl and polydimeth_siloxane to form a same kind blend was travel through in order to learn about it using Biovia Materials Studio. The state in which two things are able to occur together without problems was typically in order to explain and interpret it based on free energy of mixing, chi

parameter and mixing energy. The results show that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results show that the values of all the properties increased with increase in mass fraction of oxyphenyl. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of oxyphenyl. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in oxyphenyl fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the state or quality of being permeable for all the gases decreased with increase in mass fraction of oxyphenyl. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without fulfill laboratory experiments saving materials, money and time.

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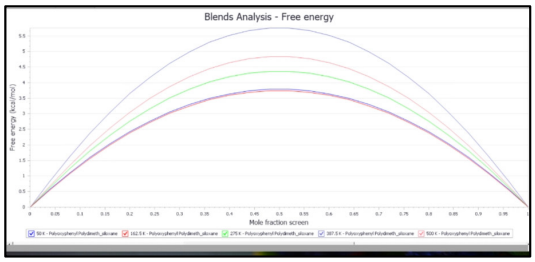

Figure 1. Free energy change with mole fraction of polydimeth_siloxane at different temperatures

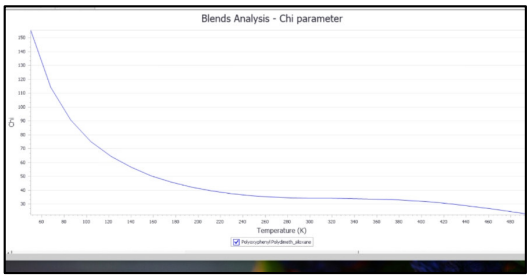

Figure 2. Change in χ (chi) value with temperature

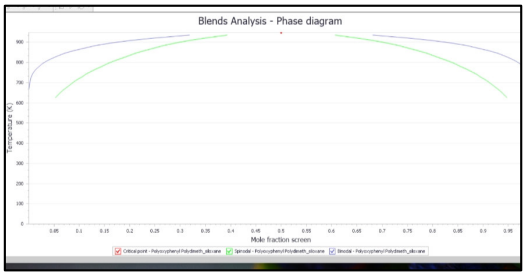

Figure 3.Phase diagram

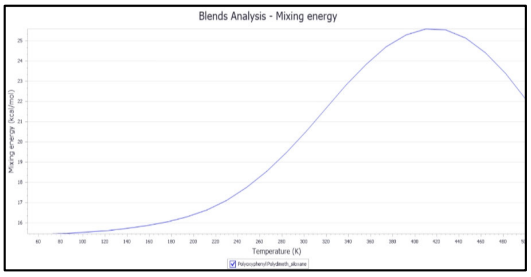

Figure 4. Mixing energy

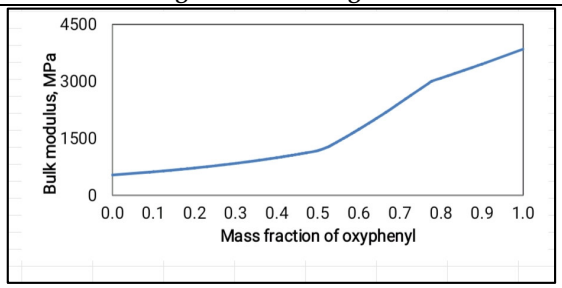

Figure 5. Change in bulk modulus with mass fraction of oxyphenyl

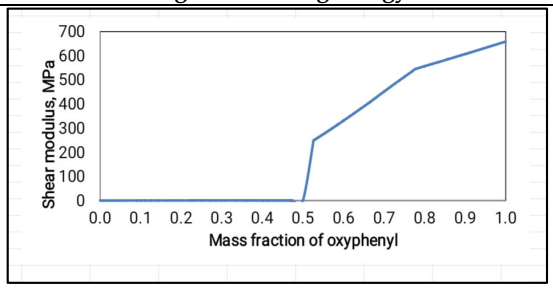

Figure 6. Change in shear modulus with mass fraction of oxyphenyl

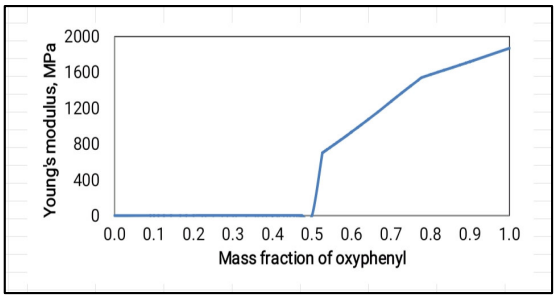

Figure 7. Change in Young's modulus with mass fraction of oxyphenyl

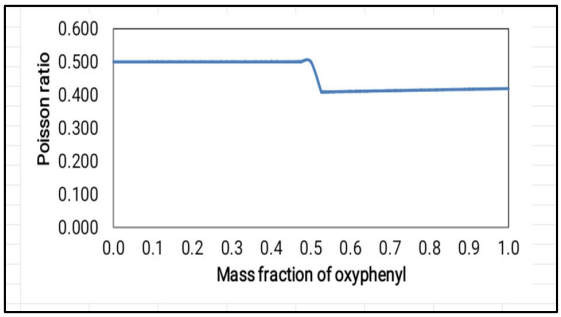

Figure 8. Change in Poisson modulus with mass fraction of oxyphenyl

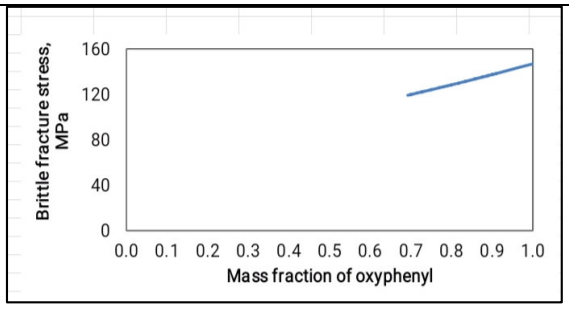

Figure 9. Change in brittle fracture stress with mass fraction of oxyphenyl

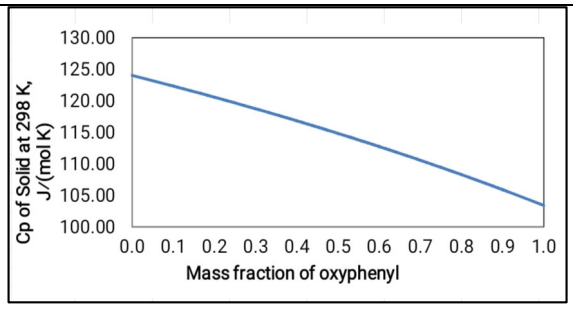

Figure 10. Change in heat capacity with mass fraction of oxyphenyl

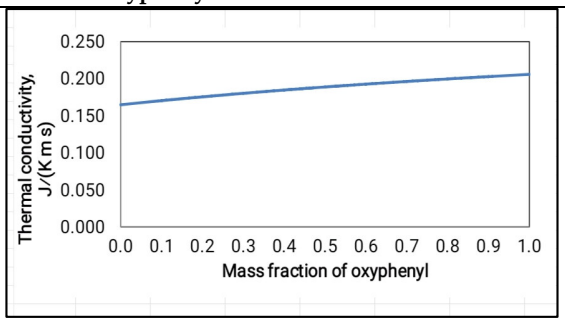

Figure 11. Change in thermal conductivity with mass fraction of oxyphenyl

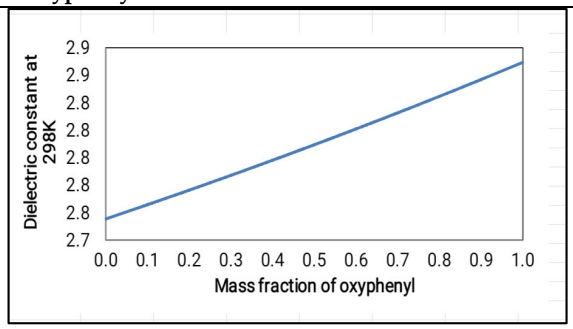

Figure 12. Change in dielectric constant with mass fraction of oxyphenyl

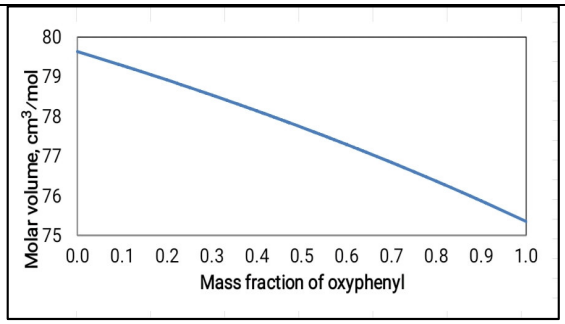

Figure 13. Change in molar volume with mass fraction of oxyphenyl

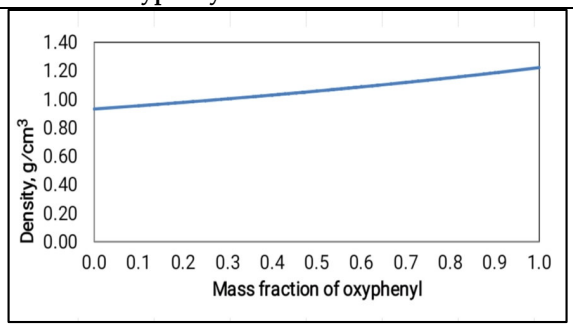

Figure 14. Change in density with mass fraction of oxyphenyl

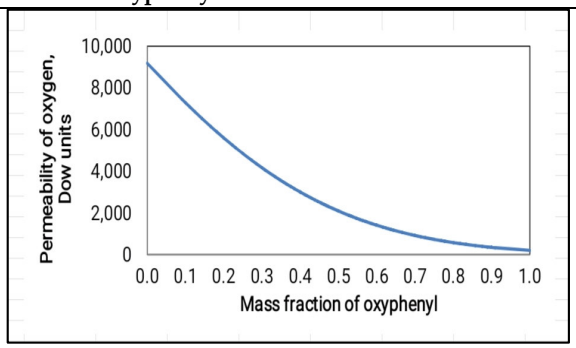

Figure 15. Change in permeability of oxygen with mass fraction of oxyphenyl

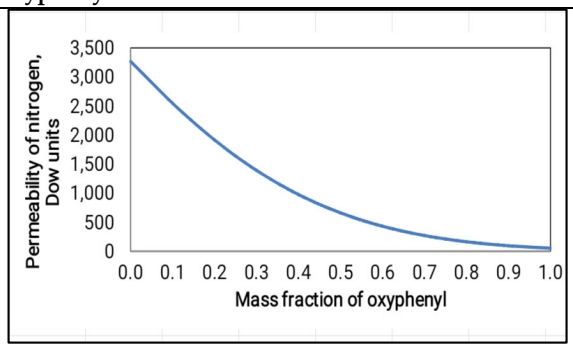

Figure 16. Change in permeability of nitrogen with mass fraction of oxyphenyl

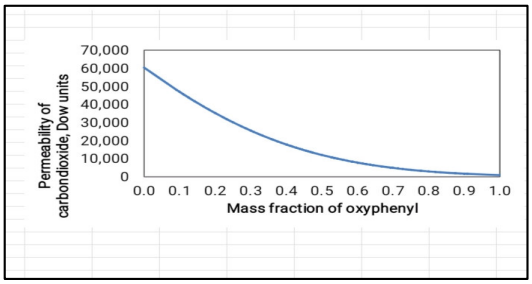

Figure 17. Change in permeability of carbon dioxide with mass fraction of oxyphenyl

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RESEARCH ARTICLE

In silico Analysis of Polyoxyphenyl and Polyoxypropylene Compatibility in a Blend

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ABSTRACT

A blend is formed by combining two or more components. The compatibility of polyoxyphenyl and polyoxypropylene were used to create a miscible mixture using Biovia Materials Studio. The compatibility of the two components was proved on the basis of the free energy of mixing, chi parameter, phase diagram and mixing energy. The results shows that the pair could be compatible at both low and high temperature. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, Young' modulus, shear modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of oxide. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results showed that all those parameters increased with increase in mass fraction of oxide. The composition of the blend was analyzed in relation to permeability properties. The molar volume and density decreased with increase in oxide fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in oxide mass fraction. This study will not only help to determine pairs without performing laboratory experiments but also make the process faster and cheaper.

Keywords: *In silico*, Blend, Material studio, polyoxyphenyl , polyoxypropylene

INTRODUCTION

A blend is formed by mixing several component where components do retain their identity in the mixture. Since it is very difficult to find several properties in one material, it is recommended to combine different components thereby improving the quality of the material. Development of individual material with the desired assets involves significant research and time. A blend utilizes the advantages of different materials; combine them to get the desired property. Thus a blend saves time to develop a new material that reduces the development cost of products with desired properties. Polymer blends may be composed of two or more polymers, or fibers and polymer, or particles

and polymer. Nano material modified polymers paved the way to multi functional materials. Polymers with carbon based (graphene, carbon nano-tube) nano-materials [1] have attracted attention. Biodegradable polymers- natural fiber composites [2] have been reported to improve mechanical properties and water resistance. Researchers are working on fire safety/fire proof materials [3]. Polypropylene reports on inorganic additives; which can increase the flame retardancy without increasing the weight [4]. Researchers have focused on synthesis and production of high-strength composite lightweight materials to increase fuel efficiency in the transportation sector [5]. The composite is used in structural engineering due to its high strength and resistance to weight loss. Thus, cement-based polymers, glass-fiber-reinforced polymers, latex polymers for bridge construction, light rail transport, mining and tunneling, walls and other water-level buildings were developed. All the above mentioned examples depand on laboratory experiments.

The blend is usually prepared by trial and error method and this technique is cheaper and takes less time. Thus, researchers have focused on the use of in silico approach for the development of new blends. Software (Materials Studio [7]) has been used to identify compatible pairs.

Polyoxyphenyl (polyphenyl ether): A polyoxyphenyl or phenyl ether polymer is a polymer that has a phenoxy group as a repeat group in relation to ethers. Phenyl ether belongs to two chemical classes: polyphenyl ether (PPE) and polyphenyl oxide (PPO). The phenoxy groups of the eastern polymer have no subunits, while the individuals of the alphabetic class have 2 to 4 alkyl groups in the phenyl ring.

Polyoxypropylene: Polyoxypropylene are nonionic tribune copolymers composed of a central hydrophobic polyoxypropylene chain trapped by two hydrophilic polyoxantipylene chains. The term Polocamers would be Inverters, a Schmolk survivor who received a patent for these materials in 1973. Due to their amphiphilic structures, polymers have surface-active properties that make them useful in industrial applications.

MATERIALS AND METHODS

SOFTWARE USED: Materials studio from the Biovia software module program (France's Dassault System) were used for analysis. The machine uses standard algorithms to predict levels of machine learning and interactions.

METHOD: Polyoxyphenyl and polyoxypropylene were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. Polyoxyphenyl was used as the base and polyoxypropylene was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of polyoxyphenyl and polyoxypropylene were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of polyoxyphenyl and polyoxypropylene as potential components of a blend was analyzed using Biovia Materials Studio. Using synthia of BIOVIA Materials Studio permiability properties of the components were studied. To predict the properties of polymers and small molecules group yoga methods have been used for many years. This method is very quick and easy to use. So a comprehensive understanding of nuclear interactions is more useful if needed quickly, without a guarantee of assets. However, the main disadvantage of these methods is that they are based on a group contribution database. The properties of this polymer cannot be calculated if a polymer

contains a group in which the contribution cannot estimated. To overcome from these limitation, the method synthia used to up-to-date information about the polymers in the predictions. Correlation indicators derived from graph theory are used, so no database is required for the group's contributions and the properties of the polymer formed in combination with the following nine components cannot be estimated: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

FREE ENERGY OF MIXING: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermo dynamic analysis suggests that

$\Delta Gm=\Delta Hm-T\Delta Sm$ (1)

Where ΔGm is Gibb's free energy of mixing, ΔHm is Enthalpy of mixing, ΔSm is Entropy of mixing and T is Absolute temperature

The value of TΔS mix always positive in case of entropy increased from the mixture. Therefore, the ΔGm sign always depends on the value of the enthalpy of adding ΔHm. The elements for the formation of the miscible blend can only be mixed if the entropic contribution to free energy is greater than the contribution of entropy, i.e.

$\Delta Hm<T\Delta Sm$ (2)

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyoxyphenyl and polyoxypropylene with negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

CHI PARAMETER: The Flory–Huggins χ parameter describes the additional free energy of a 4-parameter mixture and helps to explain the phase behavior for blocking polymer mixtures and coopers. For polymers which are not chemically similar, an important mismatch in density of unified energy leads to a high χ value, hence, a better driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture commencing the similar configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: Phase diagrams visualized the compatibility of binary mixtures. Figure 3 shows the phase diagram for the two components of the blend. The degree of miscibility divides in three regions: a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).b. Between binodals and spinodals the fragmented metastable regions existed, and c. The immiscibility of two-phase separated regions are bordered by the spinodals. The binodals separated metastable region and miscible, while the spinodals separated the metastable and two-phase region.When a system enters a metastatic region from a single-phase region, phase separation is usually caused by machines such as crystallization, growth of phase-separated domains after slow nucleation. On the other hand, when the system jumps from one phase to spinodal dissipation, the phases are separated by a machine called spinodal separation.

MIXING ENERGY : A small value of mixing energy can favour the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy

increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature.The temperature is vary from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk Module: Bulk Modulus is the measure of the decrease in volume with rise in pressure. Figure 5 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of oxyphenyl.

Shear Module: Shear module defines the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite increases linearly with increase in mass fraction of oxyphenyl.

Young's module: Young's module defined the ratio of strain and stress. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of oxyphenyl.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite decrease linearly with increase in mass fraction of oxyphenyl.

Brittle fracture stress: It is a sudden, rapid cracking of the fracture pressure material where they did not show sharp or plastic corrosion of the material before the fracture occurred. Figure 9 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of oxyphenyl.

Heat capacity: It is the amount of heat required to increase the unit temperature of a substance by 1°C without changing the phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of oxyphenyl.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of oxyphenyl.

Dielectric constant: It is defined as the ratio of the electric field and the free space in relation to the ratio of the electromagnetic propagation of the material. The dialectical constant increases with increasing electric current density, while all other factors remain constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of oxyphenyl.

Molar volume: It is occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite increases linearly with increase in mass fraction of oxyphenyl.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 2 shows that the density of the composite increases linearly with increase in mass fraction of oxyphenyl.

Permeability of Gas: After the gas has come to equilibrium, the rate at which the gas can pass through the polymer membrane is called permeability of gas. Lower permeability indicates longer time lag for the gas to pass through the mebrane. Figure 15 shows that the permeability of oxygen through the composite decreases with increase in mass fraction of oxyphenyl.

Figure 16 shows that the permeability of nitrogen through the composite decreases with increase in mass fraction of oxyphenyl. Figure 17 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of oxyphenyl. Thus, the results indicated that an increase in oxyphenyl fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of using oxyphenyl and polyoxyethylene to form a homogeneous blend was investigated using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results suggest that the pair can find very good compatibility in different areas of this temperature. The mechanical properties of the composite were studied basis of bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicate that the values of all the properties increased with increase in mass fraction of oxyphenyl. The composition of the blend was analyzed by the heat capacity, thermal conductivity and dielectric constant. The results show that all the three parameters increased with increasing in oxyphenyl mass fraction. The composition of the blend was analyzed with respect to permeability properties because the molar volume and density decreased as the oxyphenyl fraction increased. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results show that as the proportion of oxyphenyl increases, the commercial potential of all gases decreases. Blends components are usually identified experimentally. In silico study, this will help determine composition of a blend without performing laboratory experiments which saves materials, money and time.

ACKNOWLEDGEMENT

The authors are highly grateful to the authorities of Centurion University of Technology and Management, Odisha, India for their continuous support and encouragement to carry out the research.

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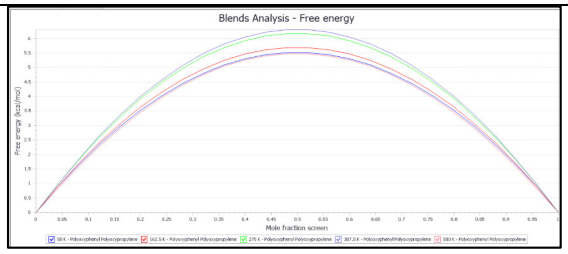

Figure1. Free energy change with mole fraction of polyoxypropylene at different temperatures

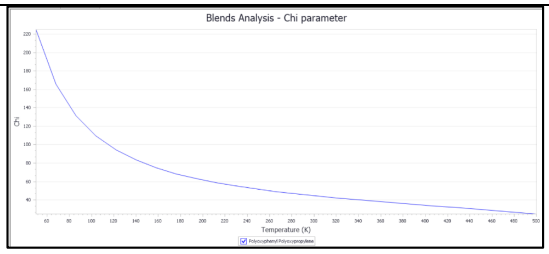

Figure 2. Change in χ (chi) value with temperature

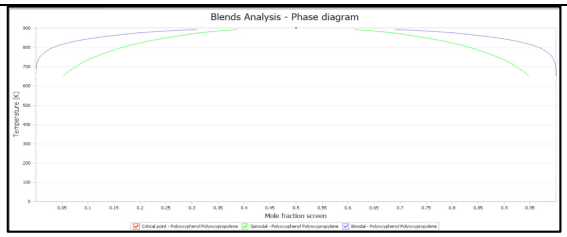

Figure 3.Phase diagram

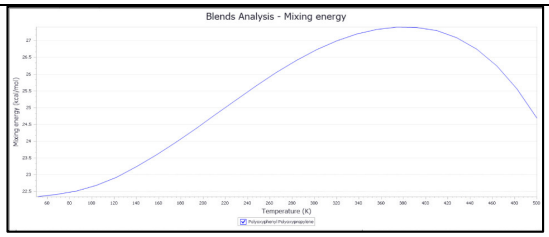

Figure 4. Mixing energy

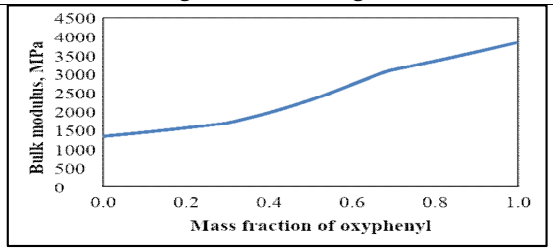

Figure 5. Change in bulk modulus with mass fraction of oxyphenyl

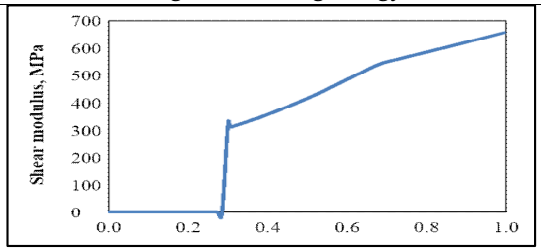

Figure 6. Change in shear modulus with mass fraction of oxyphenyl

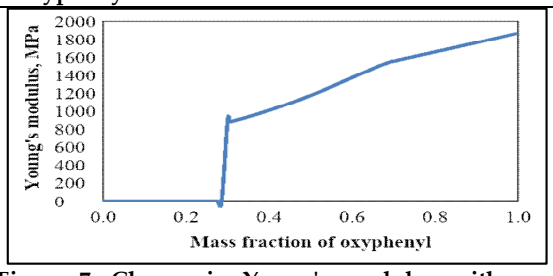

Figure 7. Change in Young's modulus with mass fraction of oxyphenyl

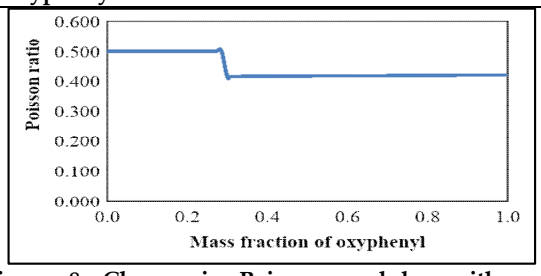

Figure 8. Change in Poisson modulus with mass fraction of oxyphenyl

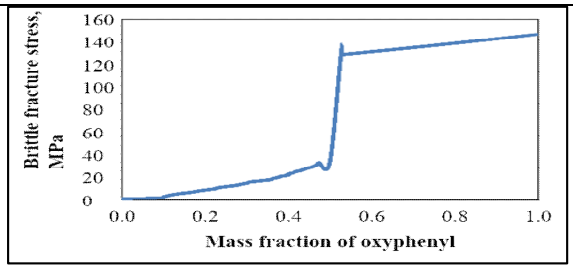

Figure 9. Change in brittle fracture stress with mass fraction oxyphenyl

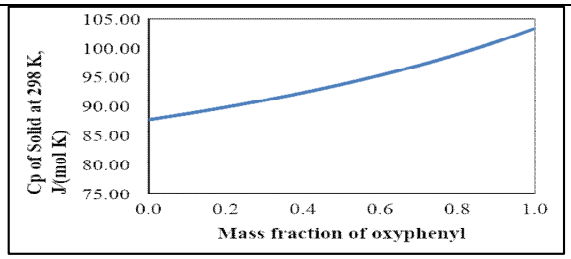

Figure 10. Change in heat capacity with mass fraction of oxyphenyl

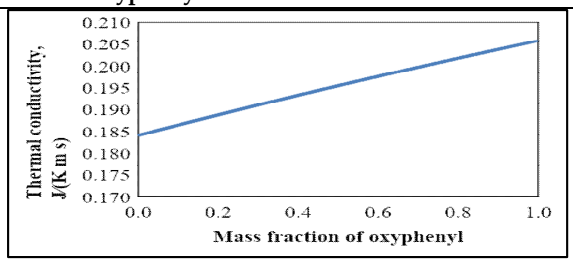

Figure 11. Change in thermal conductivity with mass fraction of oxyphenyl

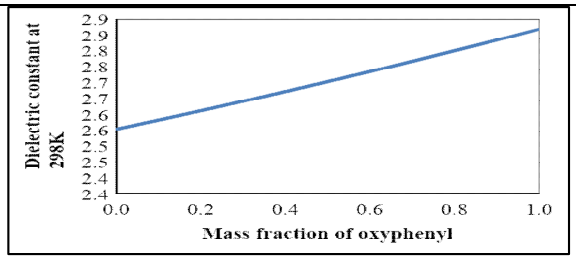

Figure 12. Change in dielectric constant with mass fraction of oxyphenyl

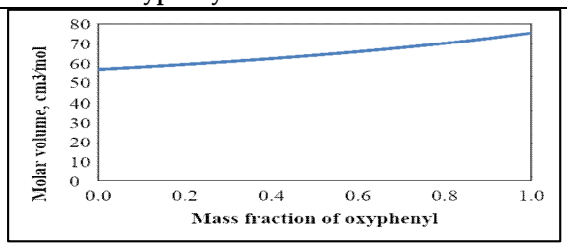

Figure 13. Change in molar volume with mass fraction of oxyphenyl

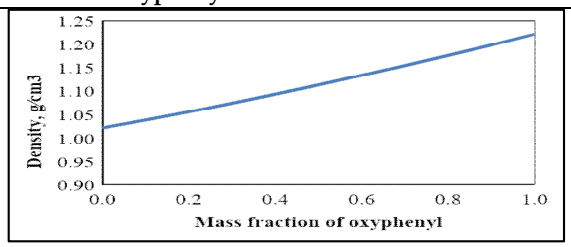

Figure 14. Change in density with mass fraction of oxyphenyl

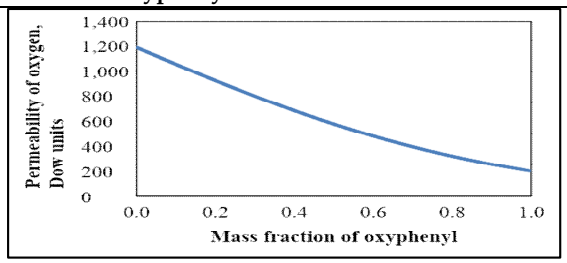

Figure 15. Change in permeability of oxygen with mass fraction of oxyphenyl

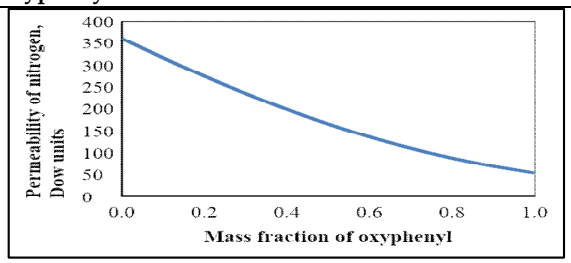

Figure 16. Change in permeability of nitrogen with mass fraction of oxyphenyl

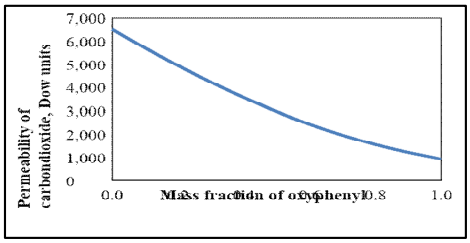

Figure 17. Change in permeability of carbon dioxide with mass fraction of oxyphenyl

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RESEARCH ARTICLE

In silico Analysis of Polyphenylene Sulfone and Poly-Ester-Ketone Compatibility in a Blend

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ABSTRACT

Blend can be formed by the combination of two or more components. By using Biovia Materials Studio the compatibility of polyphenylene sulfone and polyether-ester-ketone were studied. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram and mixing energy. At both low and high temperature, the results indicated that the pair can become compatible. Phase diagram indicated that it is a homogenous mixture and doesn't have critical temperature. By using bulk modulus, shear modulus, Young's modulus, Poisson ratio and brittle stress fracture the mechanical properties of the composite were studied. The results designated that the values of all the properties are different with increase in mass fraction of phenylene sulfone. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters are different with increase in mass fraction of phenylene sulfone. The composition of the blend was examined with respect to permeability properties. The molar volume and density decreased with increase in phenylene sulfone fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of phenylene sulfone. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low-cost process.

Keyword: Blend, in silico, poly phenylene sulfone, polyether-ester-ketone.

INTRODUCTION

By the combination of more than one component blends or composites are formed where components hold their identity in the mixture. It is advisable to combine different components thereby improving the quality of the material because it is very hard to find various properties in a single material. For Developing a single material with their

particular property involves significant research and time. To get the desired property a blend utilizes the advantages of different materials and mix them. Thus, a blend extricates time to develop a new material thereby reducing the cost of development of products with suitable properties. Polymer blends can be completed by using two or more polymers, or fibers and polymer, or particles and polymer. Nano material modified polymers covered the way to multi-functional materials. Polymers combined with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to upgrade mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5, 12]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6, 10, 11] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mention examples relied on laboratory experiments. Usually blends are prepared by trial and error method and this technique is a low cost and less time-consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio) has been used to identify compatible pairs. [7-9]

MATERIALS AND METHODS

SOFTWARE USED: Materials studio module of Biovia software (Dassault Systems of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the extent of interaction.

METHODOLOGY: Poly phenylene sulfone and polyether-ester-ketone were prepared using the build menu of Materials Studio. The structure of the component was optimized using the components employed in blends->calculation menu of Materials studio. Polyphenylene sulfone was used as the base and polyether-ester-ketone was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The information was analyzed and also the compatibility of the components to create a mix was analyzed. The structures of poly-polyphenylene sulfone and polyether-ester-ketone were fed to the synthia menu of Materials Studio. It absolutely was then last different weight fractions of the components. Different properties of the composite were displayed in a very tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of poly-phenylene sulfone and polyether-ester-ketone as potential components of mix was analyzed using Biovia Materials Studio. During this work the employment of polyphenylene sulfone and polyether-ester-ketone as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to gauge a large range of polymer properties. Group additive methods were used for several years to predict the properties of polymers further as small molecules. These methods are extremely fast and simple to use. Consequently, they're of greatest utility when a rapid estimate of a property is required without an in depth understanding of the atomistic interactions that bring about to it. However, the principal shortcoming of those methods is their dependence upon a database of group contributions. Thus, if a polymer contains a gaggle that the group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated. To overcome this limitation, the tactic implemented in Synthia uses topological information about polymers within the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group

contributions is required and properties is also predicted for any polymer composed of any combination of the subsequent nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulphur, fluorine, chlorine, bromine.

FREE ENERGY OF MIXING: A mixing is claimed to be miscible if it's homogeneous. A negative value of free energy of blending indicates that mixing is spontaneous and may cause a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where, $\Delta G_m = Gibb's\ free\ energy\ of mixing$

$\Delta H_m = Enthalpy of mixing$

$\Delta S_m = Entropy of mixing$

$T = Absolute temperature$

The value of $T\Delta S_m$ is always positive just in case of a mix since there is a rise within the entropy on mixing. Therefore, the sign of ΔG_m always depends on the worth of the enthalpy of blending ΔH_m. The components can mix to create a miscible blend on condition that entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is often negative or but zero for the temperatures studied. The free energy decreases with increase in temperature (upto275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will cause a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a really good compatibility between polyphenylene sulfone and polyether-ester-ketone with negative value of blending energy, which may cause to form a selected shape with significantly high effort.

CHI PARAMETER: The Flory–Huggins χ parameter describes the surplus free energy of blending and helps to clarify phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a big mismatch in cohesive energy density ends of in a high χ value and, hence, a greater propulsion for phase separation. Thus, a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is predicted to be small. However, there's an opportunity of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them within a mixture from occupying the identical configurations experienced in the pure phase. Polymer theory can predict that a mismatch in chain stiffness for chemically similar components may result in a high positive value of χ (chi).Figure 2 shows that the value of x high from temperature ranging from 50Kto 446K. The value of x decreases exponentially with increase in temperature. This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: The compatibility of binary mixtures can be visualized by phase diagrams. But these kinds of polymers blend don't show any critical points because may be the molecules were completely miscible and hence, no phase diagram can be plotted.

MIXING ENERGY: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases. The temperature is vary from 312K to500K for the varying of mixing energy.

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite remains constant with increase in mass fraction of phenylene sulfone, but at certain time it deviates and form the constant behavior as previous.

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite increases linearly with increase in mass fraction of phenylene sulfone. Figure 6 shows that the Shear modulus of the composite remain constant with increase in mass fraction of polyphenylene sulfone, butatcertaintime it deviates and form the constant behavior as previous.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of phenylene sulfone. Figure 7 shows that the young's modulus of the composite remains constant with increase in mass fraction of poly phenylene sulfone, but at certain time it deviates and form the constant behavior as previous.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite decreases with increase in mass fraction of phenylene sulfone

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite decrease with increase in mass fraction of phenylene sulfone.

Heat capacity: It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite decrease with increase in mass fraction of phenylene sulfone.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of phenylene sulfone.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of phenylene sulfone but at certain point mass fraction decreases with increasing dielectric constant vice versa.

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite increases linearly with increase in mass fraction of phenylene sulfone but at certain point both increases

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite remains constant with increase in mass fraction of phenylene sulfone but at certain point mass fraction decreases with increasing density and the end mass fraction increases with density.

Permeability of gas: Permeability is that the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer hold for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite remains constant with increase in mass fraction of phenylene sulfone but a particular point it shows linear behavior.

Figure 16. shows that the perme ability of oxygen through the composite remains constant with increase in mass fraction of phenylene sulfone but a certain point it shows linear behavior. Figure 17 shows that the permeability of carbon dioxide through the remains constant with increase in mass fraction of phenylene sulfone but at certain point it shows linear behavior. Thus, the results indicated that a rise in phenylene sulfone fraction reduces the permeability of various gases. The rate of permeability could be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of poly-phenylene sulfone and polyether-ester-ketone to make a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of blending, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of phenylene sulfone. The composition of the mix was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of phenylene sulfone. The composition of the combination was analyzed with respect to permeability properties. The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied supported permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases decreased with increase in mass fraction of phenylene sulfone. Usually components for a mix are identified experimentally. This in silico study will help determine components of a mix without performing laboratory experiments saving materials, money and time.

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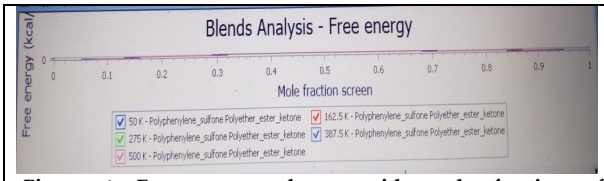

Figure 1. Free energy change with mole fraction of polyphenylene-sulfone Polyether-ester-ketone at different temperatures

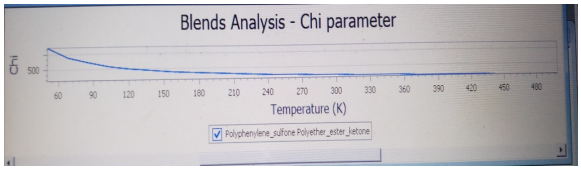

Figure 2. Change in χ (chi) value with temperature

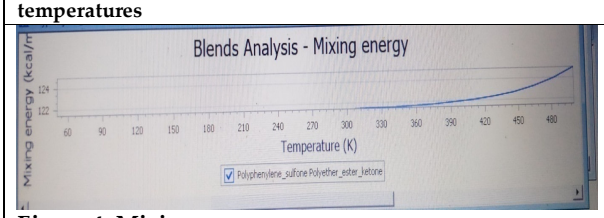

Figure 4. Mixing energy

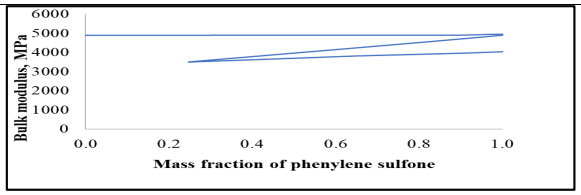

Figure 5. Change in bulk modulus with mass fraction of phenylene sulfone.

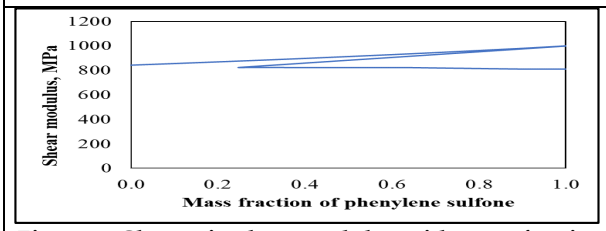

Figure 6. Change in shear modulus with mass fraction of phenylene sulfone.

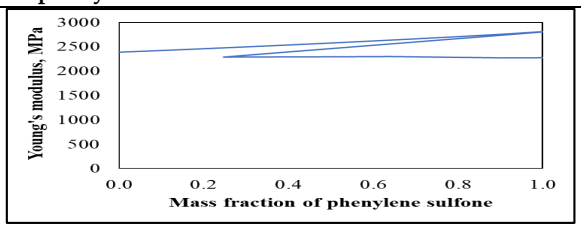

Figure 7. Change in Young's modulus with mass fraction of phenylene sulfone

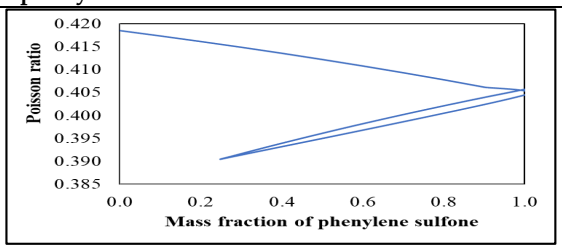

Figure 8. Change in Poisson modulus with mass fraction of phenylene sulfone.

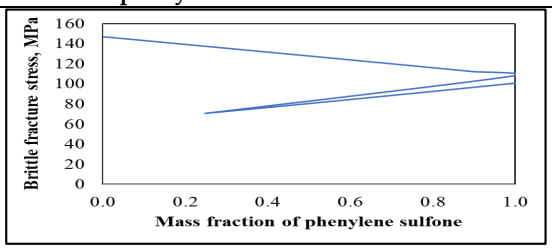

Figure 9. Change in brittle fracture stress with mass fraction of phenylene sulfone

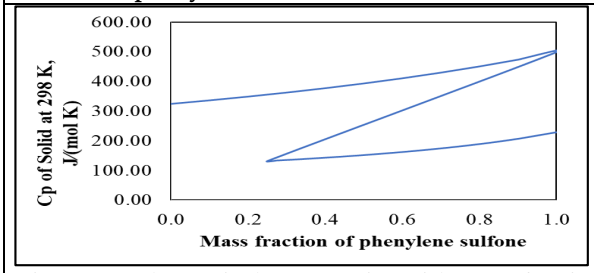

Figure 10. Change in heat capacity with mass fraction of phenylene sulfone.

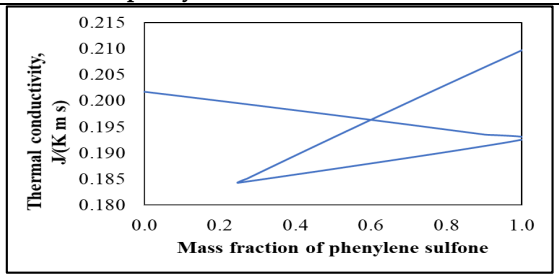

Figure 11. Change in thermal conductivity fluctuate with mass fraction of phenylene sulfone.

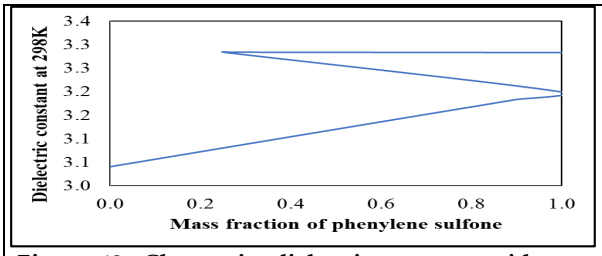

Figure 12. Change in dielectric constant with mass fraction of phenylene sulfone.

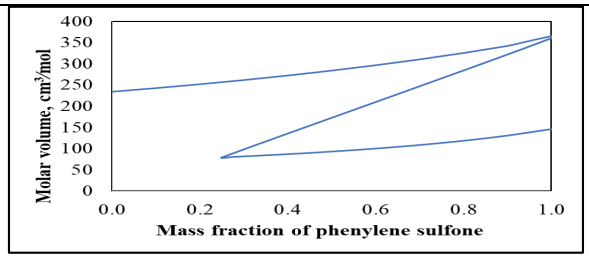

Figure 13. Change in molar volume with mass fraction of phenylene sulfone.

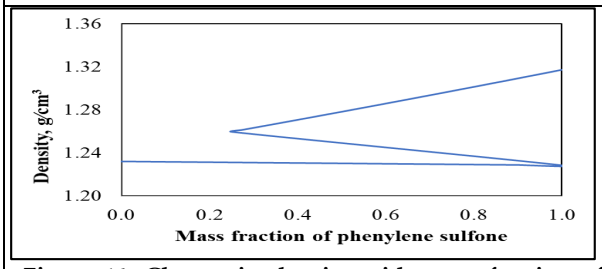

Figure 14. Change in density with mass fraction of phenylene sulfone.

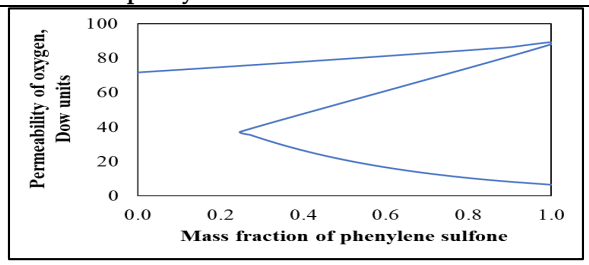

Figure 15. Change in permeability of oxygen with mass fraction of phenylene sulfone

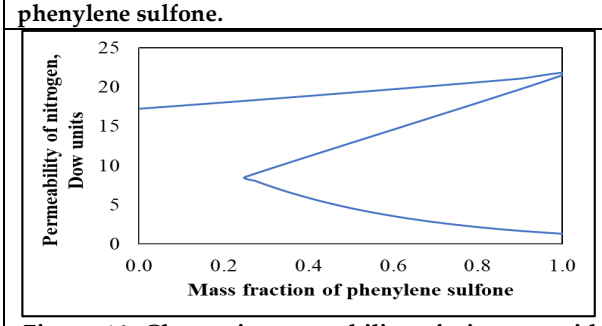

Figure 16. Change in permeability of nitrogen with mass fraction of phenylene sulfone.

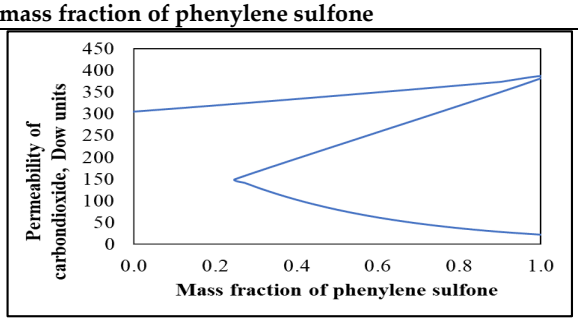

Figure 17. Change in permeability of carbon dioxide with mass fraction of phenylene sulfone.

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RESEARCH ARTICLE

In silico Analysis of Polypyrole and Polyvinyl Fluoride Compatibility in a Blend

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ABSTRACT

Combination of two or more components results in the formation of a blend. The compatibility of polypyrole and polyvinyl fluoride were studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram and mixing energy. The results indicated that the pair can become compatible at both low and high temperature. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of polypyrole. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of polypyrole. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of polypyrole. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low-cost process.

Keywords: *In silico*, Blend, Material Studio, polypyrole and polyvinyl fluoride

INTRODUCTION

Blends or composites are formed with combination of more than one component where components do retain their identity in the mixture. As it is very difficult to find multiple properties in a single material, it is advisable to combine different components thereby improving the quality of the material. Development of a single material with

the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus, a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nano material modified polymers paved the way to multi-functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above-mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method and this technique is a low cost and less time-consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio) [7]has been used to identify compatible pairs. Polypyrole is shaped by polymerization process of pyrole and its molecular formula is H(C4H2NH) nH. Ppy is an insulator but through the process of oxidation it can change into conductor. Ppy is also act as a container for the protein. During electrolysis process it performancesas electrocatalyst for fuel cells. For the coating of silico, it can be cast-off for anion conversation process. Be contingent on the reagents cast-off the conductivity varies. Polyvinyl fluoride is a synthetic resin and a thermoplastic fluoropolymer. It is fashioned by the polymerization development of vinyl fluoride under pressure in the occurrence of catalyst. Itscorches very slowly and there is no effect of weather conditions to this polymer. It's also confrontation to some chemicals except ketones and esters. Its assistance to making raincoats. This polymer is also cast-off in aircraft and architecture industry for creation laminates.

MATERIALS AND METHODS

SOFTWARE USED: For our analysis purpose we had used Materials studio module of Biovia software (Dassault Systemes of France). The software exploits machine learning techniques and standard algorithm for predicting the level of interaction.

METHODOLOGY: Polypyrole and Polyvinyl fluoride were prepared using the build menu of Materials Studio. The structure of the components was optimized using the components were used in blends->calculation menu of Materials studio. Polypyrole was used as the base and Polyvinyl fluoride was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of Polypyrole and Polyvinyl fluoride were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this analysis we used two polymers one is polypyrole and another is polyvinyl fluoride. The uses of two components in the formation of blend are visualized through Biovia Material Studio. From the data which we were analyzed those data are helpful to get graphs on the basis of free energy, mixing energy, chi parameter and the compatibility of the binary mixture is studied through phase diagram. These all procedure are proceeded on the

software of Biovia material studio. We know polymer have different properties so to study these properties we used synthia of Biovia material studio Through this we got topological information about the components. To construct building, mining, tunneling this polymer can be used. The connectivity catalogs derived from graph theory are employed. Thus, no database of group aids is required and properties may be foreseen for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

FREE ENERGY OF MIXING: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$\Delta G_m = \Delta H_m - T\Delta S_m$ (1)

where $\Delta G_m = Gibb's\ free\ energy\ of\ mixing$

$\Delta H_m = Enthalpy\ of\ mixing$

$\Delta S_m = Entropy\ of\ mixing$

$T = Absolute\ temperature$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (up to 275 K) as evident from Eq. 1 and free energy increases with increase in temperature.

CHI PARAMETER: A high value of χ for chemically dissimilar polymers indicate unfortunate mixing. For chemically identical polymers having small cohesive energy difference χ value is anticipated to be small. However, there is a unplanned of demixing for satisfactorily long chains. Architectural and geometric differences between the components prevent them in a mixture from dwell in the same configurations knowledgeable in the pure phase. Polymer field theory can predict that a mismatch in chain arduousness for chemically similar mechanisms may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K The value of x decreases exponentially with increase in temperature. This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e., slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

MIXING ENERGY: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature. The temperature is varying from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus: Figure 5 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of polypyrole.

Shear modulus: Figure 6 shows that the shear modulus of the composite increases linearly with increase in mass fraction of polypyrole.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of polypyrole.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 4 shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of polypyrole.

Brittle fracture stress: Figure 9 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of polypyrole

Heat capacity: Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of polypyrole

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of polypyrole.

Dielectric constant: As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of polypyrole.

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with increase in mass fraction of polypyrole.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite decreases linearly with increase in mass fraction of polypyrole.

Permeability of gases: Lower permeability indicates longer time lag for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite decreases with increase in mass fraction of polypyrole. Figure 16 shows that the permeability of nitrogen through the composite decreases with increase in mass fraction of polypyrole.Figure 17 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of polypyrole. Thus, the results indicated that an increase in polypyrole fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSION

The possibility of use of polypyrole and polyvinyl fluoride to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of polypyrole. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of polypyrole. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases decreased with increase in mass fraction of polypyrole. Usually

components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

ACKNOWLEDGEMENT

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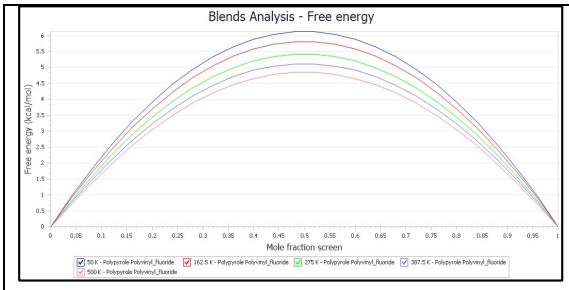
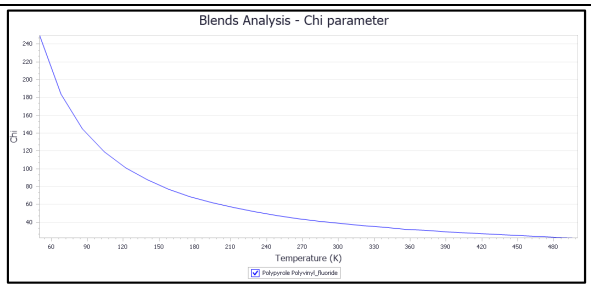


Figure 1. Free energy change with mole fraction at different temperatures



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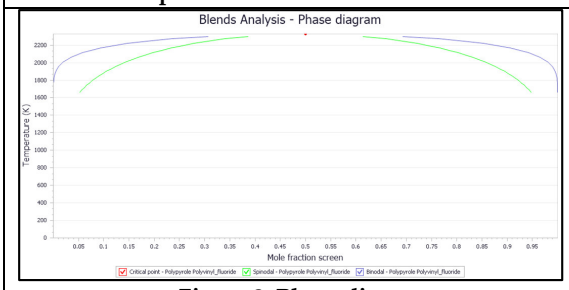
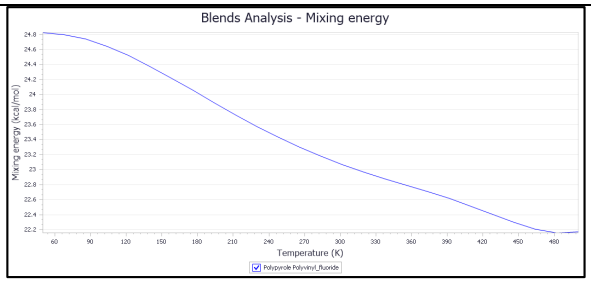


Figure 3. Phase diagram



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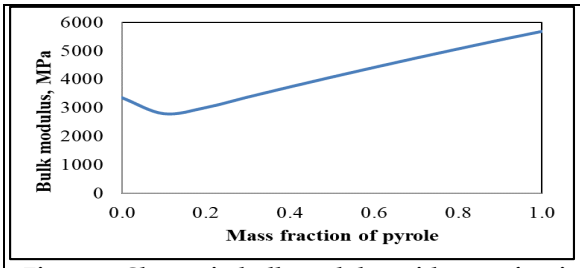


Figure 5. Change in bulk modulus with mass fraction of polypyrole

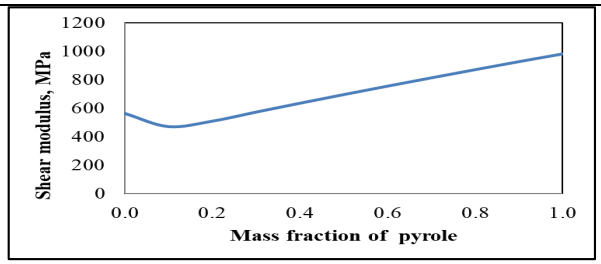


Figure 6. Change in shear modulus with mass fraction of polypyrole

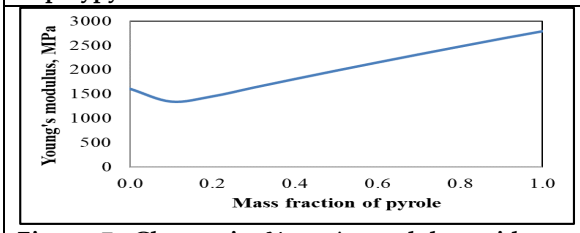


Figure 7. Change in Young's modulus with mass fraction of polypyrole

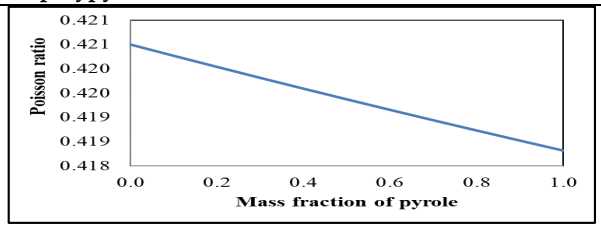


Figure 8. Change in Poisson modulus with mass fraction of polypyrole

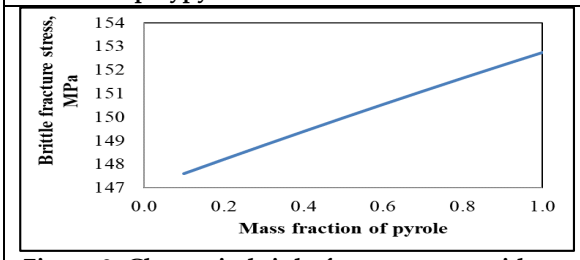
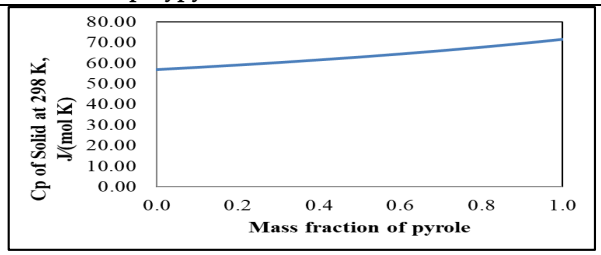


Figure 9. Change in brittle fracture stress with mass fraction of polypyrole



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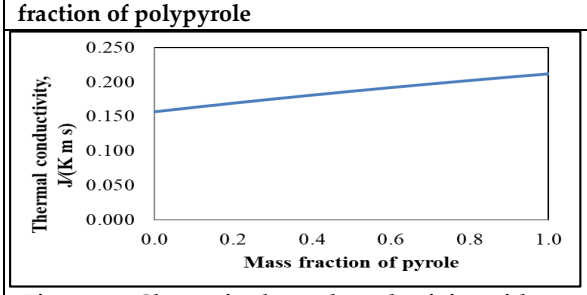

Figure 11. Change in thermal conductivity with mass fraction of polypyrole

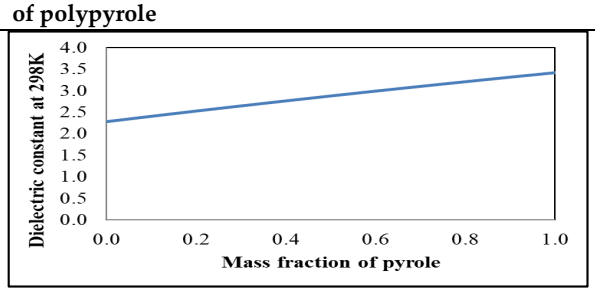

Figure 12. Change in dielectric constant with mass fraction of polypyrole

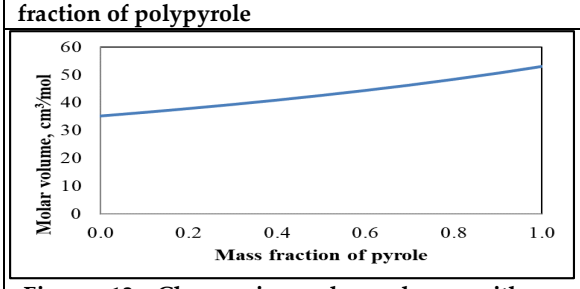

Figure 13. Change in molar volume with mass fraction of polypyrole

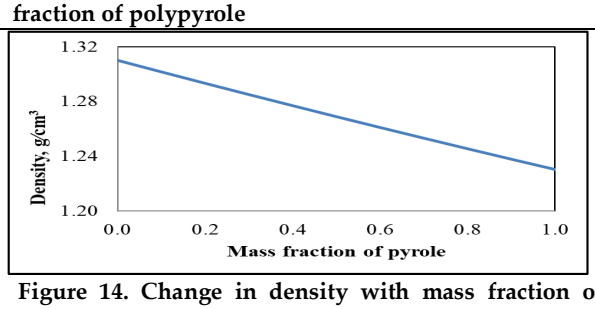

Figure 14. Change in density with mass fraction of polypyrole

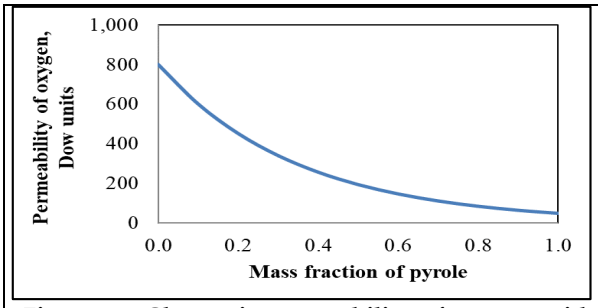

Figure 15. Change in permeability of oxygen with mass fraction of polypyrole

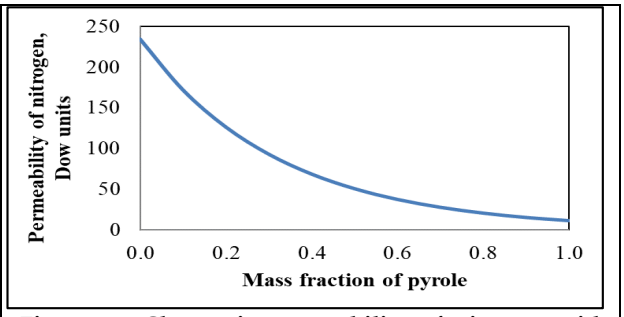

Figure 16. Change in permeability of nitrogen with mass fraction of polypyrole

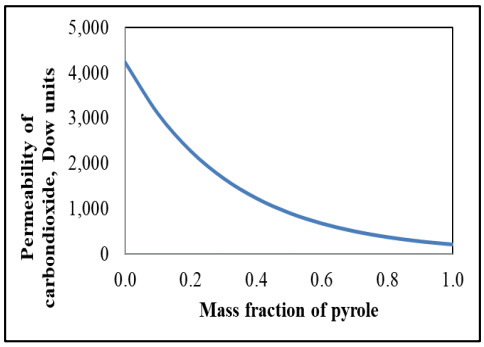

Figure 17. Change in permeability of carbon dioxide with mass fraction of polypyrole

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RESEARCH ARTICLE

In silico Analysis of Polyvinyl Amide and Polyvinyl Chloride Compatibility in a Blend

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ABSTRACT

Two or more components are mixed to form a blend. Using Biovia Materials studio we studied the compatibility of polyvinyl amide and polyvinyl chloride. On the basis of free energy of mixing, chi parameter, phase diagram, and mixing energy the compatibility of two components was indicated. Both the components were indicated at low and high temperature and both are compatible. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. Based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture the mechanical properties of components were studied. The results indicated that the values of all the properties increased with an increase in the mass fraction of vinyl amide. The resultant blend contains different composites were studied through heat capacity, thermal conductivity, and dielectric constant.The results indicated that all those parameters increased with an increase in the mass fraction of vinyl amide.Through permeability properties of the composition of the blend was analyzed.With an increase in the molar fraction of vinyl amide decrease in molar volume and density. Based on the permeability of oxygen, nitrogen, and carbon dioxide the permeability properties of the components were calculated. The results showed that with an increase in the molar fraction of vinyl amide decrease in all the permeability properties of all the gases. This analysis will help to find results without a laboratory experiment and this is a less time consuming and low-cost process.

Keywords: Blend, polyvinyl amide, and polyvinyl chloride, *In silico.*

INTRODUCTION

Two polymers or copolymers are mixed to form a polymer blend. It is the process of imparting specific properties to the polymer. Its help to reduce material cost enhanced ozone resistance, improved modulus, and hardness, etc. Now a day 30-40% of plastic is used for making polymer blend. It reduces the investment cost during new material design. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Biodegradable polymer enhances the mechanical properties of the component. Blending helps to get desired properties of the lowest cost, improve solvent and chemical resistance, improve flame resistance. Researchers are working on fireproof material. Researchers are synthesized thin type composite materials but it will have high strength which helps to enhance fuel efficiency in the transportation field. Now a day's composite materials used in many applications in which lightweight and high specific modulus and strength are critical issues.The degree of control over materials properties that is typified by the hybrid composite is transforming engineering design. To construct bridges, light rail transit, mining, and tunneling, retaining walls, and other waterside buildings different techniques were developed by the use of composite materials. The trial and error method is used to prepared blends and this method is less time-consuming. So the researcher is working to develop new blends through Biovia software material studio.Polyvinyl chloride (PVC) is prepared by polymerization of vinyl chloride. It is used for making pipes, handbags, helmets, raincoats, etc.

MATERIALS AND METHODS

Softwares of biovia material studio were used for the analysis. Different machine learning techniques were also used for the analysis.The biovia software contains different machine techniques that were used for this analysis. By the use of materials studio polyvinyl amide and polyvinyl chloride were prepared for the analysis. The blends->calculation menu of Materials studio was used for the optimization of structure of the both components.During calculation one component was used as a base and another was used as a screen means polyvinyl amide was used as a base and polyvinyl chloride was used as a screen. After calculation, various data were produced by the blends->analysis menu of Materials studio.The generated data were analyzed and then the compatibility of both the components results in a blend was also analyzed. Using the synthia menu of materials studio the structures of polyvinyl amide and polyvinyl chloride were obtained which were running for different weight fractions of the components.In the tabular form, different properties of the components were displayed. The values were used to plot graphs between a mole fraction of vinyl amide and mechanical properties of the components.

RESULTS AND DISCUSSION

The use of component polyvinyl amide and polyvinyl chloride which results in a blend were analyzed through Biovia materials studio. Using BIOVIA Materials Studio Synthia structure, properties of the components were analyzed. This method is a very fast and easy process to use. The properties of the complex polymer as well as small molecules were also analyzed by group additive methods.These methods are depending upon the database group of contribution. The polymer containsthe different contributions of different monomers these contributions can be calculated using Synthia of material studio. By the use of Synthia we can get topological information about the polymers. Through Biovia material studio we can find the contribution of polymer and topological information about the polymer.

Free energy of mixing:A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. We know that in an ideal system $\Delta G=\Delta H-T\Delta S$, but this equation can also be applied to the thermodynamics of mixing and solved for the enthalpy of mixing so that it reads

$\Delta H_{mix}=\Delta G_{mix}+T\Delta S_{mix}$

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m = Gibb's\ free\ energy\ of\ mixing$

$\Delta H_m = Enthalpy\ of\ mixing$

$\Delta S_m = Entropy\ of\ mixing$

$T = Absolute\ temperature$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with an increase in temperature (upto 275 K) as evident from Eq. 1. The results

indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows very good compatibility between polyvinyl chloride and polyvinyl amide with a negative value of mixing energy,which may lead to form a particular shape with significantly high effort.

Chi parameter: The polymer-solvent interaction parameter (χ) depends on the various factors i.e temperature, monomer concentration. The polymer-solvent interaction parameter (χ) can be calculated from the Flory-Rehner equation by using swelling data of hydrogels at different temperatures. The Flory-Huggins χ parameter describes mixing free energy and helps to explain the phase behavior of polymer blends.The χ values should be located around 0.5. Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with an increase in temperature.This agrees with the free energy of mixing for the blend.

Phase diagram: The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility: When the system enters from a single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase-separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

Mixing energy: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when the temperature increases the mixing energy increases to the highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with an increase in temperature.The temperature is varying from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus: It is defined as the ratio between volumetric stress and volumetric strain.It is denoted by K. Figure 5 shows that the bulk modulus of the composite increases linearly with increase in the mass fraction of vinyl amide

Shear modulus: It is defined as the ratio of shear stress and shear strain. It is denoted by G.Figure 6shows that the shear modulus of the composite increases linearly with increase in the mass fraction of vinyl amide.

Young's modulus: It is defined as the ratio between tensile stress and tensile. Figure 7shows that Young's modulus of the composite increases linearly with an increase in the mass fraction of vinyl amide.

Poisson ratio: It is defined as the ratio between lateral strain and longitudinal strain. When we take a negative ratio of lateral strain and lateral strain then we get Poisson's ratio.Figure: 8shows that the Poisson ratio of the composite increases linearly with an increase in the mass fraction of vinyl amide.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs.Figure 9shows that the brittle fracture stress of the composite increases linearly with an increase in the mass fraction of vinyl amide.

Heat capacity: It is the amount of heatrequired to raise the temperature of the one-unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with an increase in the mass fraction of vinyl amide.

Thermal conductivity: It is defined as the ability of a material to conduct heat.The value of thermal conductivity depends upon solid, liquid, and gas. Figure11shows that the thermal conductivity of the composite increases linearly with an increase in the mass fraction of vinyl amide.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with an increase in the mass fraction of vinyl amide

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with an increase in the mass fraction of vinyl amide.

Density: Increase in density indicates a decrease in porosity. A higher porosity will enhance the surface area making it suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite decreases linearly with an increase in the mass fraction of vinyl amide.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates a longer time lag for the gas to pass through the membrane. Figure 15 shows that the permeability of oxygen through the composite decreases with an increase in the mass fraction of vinyl amide.

Figure 16 shows that the permeability of nitrogen through the composite decreases with an increase in the mass fraction of vinyl amide. Figure 17 shows that the permeability of carbon dioxide through the composite decreases with an increase in the mass fraction of vinyl amide.Thus, the results indicated that an increase in vinyl amide fraction reduces the permeability of different gases. The rate of permeability might be influenced by the molecular weight of the gases.

Glass Transition Temperature: The temperature at which polymer converts hard to soft state is called Glass Transition Temperature (Tg). Figure 18 shows a change in glass transition temperature with a mass fraction of vinyl amide.

Refractive Index: When a ray of light enters a medium it changes its direction.As can be seen from Figure 19, the refractive index of composite decreases with an increase in the mass fraction of vinyl amide.

CONCLUSIONS

The homogeneous mixture of polyvinyl amide and polyvinyl chloride formed a blend that was studied under Biovia Materials Studio. Based on the free energy of mixing, chi parameter, and mixing energy the compatibility of both components was analyzed. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio, and brittle stress fracture. The resultant value of mechanical properties increased with an increase in the mass fraction of vinyl amide. The composition of the blend was analyzed through heat capacity, thermal conductivity, and dielectric constant. The results indicated that all three parameters increased with an increase in the mass fraction of vinyl amide. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with an increase in vinyl amide fraction. The permeability properties of the composite were studied based on the permeability of oxygen, nitrogen, and carbon dioxide. The results indicated that the permeability for all the gases decreased with an increase in the mass fraction of vinyl amide. The components present in the blend are detected experimentally. From the analysis, it was

concluded that the components present in the blend are determined through software without using any material. Through this modern technology, we can save money and time.

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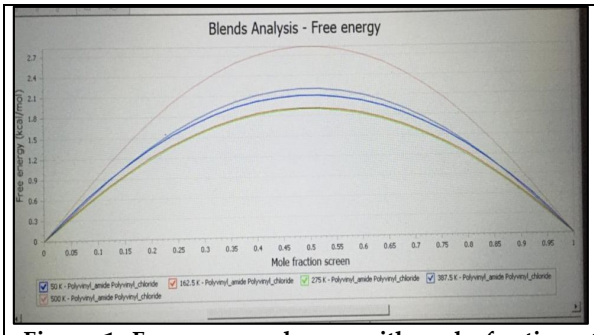

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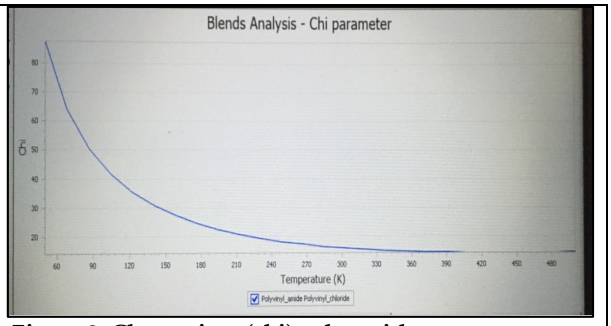

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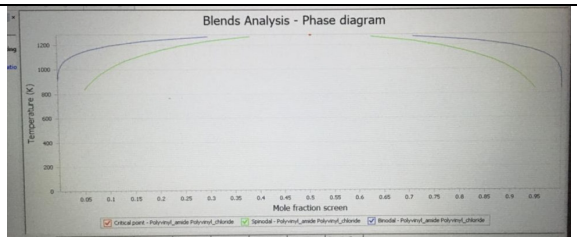
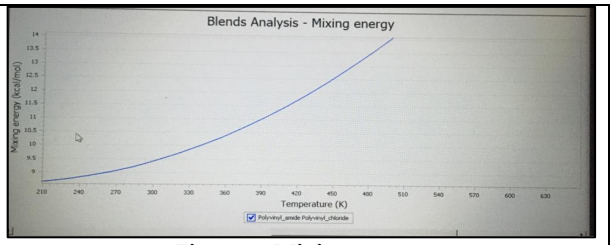


Figure 3. Phase diagram



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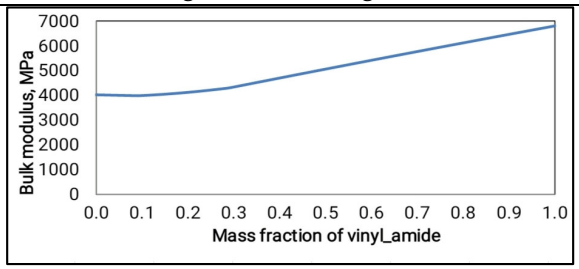

Figure 5. Change in bulk modulus with the mass fraction of Vinyl amide

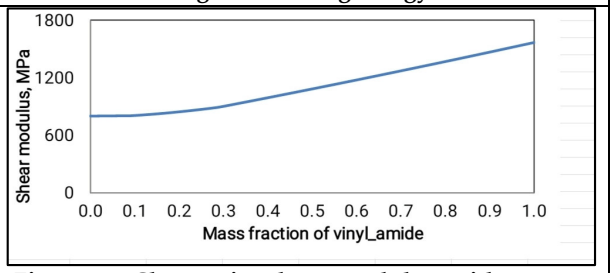

Figure 6. Change in shear modulus with a mass fraction of vinyl amide

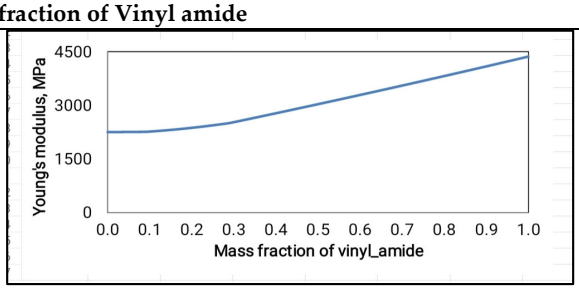

Figure 7. Change in Young's modulus with a mass fraction of vinyl amide

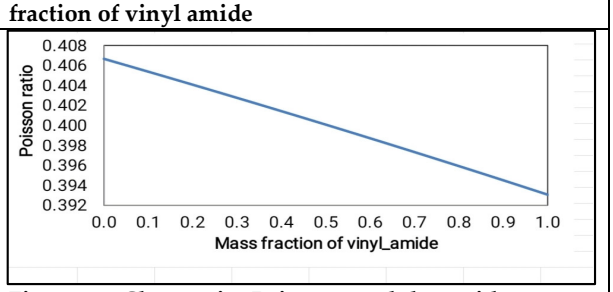

Figure 8. Change in Poisson modulus with a mass fraction of vinyl amide

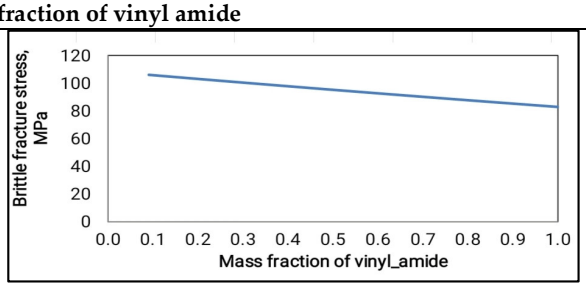

Figure 9. Change in brittle fracture stress with a mass fraction of vinyl amide

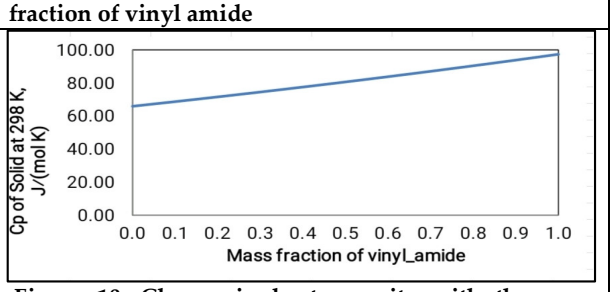

Figure 10. Change in heat capacity with the mass fraction of vinyl amide

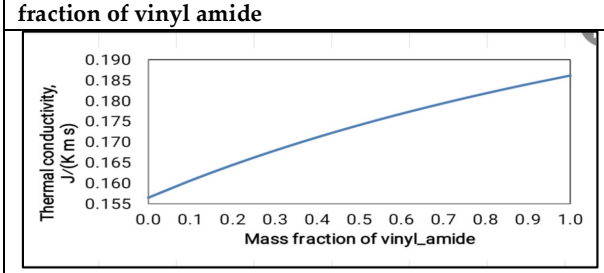

Figure 11. Change in thermal conductivity with the mass fraction of vinyl amide

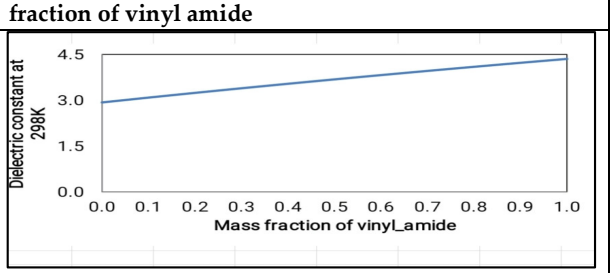

Figure 12. Change in dielectric constant with the mass fraction of vinyl amide

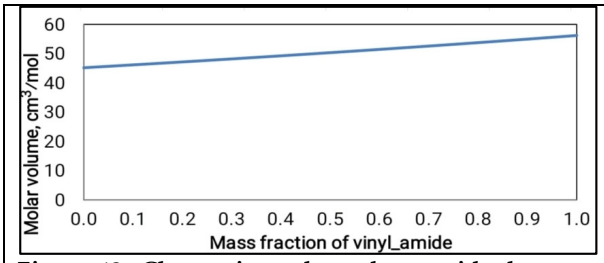

Figure 13. Change in molar volume with the mass fraction of vinyl amide

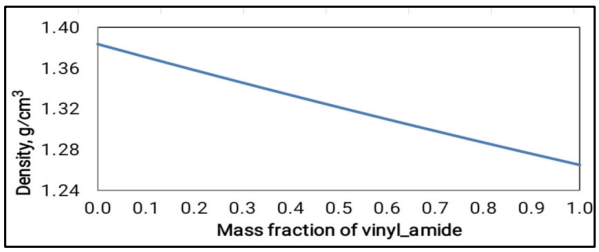

Figure 14. Change in density with the mass fraction of vinyl amide

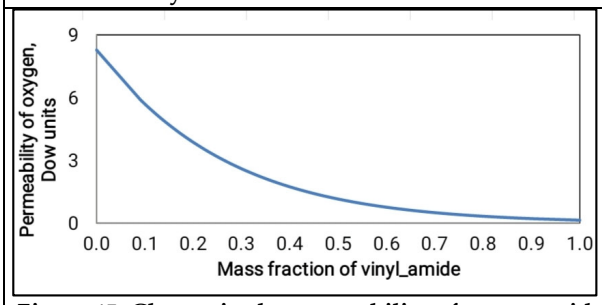

Figure 15. Change in the permeability of oxygen with a mass fraction of vinyl amide

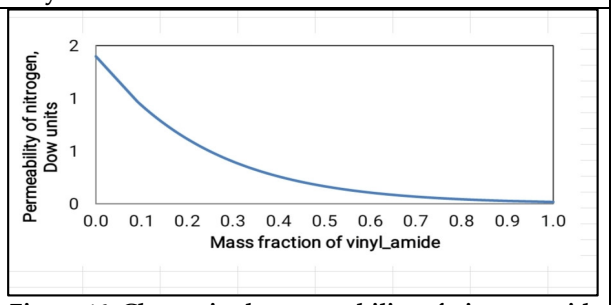

Figure 16. Change in the permeability of nitrogen with a mass fraction of vinyl amide.

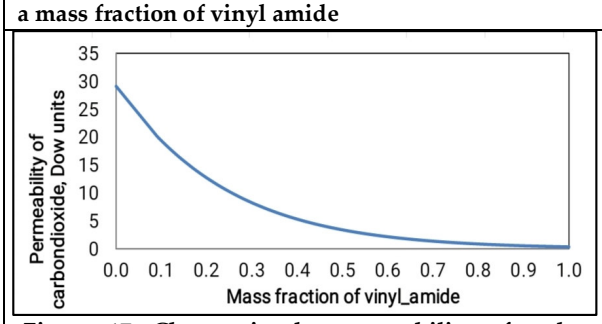

Figure 17. Change in the permeability of carbon dioxide with a mass fraction of vinyl amide

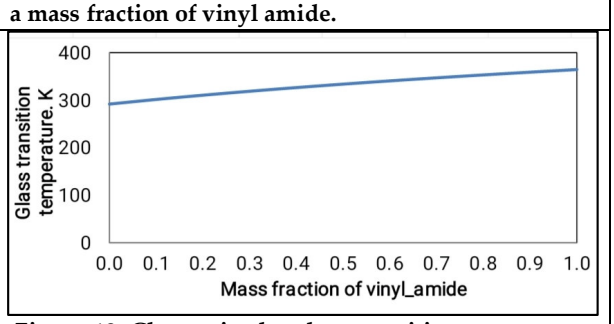

Figure 18. Change in the glass transition temperature with the mass fraction of vinyl amide

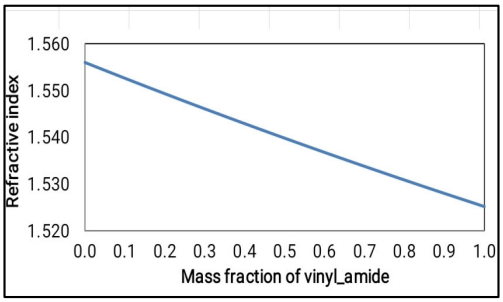

Figure 19. The graph between the refractive Index and the mass fraction of vinyl amide.

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RESEARCH ARTICLE

In silico Analysis of Prevention of COVID-19 by Blocking 6lvn Protein using *Adhatoda vasica*

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researcher are working seriously to develop drugs or vaccine against COVID-19. This docking was done by Biovia Discovery studio to analyze the interaction of phytochemicals of Aloe-vera with 6lvn of NSP3 protein. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like Aloe-emodin. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of COVID-19.

Keywords: *Aloe emodin* , *Aloe vera*, Biovia, Discovery studio, COVID-19, Phytochemicals

INTRODUCTION

A novel corona virus (nCoV-2019) emerges with a unique characteristic of human-to-human transmission on December 2019 in Wuhan province of China [1] and cause severe acute respiratory syndrome (SARS) .This infection has marked as dead-threatening to numerous people around the world within short period of time. On 30th January, 2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2].The actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. Therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as

phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc. [4,5]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry.Among different medicinal plants, Aloe vera (*Aloe barbadensis miller*) plant has been known for its medicinal properties. [6,7]. All these have anti-inflammatory activity and lupeol additionally has pain relieving properties. The main objective of this article to identify the phytochemicals of *Aloe barbadensis miller* responsible for inhibiting COVID-19.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that Aloe vera (*Aloe barbadensis miller*)contains aloe-emodin,anthraquinone,cinnamic acid,salicylic acid,aloin and glucomannan were considered for the study. etc. It has been reported that Liliaceae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19 [8].

Papain-like protease (PLpro) of COVID-19: COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that NSP3 (PDB Id **6lvn**) is involved in replication of virus. By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of Aloe vera (*Aloe barbadensis miller*) were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value show the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of ADP ribose phosphatase of NSP3 of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b) small difference between -CDOCKER energy and -CDOCKER energy interaction. High positive values of C-Docker energy are 8.46722 and the difference with Cdocker interaction energy is 4.22378. It is also represented the difference in energy which are aloe-emodin, anthraquinone, cinnamic acid, salicylic acid,aloin and glucomannan. From these findings it is found that Aloe-emodin can effectively deactivate 6vxs, thereby interrupting viral replication.On the other hand, anthraquinone shows the second highest affinity towards 6lvn of COVID-19 and therefore, it has the potential to deactivate the enzyme. cinnamic acid and salicylic acid,can less effectively inhibit the viral replication as negative -CDocker energy but shows positive -

CDocker interaction energy. Thus, the key phytochemicals Aloe-emodin can prevent COVID-19 caused by 6lvn of virus.

CONCLUSIONS

It was reported that *Aloe barbadensis miller* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals aloe-emodin can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with 6lvn of COVID-19. It was found that Aloe-emodin of *Aloe barbadensis miller* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The other phytochemicals of this plants like anthraquinone,cinnamic acid,salicylic acid,aloin and glucomannan were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals aloe-emodin provide the medicinal importance to *Aloe barbadensis miller* that can act against COVID-19

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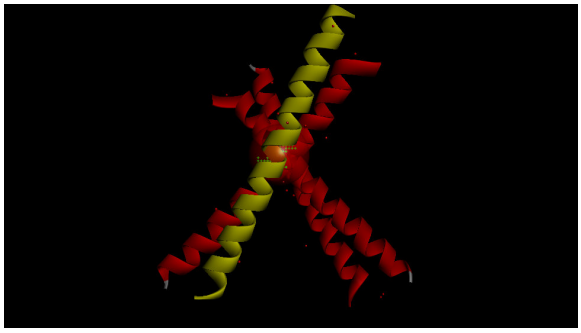

Figure 1. Receptor binding site of 6lvn of COVID-19

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RESEARCH ARTICLE

In silico Analysis of Prevention of COVID-19 by Blocking nCoV HR2 Domain (6lvn) using *Adhatoda vasica*

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researchers are working seriously to develop drugs or vaccine against COVID-19. The main aim of this study to identify the phytochemicals extracts from the plant *Adhatoda vasica* which can deactivate 6lvn of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of *Adhatoda vasica* (Vasak) were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like Kaempferol. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that covid-19virus to human cell.

Keywords: COVID-19, Kaempferol 6lvn, Biovia, *Adhatoda vasica* .

INTRODUCTION

A novel corona virus (nCoV-2019) emerge as contagious disease for human on the month of December,2019 Wuhan province of China [1] and cause severe acute respiratory syndrome (SARS). On 30th January,2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. Situation is getting worse with this viral infection and the mortality graph approaches to upward.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [4]. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. Various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir have effect on treatment of COVID. The less effective of these drugs motivated to examine the restraint of COVID-19 protease by

Indian herbal plants [5]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc.[6]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry. The main objective of this article to identify the phytochemicals of *Adhatoda vasica* responsible for inhibiting COVID-19 6lvn) by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software ((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Adhatoda vasica* contains vasicin, vasicinone, peganin, quercetin, kaempferol, etc. It has been reported that Acanthacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[7,8].COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that 6lvn is involved in replication of virus.

By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Adhatoda vasica* were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value shows the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of 6lvn (nucleocapsid protein N-terminal RNA binding domain) of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b) small difference between -CDOCKER energy and -CDOCKER energy interaction. High positive values of C-Docker energy are 4.27821 and the difference with Cdocker interaction energy 5.34789 are presented in table-I.TableI also represented the difference in energy which are kaempferol, vasicinone, vasicine, peganine. From these findings it is found that Kaempferol can effectively deactivate 6lvn, thereby interrupting viral replication. Vasicine, vasicinone, peganine can less effectively inhibit the viral replication as negative -CDocker energy but shows positive -CDocker interaction energy. Thus, the key phytochemicals Kaempferol can prevent COVID-19 caused by 6lvn of virus.

CONCLUSIONS

It was reported that *Adhatoda vasica* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like Kaempferol can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with 6lvn of COVID-19. It was found that Kaempferol of *Adhatoda vasica* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The following phytochemicals like Vasicine, vasicinone, peganine were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals Quercitin provide the medicinal importance to Kaempferol that can act against COVID-19.

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Table 1. C-Docking score of different phytochemicals with 6lvn of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Kaempferol	4.27821	9.6261	5.34789
2	Peganine	-6.38276	8.47076	14.8535
3	Vasicine	ERROR	ERROR	ERROR
4	Vasicinolone	ERROR	ERROR	ERROR
5	2-acetyle benzyle	ERROR	ERROR	ERROR

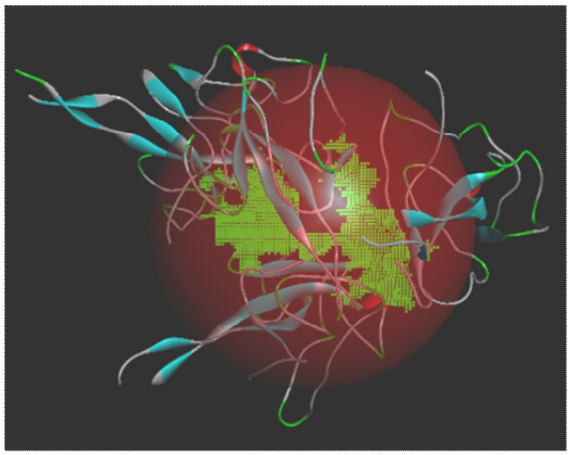

Figure 1. Binding site of 6lvn

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researchers are working seriously to develop drugs or vaccine against COVID-19. The main aim of this study to identify the phytochemicals extracts from the plant *Adhatoda vasica* which can deactivate 6lvn of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of *Adhatoda vasica* (Vasak) were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like Quercitin. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of COVID-19.

Keywords: COVID-19, 6lvn, Biovia, *Adhatoda vasica*.

INTRODUCTION

A novel corona virus (nCoV-2019) emerge as contagious disease for human on the month of December,2019 Wuhan province of China[1] and cause severe acute respiratory syndrome (SARS). On 30th January, 2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. Situation is getting worse with this viral infection and the mortality graph approaches to upward.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [4]. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. Various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir have effect on treatment of COVID. The less effective of these drugs motivated to examine the restraint of COVID-19 protease by

Indian herbal plants [5]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc.[6]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry. The main objective of this article to identify the phytochemicals of *Adhatoda vasica* responsible for inhibiting COVID-19 6lvn) by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software ((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Adhatoda vasica* contains vasicin, vasicinone, peganin, quercetin, kaempferol, etc. It has been reported that Acanthacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[7,8].COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that 6lvn is involved in replication of virus.

By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Adhatoda vasica* were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value shows the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of 6lvn (nucleocapsid protein N-terminal RNA binding domain) of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b) small difference between -CDOCKER energy and -CDOCKER energy interaction.

High positive values of C-Docker energy are11.5858 and the difference with Cdocker interaction energy 2.1942 are presented in table-I.TableI also represented the difference in energy which are kaempferol, vasicinone, vasicine, peganine. From these findings it is found that Quercitin can effectively deactivate 6lvn, thereby interrupting viral replication. Vasicine, vasicinone, peganine can less effectively inhibit the viral replication as negative -CDocker

energy but shows positive -CDocker interaction energy. Thus, the key phytochemicals Quercitin can prevent COVID-19 caused by 6lvn of virus.

CONCLUSIONS

It was reported that *Adhatoda vasica* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like quercitin can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with 6lvn of COVID-19. It was found that quercitin of *Adhatoda vasica* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The following phytochemicals like Vasicine, vasicinone, peganine were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals Quercitin provide the medicinal importance to *Adhatoda vasica* that can act against COVID-19.

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Table 1. C-Docking score of different phytochemicals with 6lvn of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Quercitin	11.5858	13.78	2.1942
2	Vasicinone	-2.29384	12.4829	14.7767
3	Peganine	-6.38276	8.47076	14.8435
4	Vasicine acetate	failed	failed	failed
5	Vasicinolone	failed	failed	failed

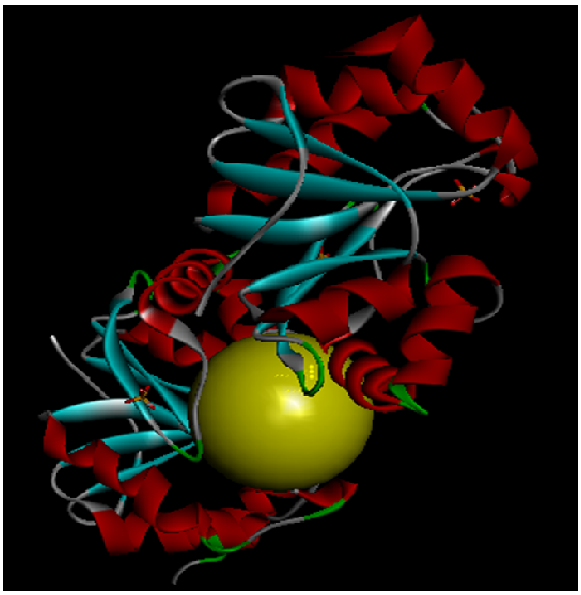

Figure 1. Binding site of 6lvn

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties Oxyethylene and Oxymethylene Suitable Compatibility in a Blend

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ABSTRACT

A blend is generally formed by combining two or more polymer. The compatibility of Oxyethylene and Oxymethylene were studied to form a miscible blend using Biovia Materials Studio. The results show that the values of all the properties changes with increase in mass fraction of Oxoethylene. The composition of the blend with respect to heat capacity, thermal conductivity and dielectric constant were thoroughly studied. The results indicated that all the three parameters also changes with increase in mass fraction of Oxoethylene, The components for a blend are usually identified experimentally. Thus in silico study will help to determine the components of a blend without performing laboratory experiments saving materials, money and time.

Keywords: Blend, in silico, Oxyethylene, Oxymethylene

INTRODUCTION

In this days polymer have more values and it have also used in plenty amounts. In the modern society it is use for many reasons and it is all around us. Polymers are being used in almost every area starting from home to industries like grocery bags, soda and water bottles, textile fibers, phones, computers, food packing, auto parts etc [1]. Most of the natural polymers are formed from monomers with the removal of water by condensation process. Synthetic polymers are human made polymers. They are generally prepared in the laboratories, for e.g.:- PVC, Styrene etc. The most common types are nylon and polythene is used in our everyday life [2]. Low density polythene polymer is the most common kind of synthetic polymer being used in household products. Most of some common uses of synthetic polymers include plastic containers of all shapes and sizes. They are lightweight and economically less expensive than common traditional containers .Some common polymers are very demanding now days [3]. These are produced by adding of many monomer molecules held together by strong covalent bonds.Polymer composites are a kind of high performance and versatile materials formed from `a combination of different polymers or co-polymers in which one of the component is taken as matrix(base)[4]. The combination of these components results in a product with

unique mechanical and thermal properties that are infeasible to be achieved with a single material.. These two phases are usually composed of organic polymers as the matrix and fibre as the reinforcement. Generally, fibre materials have high strength and stiffness compared to those of the base material and thus making the fibre the widely used component in polymer composites. On the other hand, when force is applied on the fibre, the matrix distribute the load among the fibre evenly, which in turn increases the mechanical properties of the polymer composites. A numerous mechanical tests and testing instruments with standardized and non standardized testing methods have been developed to determine the mechanical properties of polymer composites. Tensile properties is one of the key factor in determining the performance of polymer composites materials. The ultimate elongation is 0.32-2.5% where the lower elongation corresponds to the higher stiffness and vice-versa. Carbon fibres don't absorb water and are resistant's too many chemical solutions. They withstand fatigue excellently and neither corrodes nor show any creep or relaxation [5].Polymer composites with functionalised nano particles are a growing group of materials whose properties can be controlled not only through the kind and the size of nano materials but also via its fictionalisation. Nanoparticles have been extensively used in biomedical application such as tissue engineering, drug therapies, cellular therapies because of their unique interaction by mimicking native tissue structure and properties[6]. Usually blends are prepared by trial and error method and this technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs.Polyoxymethylene or polyformaldehyde is also known as acetal. It has high strength, hardness, rigidity to -40C. Because of its crystallised composition it is intrinsically opaque white but a wide variety of colours are also available [8].

MATERIALS AND METHODS

SOFTWARE USED: For the analysis of compatibility of the blend, Materials studio module of Biovia software (Dassault Systemes of France) was used. It utilizes machine learning techniques and standard algorithms for predicting the level of interaction

METHODOLOGY: The structure of Oxyethylene and Oxymethylene were prepared using the build menu of Materials Studio. From the built polymer option and homopolymer was selected shoeing a number of desirable polymer. Then the structure of the components were optimized in blends-calculation menu of Materials studio and then Oxyethylene was used as the base which was taken in large quantity and Oxymethylene was used as screen which was taken in small quantity. After calculation, the blends->analysis menu of Materials studio was used to generate various data that includes chi parameter, free energy, mixing energy, phase diagram. The data were analyzed and the compatibility of the components to form a blend was predicted depending upon the data. For synthia calculation the structures of Oxyethylene and Oxyethylene were then fed to the Materials Studio by selecting co-polymers and then adding up our polymer within the limit 0-1. It was then run for different weight fractions of the components. The various properties of the composite were displayed in a tabular form. The values obtained from the tabular form were fed to plot graphs to identify the effect of weight fraction of Oxyethylene on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of Oxyethylene and Oxyethylene as potential components of a blend was analyzed using Biovia Materials Studio. In this work the use of polyoxyethylene and poly Oxymethylene as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are very fast and convininet for use. Even without proper understanding of interactions among atoms, we can calculate various property. However, the principal shortcoming of these methods is their dependence

upon a database of group contributions. Thus, the property of that polymer cannot be calculated if group ccontribution of a group is not known.To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties of any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulphur, fluorine, chlorine, bromine can be estimated.

Heat capacity : The amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase is termed as heat capacity. Figure 1 shows that with increase in mass fraction of oxyethylene the heat capacity (Cp) of the composite increases.

Thermal conductivity : The correlation between heat flux per unit area and temperature gradient is described as thermal conductivity. It refers to the intrinsic heat transfer ability of a material. Fig.2 shows that the thermal conductivity of the composite decreases linearly with increase in mass fraction of oxyethylene

Dielectric constant : It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant decreases linearly From fig. 3 it was observed that with increase in mass fraction of oxyethylene dielectric constant of the composite decreases with increase of mass fraction of ox ethylene.

CONCLUSIONS

The use of poly oxyethylene and Oxymethylene to form a possible homogeneous blend was explored using Biovia Materials Studio. The results show that the values of all the properties changes with increase in mass fraction of Oxoethylene. The composition of the blend with respect to heat capacity, thermal conductivity and dielectric constant were thoroughly studied. The results indicated that all the three parameters also changes with increase in mass fraction of Oxoethylene, The components for a blend are usually identified experimentally. Thus in silico study will help to determine the components of a blend without performing laboratory experiments saving materials, money and time.

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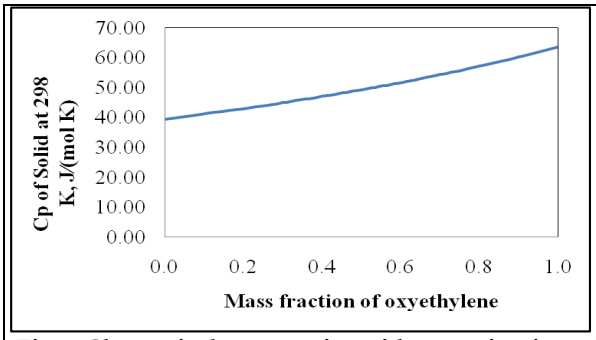

Fig.1. Change in heat capacity with mass fraction of oxyethylene

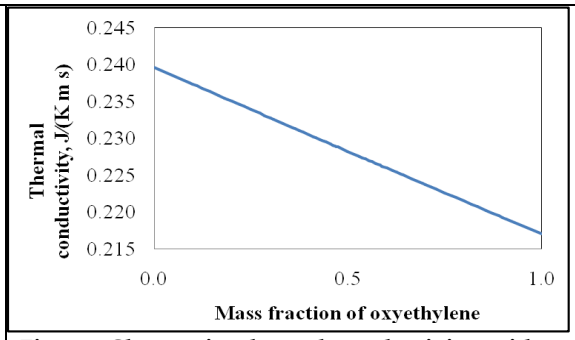

Fig. 2. Change in thermal conductivity with mass fraction of oxyethylene

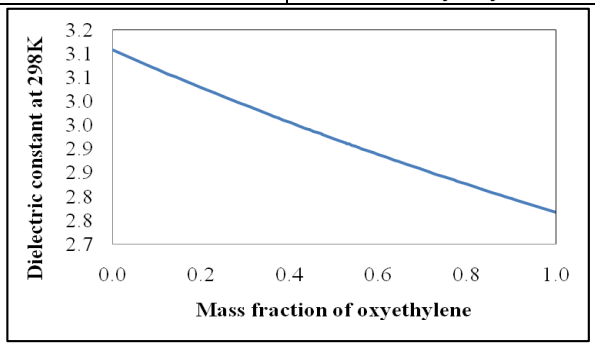

Fig. 3. Change in dielectric constant with mass fraction of oxyethylene

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RESEARCH ARTICLE

In silico Analysis of Urea and Oxo Phenyl Compatibility in a Blend

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ABSTRACT

Combination of two or more components results in the formation of a blend. The compatibility of urea and oxo phenyl was studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram and mixing energy. The results indicated that the pair can become compatible at both low and high temperature. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of Urea. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of Urea. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in Urea fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of Urea. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low-cost process.

Keywords: Blend, *In silico*, Urea, Oxo phenyl

INTRODUCTION

Blends or composites are formed with combination of more than one component where components do retain their identity in the mixture. As it is very difficult to find multiple properties in a single material, it is advisableto combine different components thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materialshave drawn attention. Biodegradable polymers- natural fiber composites have been reported to enhance mechanical properties and water

resistance. Researchers are working on fire retardant/fire proof materials. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method andthis technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio) has been used to identify compatible pairs. Urea (carbamide), with chemical formula $CO(NH_2)_2$ having two $–NH_2$ groups linked by a carbonyl functional group. Urea finds its role in the animal metabolism with nitrogen-containing compounds and present in the urine of mammals as nitrogen containing group. Phenylglyoxylic acid with the formula $C_6H_5C(O)CO_2$ having the conjugate base, known as benzoylformate is the substrate of benzoylformate decarboxylase, a thiamine diphosphate-dependent enzyme:

Benzoylformate + H^+ ⇌ Benzaldehyde + CO_2

It is a colourless solid with a melting point of 64–66 °C and is moderately acidic (pKa = 2.15).

MATERIALS AND METHODS

SOFTWARE USED: In this study, Biovia software (Dassault Systemes of France) with Materials studio module was used for analysis. Machine learning techniques and standard algorithms were used to predict the point of interaction.

METHODOLOGY: Urea and Oxo phenyl were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. Urea was used as the base and Oxo phenyl was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of Urea and Oxo phenyl were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of oxophenyl on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of Urea and Oxo phenyl as potential components of a blend was analyzed using Biovia Materials Studio.In this work the use of Urea and Oxo phenyl as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a number of polymer properties. Group additive methods were used for many years to evaluate the properties of polymers as well as small molecules. AS these methods are very simple to analyses the properties, so they are of greatest utility when a rapid estimate of a property is required without having an atomistic interactions that give rise to it. However, the disadvantages of these methods is that with numerous data base requirement .For this reason the property of that polymer cannot be calculated if the group present in that particular polymeric compound cannot be quantitatively identified and estimated. To modify this condition, a scheme implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. However properties may be identified for any

polymer having the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

FREE ENERGY OF MIXING: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m = Gibb's free energy of mixing$

$\Delta H_m = Enthalpy of mixing$

$\Delta S_m = Entropy of mixing$

$T = Absolute temperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to ahomogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between Urea and Oxo phenyl with negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

CHI PARAMETER: The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus, a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2 shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature. This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: The compatibility of binary mixtures can be obtained from phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. It has been seen that the different degree of miscibility which may be due to three different region . The three region are as follows :

a. The single-phase miscible region existed above the critical temperature of around 750 K which indicates a single phase blend can be formed at a high temperature (higher than 750 K).

b. The area between binodals and spinodals is the fragmented metastable

c. The two-phase separated regions of immiscibility are bordered by the spinodals.

The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region.

Again it has been known that when the system enters from single-phase to the metastable region, the phase region , separation usually occurs by slow nucleation followed by growth of the phase separated domains known as resembling crystallization .On the other hand, when the system moves from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition

MIXING ENERGY: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value after that when again temperature increases the mixing energy becomes decreases and again further increases with increase in temperature.The temperature is vary from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of Urea.

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6 shows that the shear modulus of the composite increases linearly with increase in mass fraction of Urea.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 7 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of Urea.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8 shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of Urea.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of Urea.

Heat capacity: It is the amount of heatrequired to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of Urea

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of Urea.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12 shows that the dielectric constant of the composite increases with increase in mass fraction of Urea

Molar volume: It is the volume occupied by one mole of a substance. Figure 13 shows that the molar volume of the composite decreases linearly with increase in mass fraction of Urea.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14 shows that the density of the composite decreases linearly with increase in mass fraction of Urea

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the mebrane. Figure 15 shows that the permeability of oxygen through the composite decreases with increase in mass fraction of Urea.

Figure 16 shows that the permeability of carbon dioxide through the composite decreases with increase in mass fraction of Urea. Thus, the results indicated that an increase in acrylic acid fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of urea and oxo phenyl to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of Urea. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of Urea. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases decreased with increase in mass fraction of Urea. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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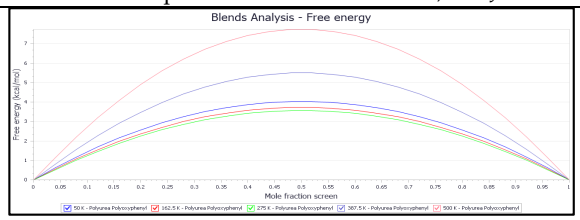

Figure 1. Free energy change with mole fraction of Urea at different temperatures

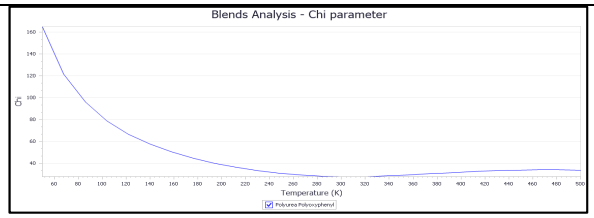

Figure 2. Change in χ (chi) value with temperature

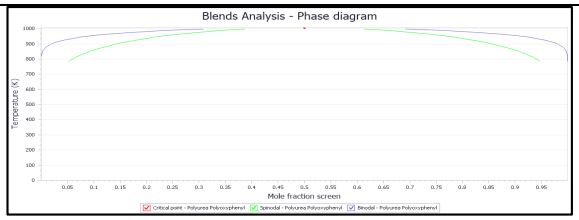

Figure 3.Phase diagram

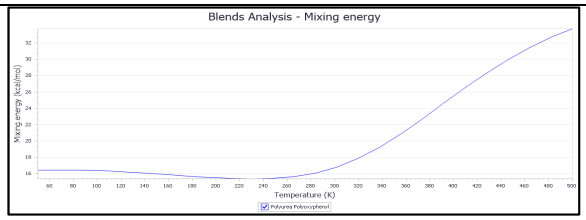

Figure 4. Mixing energy

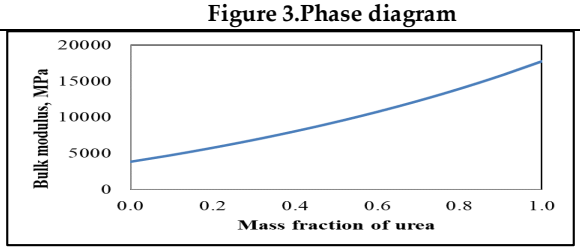

Figure 5. Change in bulk modulus with mass fraction of Urea

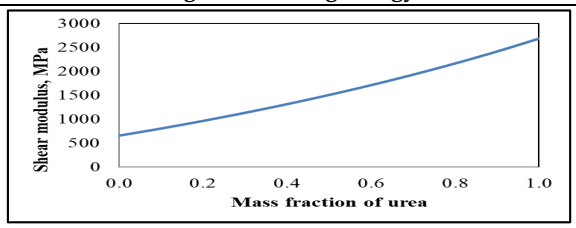

Figure 6. Change in shear modulus with mass fraction of Urea

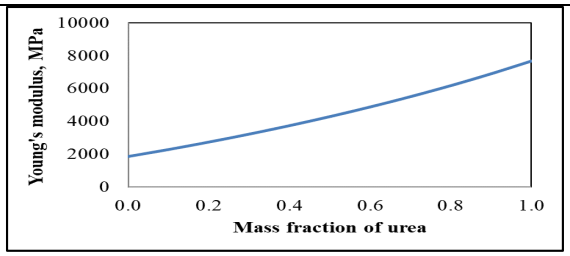

Figure 7. Change in Young's modulus with mass fraction of Urea

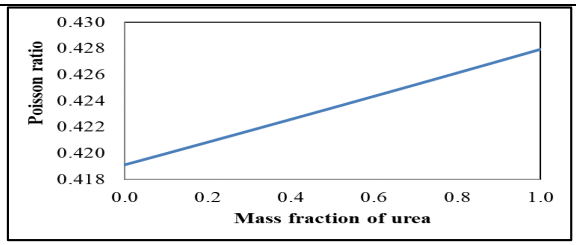

Figure 8. Change in Poisson modulus with mass fraction of Urea

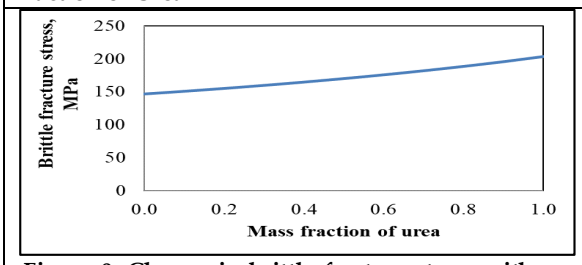

Figure 9. Change in brittle fracture stress with mass fraction of Urea

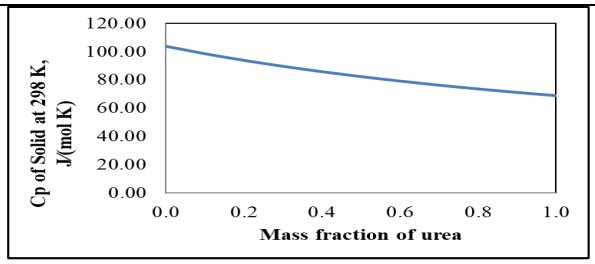

Figure 10. Change in heat capacity with mass fraction of Urea

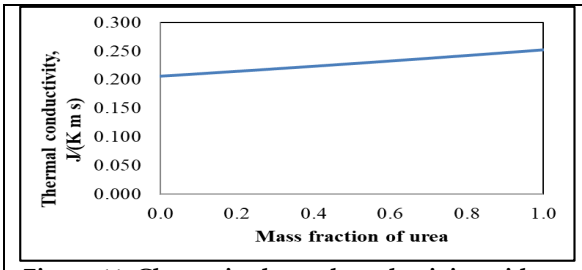

Figure 11. Change in thermal conductivity with mass fraction of Urea

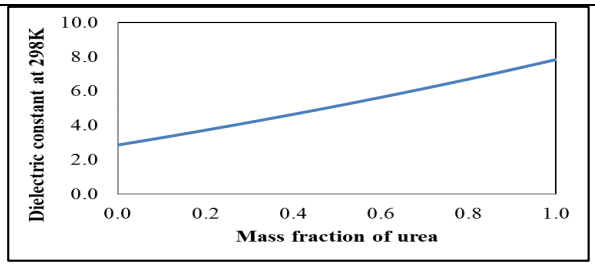

Figure 13. Change in dielectric constant with mass fraction of Urea

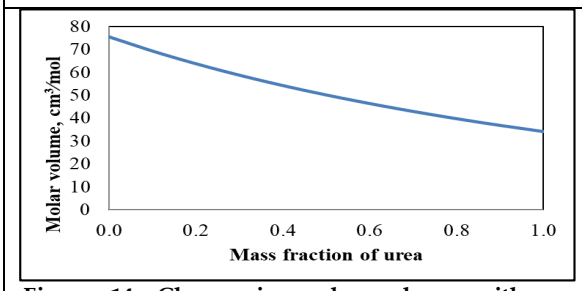

Figure 14. Change in molar volume with mass fraction of Urea

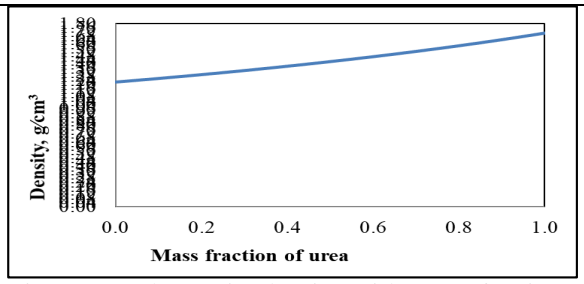

Figure 15. Change in density with mass fraction of Urea

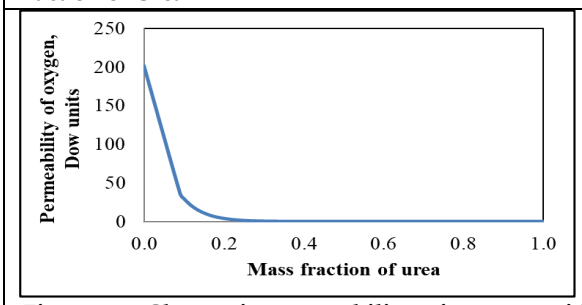

Figure 11. Change in permeability of oxygen with mass fraction of Urea

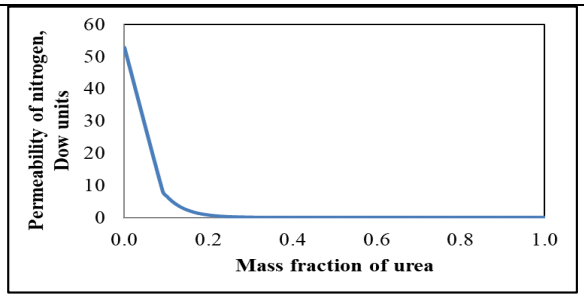

Figure 12. Change in permeability of nitrogen with mass fraction of Urea

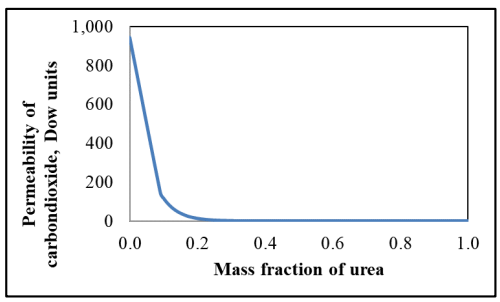

Figure 16. Change in permeability of carbon dioxide with mass fraction of Urea

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RESEARCH ARTICLE

Inhibition of COVID-19 by Blocking SARS-CoV-2 Enzyme using Bhringraj [*Eclipta alba* (L.) Hassk.] Plant Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by novel corona virus SARS-CoV-2. The molecular docking of the phytochemicals with PDB code 6LNV enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" revealed that citric acid of bhringraj (*Eclipta alba* (L.) Hassk.) plant extract can effectively fight against"SARS-CoV-2 virus".

Keywords: Biovia, COVID-19, Discovery studio, Phytochemical, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" has been spread over 100 countries and becomes pandemic. [1][2], There is no confirmed treatments till now. [3] Research is going on across the globe to develop the vaccines and also in searching the immune boosting alternative medicines. From the ancient time plants are used to treat various diseases. [4] Different phytochemicals present in plants are used for safety in comparison to synthetic drugs. Among the medicinal plants, *Eclipta alba* (L.) Hassk. commonly known as 'Bhringraj' is one of the important plants which belongs to family Asteraceae. It contains 6, 10, 14-trimethyl-2-pentadecanone, 7, 11-Dimethyl-3-methylene-1,6Z, 10-dodecatriene, octadea-9-enoic acid, Phytol, Pentadecane and Citric acid etc. This study aims to identify the phytochemicals present in *E. alba* (L.) Hassk to protect from "COVID-19" infection.

MATERIALS AND METHODS

"Biovia Discovery studio" is the software tool developed by Dassault Systems of France was used for computational approaches for fast to analyze the predictions for a large set of phytochemicals as the primary drug development process. It was revealed that *E. alba* contains 6, 10, 14-trimethyl-2-pentadecanone; 7, 11- Dimethyl-3-methylene-1; 6 Z-10 Dodecatriene; Octadea-9-enoic acid, Phytol, Pentadecane and citric acid etc. From ancient times plants are used

for curing various diseases. In silico analysis confirms the particular phytochemicals responsible for inhibiting the PDB code 6LNV enzyme of this virus and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Computational molecular docking approaches was used to recognize the particular phytochemicals of the experimented plant which can inhibit the PDB code 6LNV enzyme. The method has been enumerated elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was known for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". Confirmations of ligand were acquired by "Molecular Dynamic methods". High positive –CDOCKER energy value and the difference between –CDOCKER energy and –CDOCKER interaction energy are taken to recognize the drug. This study identifies those phytochemicals which can cure COVID-19 attack. Data depicted in Table 1 showed that citric acid can effectively inhibit from COVID 19.

CONCLUSIONS

Citric acid present in *E. alba* (L.) Hassk. Can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was noticed that citric acid can interact significantly with PDB code 6LNV enzyme.

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Table 1. Results of C Docking of phytochemicals with PDB code 6LNV enzyme (receptor)

Sl No	Ligand	-C Docker energy	– C Docker interaction energy	Difference Between -C Docker Interaction Energy and - C Docker Energy	Remarks
1	6,10,14-trimethyl-2-pentadecanone	20.1835	20.297	0.1135	
2	7,11-Dimethyl-3-methylene-1,6Z,10-dodecatriene	-28.7715	30.4083	59.1798	Minimum inhibition of viral protein
3	octadea-9-enoic acid	25.2062	33.2391	8.0329	
4	Phytol	13.3508	38.3735	25.0227	
5	Pentadecane	FAIL		NA	
6	Citric acid	32.8882	32.2613	0.6269	Maximum inhibition of viral protein

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RESEARCH ARTICLE

In-silico Analysis of COVID-19 Prevention by Blocking SARS-CoV-2 using *Guava* Phytochemicals Extract

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is an infectious disease produced by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". "Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with enzyme6W4Hof SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Malonic acid ofguavaextract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Psidium guajava*(Guava) belongs to myrtle family (Myrtaceae) and the leaf of it contains phytochemicals likeMALONIC ACID, ASCORBIC ACID , KAEMPFEROL, CATECHIN, GALLIC ACID, CITRIC ACID etc. This study focuses on exploring the possibilityof using these phytochemicals in curing the disease caused by COVID-19.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Psidium guajava*contains Malonic acid,Ascorbic acid, kaempftrol,Catechin,Gallic acid and Citric acid etc. It is known that plants belonging to this family Myrtaceaeare effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting enzyme 6W4Hand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract,that can deactivate the enzyme 6W4Hviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Malonic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Psidium guajava* (Guava)plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatMalonic acid can significantly interact with the viral enzyme i.e.6W4H.

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Table 1. Results of CDocking of phytochemicals with (Enzyme 6W4H)(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	MALONIC ACID	30.1529	26.5013	3.6516	
2	ASCORBIC ACID	5.8796	26.1182	20.2386	Least Effective
3	KAEMPFEROL	18.4587	23.2016	4.7429	
4	CATECHIN	21.694	29.3748	7.6808	
5	GALLIC ACID	21.8893	22.9785	1.0892	
6	CITRIC ACID	31.5584	24.4735	7.0849	

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RESEARCH ARTICLE

In silico Analysis of Prevention of COVID-19 by Blocking Nucleocapsid Protein N-terminal RNA Binding Domain (6M3M) using *Adhatoda vasica)*

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ABSTRACT

An infectious disease COVID-19 also known as "Corona virus disease 2019" which is caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).This global epidemic has been affecting millions of people within a short period of time. Epidemic researchers are putting lot of efforts to discover a preventive traditional vaccine. As there is no specific medicines discovered to fight against the disease, researcher are working seriously to develop drugs or vaccine against COVID-19. The main aim of this study to identify the phytochemicals extracts from the plant *Adhatoda vasica* which can deactivate 6M3M of SARS COVID-19. This deactivation can help to fight against COVID-19. The molecular C-docking of phytochemicals of *Adhatoda vasica* (Vasak) were analysed by using Biovia Discovery Studio. According to the "–C Docker energy and –C Docker interaction energy" the strength of interaction was determined. For both the parameters, high positive values were considered from phytochemicasl like kaempferolcan. These phytochemicals deviate the enzymatic process significantly and interfere with the infection of that virus to a human cell by interrupting the life cycle of COVID-19.

Keywords: COVID-19, 6M3M, Biovia, *Adhatoda vasica*, NSP3.

INTRODUCTION

A novel corona virus (nCoV-2019) emerge as contagious disease for human on the month of December,2019 Wuhan province of China[1] and cause severe acute respiratory syndrome (SARS). On 30th January, 2020 World Health Organisation has issued public health emergency of international concern under International Health regulations [2]. Situation is getting worse with this viral infection and the mortality graph approaches to upward.Therefore, the actual number is much higher than reported one and it is because of the lack of huge testing facility [3]. Shockingly, there has been no recognizable forward drive in the administration of this sickness to date and the patient is given a treatment dependent on his noticeable and diagnosable side effects [4]. Even though a few endeavors have been made in the innovative work of the diagnostics, therapeutics and immunizations for this novel corona virus, there

exists no vaccines, so far which has been demonstrated unequivocally to be viable in treating human maladies because of a tiny virus. Various traditional drugs like chloroquine, hydroxyl-chloroquine, remdesivir have effect on treatment of COVID. The less effective of these drugs motivated to examine the restraint of COVID-19 protease by Indian herbal plants [5]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain regulatory function in physiology of human. These chemicals are known as phyto-chemicals. Generally seeds, fruits, flowers, leaves, barks, flowers, roots and fruits are the main source for these medicinal values. Plant extracts of some plants have their specific function towards anti-oxidation, anti-inflammatory, anticancer and anti-diabetes etc.[6]. From ancient period plants have been used as a source of novel chemical substances which serve as a new material for the pharmaceutical industry.The leaves of vasak have the following phytochemicals like alkaloids, tannins, saponin and phenolic compounds.The main objective of this article to identify the phytochemicals of *Adhatoda vasica* responsible for inhibiting COVID-19 6M3M) by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

The entire insilico analysis was done by the help of Discovery studio of "Biovia Software ((Dassault Systemes de France).Molecular level of interaction can be predicted through machine learning by using this software. Plants protect itself from its predators by its own secondary metabolites. Plants may face some threats including bacteria, viruses, fungi etc. Such phytochemicals ward off health risks when certain plants or their parts are eaten by humans. Recent studies demonstrated that *Adhatoda vasica* contains vasicin, vasicinone, peganin, quercetin , kaempferol, etc. It has been reported that Acanthacae have potential to fight against various diseases.This study focuses on identifying specific phytochemical which can control COVID-19[7,8].

Papain-like protease (PLpro) of COVID-19: COVID 19 can infect an individual with its various metabolic pathway. These metabolism and lifecycle are controlled by various proteins or protein like enzymes. The enzymes were identified by using Brenda database which found in COVID-19. It has been found that 6M3M (nucleocapsid protein N-terminal RNA binding domain) is involved in replication of virus. By molecular docking method, it can be identified the phytochemicals which can be used as ligand and interact with the receptor of enzyme or protein of pathogen. Biovia Software's Discovery Studio modules have been used to define interaction of molecules through molecular docking. Phytochemicals of *Adhatoda vasica* were downloaded in sdf format. The PDB code has protein database code has been identified at the RCSB website. The enzyme's active site was established through a protocol called "Define receptor binding site" found under the menu receptor-ligand interaction. The molecular docking was carried out using a C-Docker protocol by using receptor-ligand interaction. Receptor molecule was selected from the enzyme and ligands were selected from the phytochemicals. C-Docker energy and C Docker interaction energy were considered for the significant molecular CDocking. The high positive value show the good interaction of phytochemicals with the enzyme for curing the disease.

RESULTS AND DISCUSSION

Receptor binding site of 6M3M (nucleocapsid protein N-terminal RNA binding domain) of COVID-19 is represented as green colour in figure1. CDOCK is a simulated-annealing based molecular dynamics (MD) algorithm. It is a molecular docking process based on a grid and optimized for precision. It is an insilico based method for optimizing accuracy. Molecular Dynamic methods obtained the ligand conformations. The energy difference was calculated by-CDOCKER energy from the internal ligand strain and energy from the receptor-ligand interaction. -CDOCKER interaction refers to the energy of an unbonded interaction between the protein and the ligand. The best interaction criteria were chosen based on a) high positive value of -CDOCKER energy, and b)small difference between -CDOCKER energy and -CDOCKER energy interaction.

High positive values of C-Docker energy are16.6619 and the difference with Cdocker interaction energy 4.188 are presented in table-I.TableI also represented the difference in energy which are kaempferol, vasicinone, vasicine, peganine. From these findings it is found that Kaempferol can effectively deactivate 6M3M, thereby interrupting viral replication.On the other hand, kaempferol shows the second highest affinity towards 6M3M (nucleocapsid protein N-terminal RNA binding domain)of COVID-19 and therefore, it has the potential to deactivate the enzyme. Vasicine, vasicinone, peganine can less effectively inhibit the viral replication as negative -CDocker energy but shows positive -CDocker interaction energy. Thus, the key phytochemicals Kaempferol can prevent COVID-19 caused by 6M3M of virus.

CONCLUSIONS

It was reported that *Adhatoda vasica* has shown better response to COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. From this study, it is concluded that phytochemicals like kaempferol can inhibit the lifecycle of virus causing COVID19 by using insilico analysis through Biovia Discover software. These molecules as ligand can have a significant interaction with 6M3M of COVID-19. It was found that Kaempferol of *Adhatoda vasica* can have strong interaction with the enzymatic molecule that inhibit the life cycle of virus. The following phytochemicals like Vasicine, vasicinone, peganine were not suitable interaction with the enzyme of virus. From this study it can be concluded that these two phyochemicals Kaempferol provide the medicinal importance to *Adhatoda vasica* that can act against COVID-19 caused by 6M3M.

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Table 1. C-Docking score of different phytochemicals with 6M3M of COVID-19

Serial Number	Phytochemicals	- C Docker energy	- C Docker interaction Energy	Difference between - C Docker interaction and - C Docker energy
1	Vasicine	2.09314	16.5914	14.49826
2	Vasicinone	1.60423	16.3419	14.73767
3	Peganine	4.29333	18.9121	14.61877
4	Vasicinolone	Failed	Failed	Failed
5	Kaempferol	16.6619	20.8488	4.188

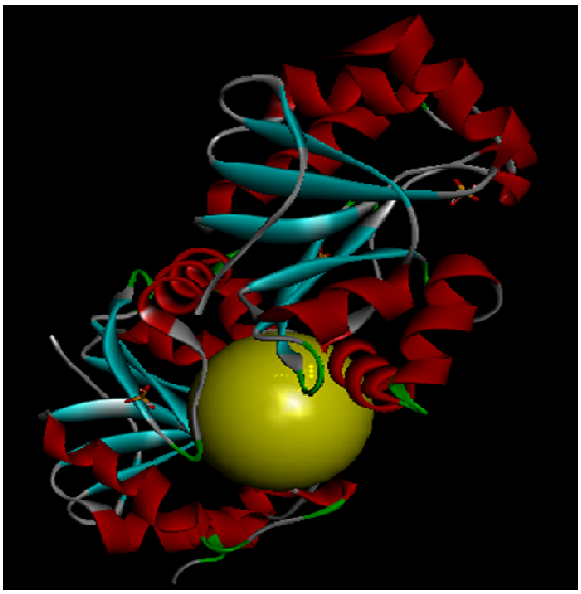

Figure 1. Binding site of 6M3M (nucleocapsid protein N-terminal RNA binding domain)

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RESEARCH ARTICLE

Prevention of COVID-19 by Blocking 6M03 Enzyme using *Helichrysum chasmolycicum* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "6M03 enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Hexadecanoic acid of *Helichrysum chasmolycicum* extract can effectively fight against "SARS-CoV-2 virus".

Keywords: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" is one of the most dangerous disease and has spread fear among people as severe pandemic disease[1][2]. While, there is no such relevant cure for this severe disease [3]. Hence, it is the need of the hour to discover the most needed drugs against the emerging pandemic. Several plants have been identified curing various illnesses [4]. Their phytochemicals will be low-cost but effective. *Helichrysum chasmolycicum* belongs to family Asteraceae. It contains phytochemicals like Hexadecanoic acid, Kaemferol, Apigenin, Palmitic acid, 3', 5-dihydroxy-3, 4', 7-trimethoxy flavone etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) has used for in silico study. After *In silico* molecular docking the result reveals that *Helichrysum chasmolycicum* contains Hexadecanoic acid, Kaemferol, Apigenin, Palmitic acid, 3',5-dihydroxy-3,4',7-trimethoxy flavone etc. It is known that plants belonging to this family are effective against viruses. In our investigation the main objective was to pick up that phytochemical which is unique and

capable to inhibit 6M03 enzyme and controlling of COVID-19. To find out numerous enzymes found in COVID-19, we have used Brenda database. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate 6M03 enzyme. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". Small difference between -CDOCKER energy and -CDOCKER interaction energy and High positive value of –CD CKER energy and are the criteria to identify the drug. Table 1 shows that is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It has concluded that *Helichrysum chasmolycicum* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it has identified that Hexadecanoic acid can significantly interact with the 6M03 enzyme.

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Table 1. Results of CDocking of phytochemicals of *Helichrysum chasmolycicum* with 6M03 enzyme

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Hexadecanoic acid	36.2155	37.9446	1.7291	Maximum inhibition of viral protein
2	3',5-dihydroxy-3,4',7-trimethoxyflavone	17.815	36.4605	18.6455	Minimum inhibition of viral protein
3	Apigenin	FAIL		NA	
4	Kaemferol	28.3298	33.3087	4.9789	
5	Palmitic acid	20.2218	31.9164	11.6946	

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RESEARCH ARTICLE

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Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

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MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. After in silico molecular docking the result reveals that *Helichrysum chasmolycicum* contains Hexadecanoic acid, Kaemferol, Apigenin, Palmitic acid, 3',5-dihydroxy-3,4',7-trimethoxy flavone etc. It is known that plants belonging to this family are effective against viruses. In our investigation, the main objective was to pick up that phytochemical which is unique and capable inhibiting 6M3M enzyme and controlling of COVID-19. To find out numerous enzymes found in COVID-19,

we have used Brenda database. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the 6M3M enzyme. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". Small difference between -CDOCKER energy and -CDOCKER interaction energy and High positive value of -CDOCKER energy and are the criteria to identify the drug. Table 1 shows that Palmitic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It has concluded that *Helichrysum chasmolycicum* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Palmitic acid can significantly interact with the viral 6M3M enzyme.

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Table 1. Results of CDocking of phytochemicals of *Helichrysum chasmolycicum* with 6M3M enzyme

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Hexadecanoic acid	41.9423	38.5978	3.3445	
2	3',5-dihydroxy-3,4',7-trimethoxy flavone	15.5968	31.6696	16.0728	
3	Apigenin	24.0931	29.2745	5.1814	
4	Kaemferol	15.1787	19.5446	4.3659	Minimum inhibition of viral protein
5	Palmitic acid	72.5252	62.6273	9.8979	Maximum inhibition of viral protein

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RESEARCH ARTICLE

Studies of Phytochemicals Presents in *Ocimum sanctum*

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ABSTRACT

Now a day"s researchers have been isolating and analyzing many medicinal plants for their medicinal properties and healing components. "Ocimum sanctum" also known as "Tulsi" or "Holi basil" is an aromatic plant and it belongs to the family "Lamiaceae" which is widely used as medicine to cure various ailments. The aim of this work is to analyse elemental content and different "phytochemicals" of "tulsi leaf" by X-Ray Fluorescence (XRF) technique for samples of different parts of "tulsi". The "phytochemical" screening revealed the presence of "alkaloids", "carbohydrates", "flavonoids", "protein", "steroids", "terpenoids", "phenols", "tannins" and "glycosides" in tulsi leaf extract. Qualitative analysis revealed high amount (1.5 to 7.%) of "phenols" being present. The amount of "alkanoid" and "flavonoids" ranged from 0.90 to 1.27% and 1.53 to 2.22% respectively. The presence of these phytochemicals can be correlated with the medicinal potential of this plant.

Keywords: Ocimum sanctum, phytochemical, medicine, methanol extract, ethanol extract

INTRODUCTION

The importance of medicinal plants is play important role to meet the medical and health needs of 70% of the populations in developed countries. (N gari etal2010). Ayurveda is a conventional Hindu medicine system which emphasizes the use of endemic plant based medicines for the medication of disease. Among different medicinal plants, "Ocimum sanctum", which is known as Tulsi, has important contribution to the such field and has been attracted the attention of many researchers owing to its large medicinal properties. In this regard, "tulsi" is considered as "Incomparable one" and is holiest and most cherished of many medicinal herbs. Moreover, in contrast to the synthetic chemicals, herbal products, are considered for their safety to human system and environment. Usually medical plants contains chemically and taxonomically diverse "secondary metabolites" with unknown function. Many phytochemicals are widely used in therapy for human beings, veterinary, agriculture, different scientific researches and also in inhibition for microorganisms "in vitro" (Vasu et al; 2009).

"Tulsi" belongs to a family of "Lamiacae" and known as an important source of medicine having many secondary metabolites, essential oils which are highly recommended for treatment of diseases such as "malaria", "diarrhea", "bronchical asthma", "dysentery", "skin disease", "arthritis", "chronic fever" and "eye disease" etc. Indeed, tulsi, is a very useful medicinal plant having wide range of medicinal properties. At the same time it is available in different parts of country in rural as well as urban areas. It is also of a great deal of spiritual value and in the bead form if worn, it is supposed to ward of all kind of negativity from life. Its medicinal value, extends from ordinary and general diseases like curing of common colds to as complex diseases as hypertensive disposition and cardiac relaxing effect. It also has great deal of soothing action upon the digestive tract. Such a combination of availability of great deal of disease removal properties along with spiritual values, makes it a sacred plant to be worshiped in different parts of country. In the present work, we proceed to evaluate different "phytochemicals" present in the dried extract of tulsi plant.

Studies from different researches has been suggested that tulsi is a "COX2inhibitor," like many modern painkiller, as it contains appreciable amount of "eugenol". Moreover, tulsi has been taken traditionallty as "herbal tea", "dried powder", "fresh leaf", or "mixed with honey" or ghee". Its dried leaves have been used to protect stored grains for repelling insects. The tulsi is a complex combination of many "nutrients" and "biological active" compounds. However, these constituents significantly change with time and cultivation and storage process. The elemental status of the medicinal herb is governed by the making "geochemical" features of the soil, capacity of the plant to accumulate elements minerals "environmental pollution" and "fertilization" (Queralt et al; 2005).

MATERIALS AND METHODS

Sample collection: Mature fresh leaves of Ocimum sanctum were collected from the trees growing around centurion university botanical garden.

Preparation of dry extracts: 100gm of fresh leaves were dried in hot air oven at 50˚C for four days. The leaves were then ground into powdery form. Ten gram (10gm) each of the grounded leaf were weighed. The extract taken for elemental analysis by using X-Ray Fluorescence(XRF).

Preparation of aqueous, methanol and ethanol extract: In a soxhlet apparatus, 20 g of dried tulsi powder was placed. For extraction procedure, to 200 mL of distilled water was used. The same extraction was also repeated with methanol and ethanol separate procedures. The extraction was continued till clear solvent was observed in the thimble of soxhlet apparatus. The extraction was concentrated using rota-evaporator, dried till dark green residue was obtained. The %age yield of the extract was calculated using the following formula:
Percentage of yield= (Final weight of dried extract/Initial weight of the powder) ×100

1. Percentage of aqueous solution= (0 2/20) ×100 = 1%
2. Percentage of methanol solution= (0.6/20) ×100 = 3%
3. Percentage of ethanol solution= (0.4/20) ×100 = 2%

Qualitative phytochemical analysis : The extract was tested following standard biochemical methods as describe below.

Test for proteins

Biuret"s test: 2ml of Biuret reagent was added to 2ml of extract. The mixture was shaken well and warm for 5 min. Appearance of red or violet colour indicated presence of proteins.

Million"s test: Crude extract was mixed with 2ml of Millon"s reagent, if precipitate appeared which turned red on gentle heating confirmed the presence of protein.

Ninhydrin test: Crude extract was mixed with 2 ml of0.2% solution of Ninhydrin and boiled for some time, if violet colour appeared indicating the presence of amino acids and proteins.

Test for carbohydrates

"Fehling's" test: 2 mL of Fehling's solution was added to the plant extract heated gently.
The emergence of brick red precipitate indicates the presence of a"reducing sugar"

Benedict's Test: 2mL of the Benedict's reagent was heated to boiling with the crude extract. The formation of the reddish brown precipitate indicates the presence of "carbohydrates".

Molisch's Test: To 0.5 mL of the crude extgract, 2 mL of the Molisch's reagent was added and shaken vigorously. To it 2 mL of conc. Sulphuric acid as added carefully from the sids of the test tube. The formation of a violet ring indicates the preseance of "carbohydrate".

Iondine Test: To 0.5 mL of the crude extract, 2 mL of iodine solution was added. A dark blue/purple colouration indicates "carbohydrate".

Test for "phenol": 2 mL of "alcohol" and 2-3 drops of "ferric chloride" solution was added to1 mL of "crude extract". Appearance of blue, green or black coloration indicated the presence of "phenols".

Test for "tannin": 1 ml of distilled water and 2-3 drops of "ferric chloride solution" was added to 0.5 mL of "crude extract". A black coloration indicated the presence of "tannin".

Test for "flavonoids": "*Shinoda test": The* "Crude extract" was mixed with small amount of "magnesium" and "concentrated HCl" was added drop wise. Appearance of pink scarlet colour after few minutes indicated the presence of "flavonoids".

Alkaline reagent test: 0.5 ml of "crude extract" was mixed with 2ml of "2% solution of NaOH". An intense yellow colour was formed which turned colourless on addition of few drops of diluted acid which indicated the presence of "favonoid".

Test for saponins: 1 mL of crude extract was mixed with 5ml of distilled water in a test tube and it was shaken vigorously. The formation of stable foam was taken as an indication for the presence of "saponins".

Test for "glycosides"

"Liebermann"s tes"t: Crude extract was mixed with each of 2 ml of "chloroform" and 2 mL of "acetic acid". The mixture was cooled in ice. Carefully "concentrated H_2SO_4" was added. If colour change from violet to blue to green which indicated the presence of "steroidal nucleus", i.e., "glycone" portion of "glycoside".

"Salk owsk I's" test: The crude extract was mixed with "chloroform". To this 2 mL of the "conc sulphuric acid" was added and gently swirled. Reddish brown colouration is due to "glycoside"

"Keller-kilani test": 0.5 ml of crude extract was mixed with 2 mL of "glacial acetic acid" containing 2-3 drops of 2% solution of "$FeCl_3$". To this 2 ml of "concentrated sulphuric acid" was added. Formation of a brown ring at the interface indicated the presence of "cardiac glycosides".

Test for steroid:
(i) 2 mL of "chloroform" was added to the crude "Tulsi" extract. To this 2 mL of each of "concentrated H2SO4" and "acetic acid" were added. The appearance of greenish coloration indicated the presence of "steroids".
(ii) The Crude extract was mixed with 2 mL of "chloroform" and gently added "concentrated H_2SO_4". A red colour was seen in the lower layer this indicated the presence of steroids.

Test for terpenoids: Crude extract was mixed in 2ml of "chloroform" and evaporated to dryness. To this, 2 mL of "concentrated H_2SO_4" was added and heated for about 2 min. A greyish colour indicated the presence of "terpenoids" at the interface.

Test for alkanoids: 2 mL of 1% "hydrochloric acid" was mixed with crude extract and heated gently. After heating, "Mayer's And Wagner's" reagents were added to the mixture. Appearance of precipitate indicated the presence of alkaloids.

Test for anthraquinone: 5ml of "chloroform" and 5 ml of "ammonia" solution was added to 0.2 g of plant extract. Appearance of pink, red or violet colour indicated the presence of "anthraquinone".

Oils & Fats: A small quantity of crude extract was pressed between two filter papers separately. An oily appearance on filter paper indicated the presence of fixed oil & fats.

Test for lactones:
Baljet"s test: Crude extract was treated with sodium picrate solution. Presence of lactone was observed by appearance of yellow to orange colour in the mixture.

Quantitative analysis of phytochemicals in the plant extract

Determination of total phenoliccontents: The amount of total phenol for aqueous, methanol and ethanol extract were determined by Folin-Ciocalteu reagent method. 2.4 ml of 10% Folin- Ciocalteu reagent and 2 ml of 2% Na2Co3 were added to 0.5 ml of plant extract. The mixture was then incubated at room temperature for 30 minutes. Gallic acid was used as standard (1mg/ml). The absorbance of the sample was measured at 765 nm. All the tests were done in triplicates and the results were determined from standard curve and were expressed as gallic acid equivalent (mg/g of extracted compound).

Determination of alkaloid: 4 g of the sample was taken and 200 ml of 10% acetic acid in ethanol was added to the sample and allowed to stand for4 hours. Then the solution was filtered and the extract was Concentrated on water bath Conc. NH4 (OH) was added drop wise and the whole solution was allowed to settle and the precipitate was then washed with dilute ammonium hydroxide and filtered. The residue was dried and weighed and this was the amount of alkaloid present in the plant material.

Determination of flavonoids: 9g of plant sample was taken and extracted repeatedly with 100ml 80% methanol. Then the solution was filtered and the filtrate was transferred into an empty crucible and evaporated into dryness over water bath and weighed. The final weight dry weight was amount of flavonoids in the plant sample.

RESULTS AND DISCUSSIONS

Determination of major& minor elements in Ocimum sanctum: The micro (Co, Cu, Ni, Fe, Mn, & Zn) and macro (K, Na, Ca, & Mg) minerals in Ocimum sanctum leaves were determined (Table1). The concentration of these elements reported as ppm on dry weight basis. Among micro elements Mn & Zn have greater value as compared

with other medicinal plants that was 61.75& 32.38 ppm. While in macro elements including K, Na, P, Mg of the leaves is same, which is 0.62, 0.74, 1.10 ppm and traces of Mg leaves respectively. This study reports investigation on the presence of five elements Cd, Cr, Pb, As & Hg in the plant leaves. The leaves were found to contain very high amount of detectable levels of Cr & As. Ocimum sanctum leaf digest shown 3.67 & 3.54 ppm of Cr & As.

Amount of plant extracts yield percentage in different solvent: The yield of residue after Soxhlet & evaporation of 20gm dried plant leaves in methanol, ethanol & and water were in Table-2. The phytochemicals analysis in Ocimum sanctum (Tulsi) leave extract in the two solvents & aqueous conditions were summarized in Table-2 various bioactive molecules were found in Tulsi leaf extract from the phytochemical screening. The amount of extraction is more in case of organic solvent then that of water.

Qualitative & Quantitative analysis: From the quantitative analysis it was found that high amount of phenols are present in Tulsi leaf ranging from 1.5 to 7.4 percentages. Consequently the amount of alkanoid & flavonoids ranged from 0.90 to 1.27 & 1.53 to 2.22 percentages respectively. *"Ocimum sanctum"* has wide range of medicinal properties like, antiseptic, anti-inmflammatory, anti-microbial, antistress, antiseptic, analgesic, immune modulatory, hypoglycaemic, hypotensive, cardio-protective and antioxidant (Williamson, 2002, Tanwar *et al*., 2015). "Eugenol (1-hydroxy-2-methoxy-4-allylbenzene)" which is the active constituent of "Occimum Sanctum, is largely responsible for the therapeutic potentials (Sailaja *et al*., 2010). In addition, studies also shows that different secondary metabolites such as tannin, carbohydrates, flavonoids, glycoside, saponins, terpenoids, water soluble phenolic compounds, eugenol, caryophyllene, and methyl eugenol and fatty acids are present in extract of the tulsi leaf.. Some of the ingredients are also act as immune stimulant and Saponins act as ntihyperlipedemic, hypotensive and cardio depressive (Bairwa *et al*., 2012).

Among the phytochemical constituents, alkaloids, steroids, tannins, flavonoids, phenols and other aromatic compounds serve as defense mechanism against predation by lots of microorganisms, insects (Bonjar *et al*., 2004).cardio stimulant action of glycosides protects against cardiac failure (Sood et al.,2005). Tannins are known for antidiarrheal and haemostasis properties (Cragg *et al*., 1999 and Khanna *etal*; 2003). *O. sanctum* leaves extract have both "specific and non-specific" responses towards immune and disease resistance against fungal and bacterial infection (Santra *et al*; 2017). It stimulated both "antibody response" and "neutrophil activity". The methanolic extract of Occimum sanctum, reportedly, have anti-cancer properties which is effected by inhibition of synthesis of nitric oxide (Kim et al; 1998). It also has "hepatoprotective" and "notropic activities" (Rajesh et al; 2013). It also is found to be helpful in treatment of congnitive disorders as the alcoholic extract increased "step down latency" and "acetyl cholinesterase inhibition". Thus, the phytochemicals from occimum sanctum plant can successfully be used in various disorders of humankind. In addition the herb is cheap, available in huge amount around, whereby greatly helpful for living organisms.

CONCLUSION

Medicinal plants have various mineral elements which are important for their curative and therapeutic properties. Various kinds of the element or minerals exist at varying parts roots, stem & leaves of the plants. Many medicinal plants are isolated and analyzed for their medicinal properties and healing components by researchers nowadays. In the medicinal plants, elements are present in the mineral form & they play a critical role in functioning & maintenance of the body. The minerals essential for humans & organisms are Calcium, Phosphorus, Potassium, Sodium, Magnesium, Iron, Copper, Zinc & Manganese. Tulsi is one of the important plants in the traditional medicinal system & characterized in Ayurveda as an "elixir of life". Tulsi is a panacea fora lots of common health problem example fever, common cold, cough, throat aching, inhaling, kidney problem, stress, insect, bites etc. The presence of various bioactive compounds in the tulsi leaves justifies the uses for various ailments by living

population. Finally, it is concluded that the results of the present study provide information that Tulsi contains many elements & phytochemicals which may be useful in the treatment of many problems related to human health.

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Table-1(Elements present in Ocimum sanctum leaf)

Elements	Unit	Concentration
Mn	ppm	61.75±2.06
Zn	ppm	32.38±1.42
Cu	ppm	14.48±0.72
Mo	ppm	0.58±0.21
Ni	ppm	5.64±0.37
Li	ppm	0.59±0.07
Al	ppm	Trace
Mg	ppm	Trace
Cd	ppm	ND
Cr2	ppm	3.67±0.020
Pb	ppm	1.17±0.045
As	ppm	3.54±0.304
Hg	ppm	0.37±0.051

Table-2(Yield percentage in different solvents)

Extract	Yield amount (%) W/W
Methanol	3%
Ethanol	3%
Aqueous	1%

Table-3(Qualitative phytochemical screening methanol extract of tulsi leaf)

Phytochemicals	Aqueous extract	Methanol extract	Ethanol extract
Protein	-	-	-
Carbohydrate	-	+	+
Phenol	+	+	-

Tannin	-	+	+
Flavonoid	+	+	+
Saponin	-	+	+
Glycosides	+	+	+
Streroid	-	-	-
Terpenoid	-	+	+
Alkanoid	+	+	+
Anthraquinone	-	-	-
Fixed oils &fatty acid	-	+	-
Test for lactone	-	-	-

Here "+" indicates present & "-" indicates absent.

Table-4(Percentage of total phenolic, alkanoid, & flavonoid contents in plant extract)

Extract	Phenolic	Alkanoid	Flavonoid
Aqueous	1.51±0.55	0.90±0.65	1.53±0.64
Methanol	7.4±0.54	1.27±0.02	2.22±1.01
Ethanol	4.61±0.56	0.94±0.58	1.91±0.56

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RESEARCH ARTICLE

In silico Analysis of Polyoxymethylene and Polyether Sulfone Compatibility in a Blend

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ABSTRACT

Combination of two or more components results in the formation of a blend. The compatibility of polyoxymethylene and polyether sulfone were studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram and mixing energy. The results indicated that the pair can become compatible at both low and high temperature. Phase diagram indicated that a single phase can be obtained above 387.5K which was the critical temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of polyoxymethylene. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of polyoxymethylene. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in polyoxymethylene fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases increased with increase in mass fraction of polyoxymethylene. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend, In silico, Polyoxymethylene, Polyether sulfone.

INTRODUCTION

Blends or composites are formed with combination of more than one component where components do retain their identity in the mixture. As it is very difficult to find multiple properties in a single material, it is advisable to combine different components thereby improving the quality of the material. Development of a single material with

the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired properties. Thus a blend not only saves time to develop a new material also reduce the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer. The aim of the work was to examine the physical, mechanical and tribological properties of modified polyacetal.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3].A key issue is the process of mixing polymers during which blends undergo a complex combination of shear and elongation and the evolution of blend microstructure becomes crucial and requires close attention. [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites concern over environmental issues and sustainability has opened up another vibrant research field, namely, biobased and biodegradable polymer blends [7-12]. An overview of major developments and recent trends in biodegradable blends with an emphasis on PLA blends are also discussed. This chapter closes with an outlook for the future of this important subject. Usually blends are prepared by trial and error method and this technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio) has been used to identify compatible pairs.

MATERIALS AND METHODS

SOFTWARE USED: "Materials studio module of Biovia software (Dassault Systemes of France)" was used for this analysis. It utilizes machine learning techniques and standard algorithms to predict the level of interaction.

METHODOLOGY: POLYOXYMETHYLENE and POLYETHER SULFONE were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. POLYOXYMETHYLENE was used as the base and POLYETHER SULFONE was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed. The structures of POLYOXYMETHYLENE and POLYETHER SULFONE were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyoxymethylene on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of POLYOXYMETHYLENE and POLYETHER SULFONE as potential components of a blend was analyzed using Biovia Materials Studio. In this work the use of polyoxymethylene and polyether sulfone as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the

property of that polymer cannot be calculated. To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

ENERGY PARAMETER:

FREE ENERGY OF MIXING: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. Thermodynamic analysis suggests that

$$\Delta G_m = \Delta H_m - T\Delta S_m \quad (1)$$

where $\Delta G_m = Gibb's free energy of mixing$

$\Delta H_m = Enthalpy of mixing$

$\Delta S_m = Entropy of mixing$

$T = Absolute temperature$

The value of $T\Delta S_m$ is always positive in case of a blend since there is an increase in the entropy on mixing. Therefore, the sign of ΔG_m always depends on the value of the enthalpy of mixing ΔH_m. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution, i.e.,

$$\Delta H_m < T\Delta S_m \quad (2)$$

Figure 1. shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to a homogenous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyoxymethylene and poly ether sulfone with negative value of mixing energy, which may lead to form a particular shape with significantly high effort.

CHI PARAMETER: The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a high value of χ for chemically dissimilar polymers indicate poor mixing. For chemically similar polymers having small cohesive energy difference χ value is expected to be small. However, there is a chance of demixing for sufficiently long chains. Architectural and geometric differences between the components prevent them in a mixture from occupying the same configurations experienced in the pure phase. Polymer field theory can predict that a mismatch in chain stiffness for chemically similar components may lead to a high positive value of χ (chi). Figure 2. shows that the value of x high from temperature ranging from 50Kto 500K Thevalue of x decreases exponentially with increase in temperature.This agrees with the free energy of mixing for the blend.

PHASE DIAGRAM: The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3. shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).

b. Fragmented metastable regions existed between binodals and spinodals, and

c. The two-phase separated regions of immiscibility are bordered by the spinodals.

The binodals separated miscible (one-phase) and metastable region, while the spinodals separated the metastable and two-phase region. When the system enters from single-phase region to the metastable region, the phase separation usually occurs by the mechanism of resembling crystallization i.e, slow nucleation followed by growth of the phase separated domains. On the other hand, when the system jumps from a single-phase into the spinodal region of immiscibility the phases separate spontaneously by a mechanism called spinodal decomposition.

MIXING ENERGY: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 4. shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that at first when temperature increases the mixing energy increases to a highest value.The temperature is vary from 50K to500K for the varying of mixing energy.it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

MECHANICAL PROPERTIES

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 5. shows that the bulk modulus of the composite decreases linearly with increase in mass fraction of polyoxymethylene

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 6. shows that the shear modulus of the composite decreases linearly with increase in mass fraction of polyoxymethylene.

Young's modulus: It is defined as the ratio of longitudinal stress and strain. It compares the relative stiffness of the composite. Figure 7. shows that the Young's modulus of the composite decreases linearly with increase in mass fraction of polyoxymethylene.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 8. shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of polyoxymethylene.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 9. shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of polyoxymethylene.

THERMAL PROPERTIES

Heat capacity: It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase. Figure 10. shows that the heat capacity (Cp) of the composite decreases linearly with increase in mass fraction of polyoxymethylene.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat. Figure 11 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of polyoxymethylene.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant. Figure 12. shows that the dielectric constant of the composite decreases with increase in mass fraction of polyoxymethylene

INTENSIVE PROPERTIES:

Molar volume: It is the volume occupied by one mole of a substance. Figure 13. shows that the molar volume of the composite decreases linearly with increase in mass fraction of polyoxymethylene.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 14. shows that the density of the composite decreases linearly with increase in mass fraction of polyoxymethylene.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium. Lower permeability indicates longer time lag for the gas to pass through the membrane. Figure 15. shows that the permeability of oxygen through the composite increases with increase in mass fraction of polyoxymethylene.

Figure 16 shows that the permeability of nitrogen through the composite increases with increase in mass fraction of polyoxymethylene. Figure 17. shows that the permeability of carbon dioxide through the composite increases with increase in mass fraction of polyoxymethylene. Thus, the results indicated that an increase in polyoxymethylene fraction increases the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of polyoxymethylene and polyether sulfone to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The results indicated that the pair can have very good compatibility at different ranges of temperature. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of polyoxymethylene. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of polyoxymethylene. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in polyoxymethylene fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeability for all the gases increased with increase in mass fraction of polyoxymethylene. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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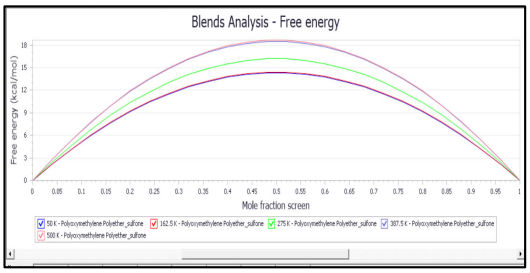

Figure 1. Free energy change with mole fraction of polyether sulfone at different temperatures

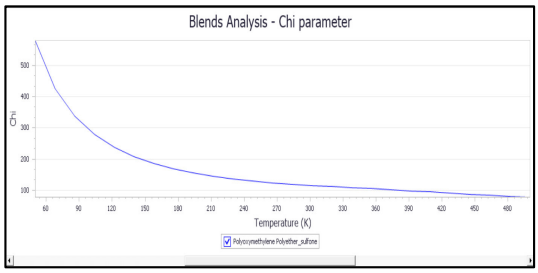

Figure 2 Change in χ (chi) value with temperature

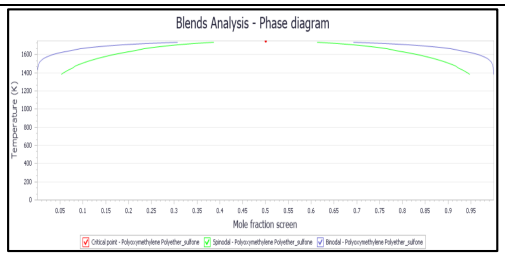

Figure 3. Phase diagram

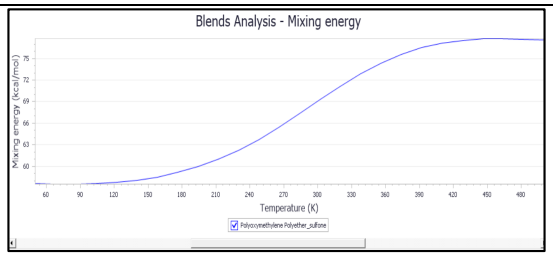

Figure 4. Mixing energy

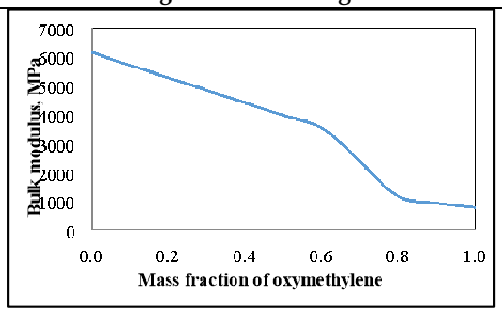

Figure 5. Change in bulk modulus with mass fraction of polyoxymethylene

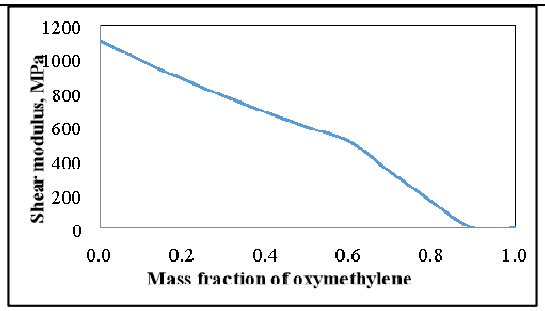

Figure 6. Change in shear modulus with mass fraction of polyoxymethylene

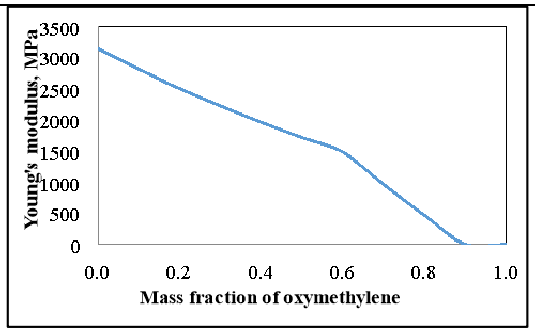

Figure 7. Change in Young's modulus with mass fraction of polyoxymethylene

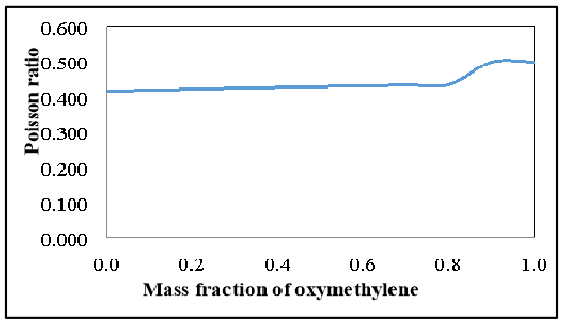

Figure 8. Change in Poisson modulus with mass fraction of polyoxymethylene

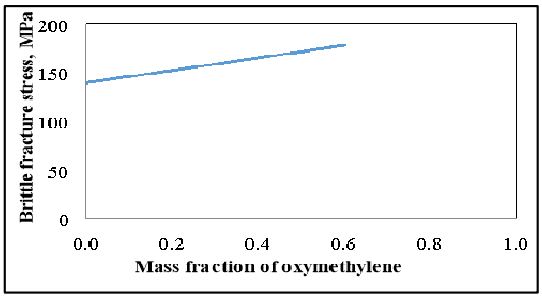

Figure 9. Change in brittle fracture stress with mass fraction of polyoxymethylene

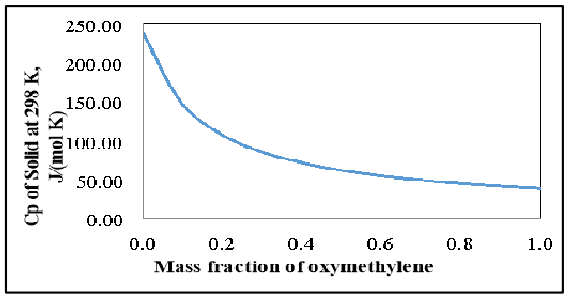

Figure 10. Change in heat capacity with mass fraction of polyoxymethylene

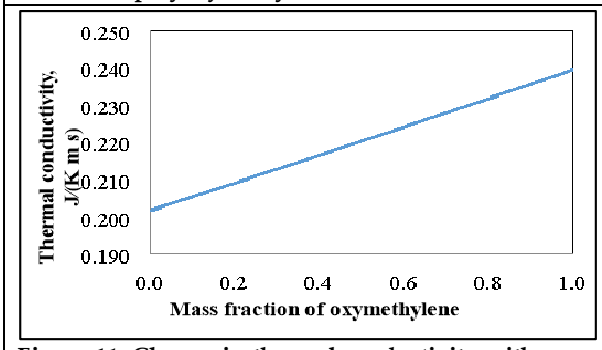

Figure 11. Change in thermal conductivity with mass fraction of polyoxymethylene

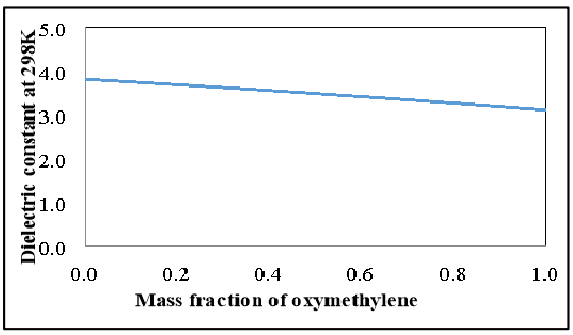

Figure 12. Change in dielectric constant with mass fraction of polyoxymethylene

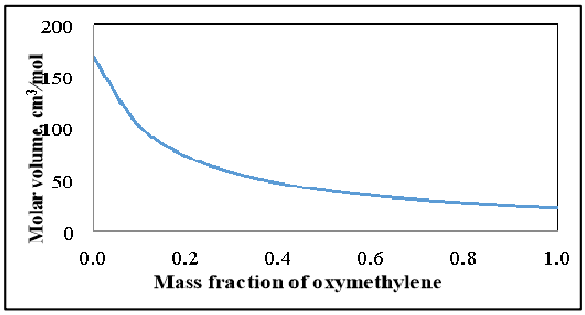

Figure 13. Change in molar volume with mass fraction of polyoxymethylene

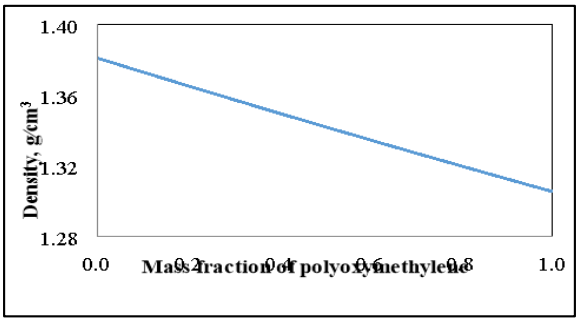

Figure 14. Change in density with mass fraction of polyoxymethylene

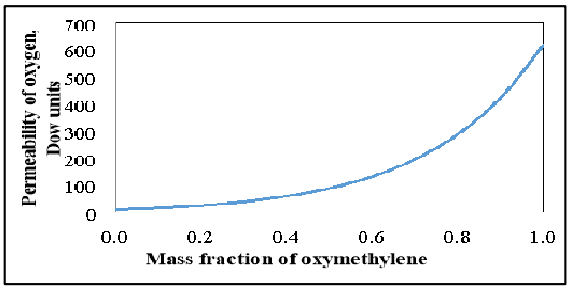

Figure 15. Change in permeability of oxygen with mass fraction of polyoxymethylene

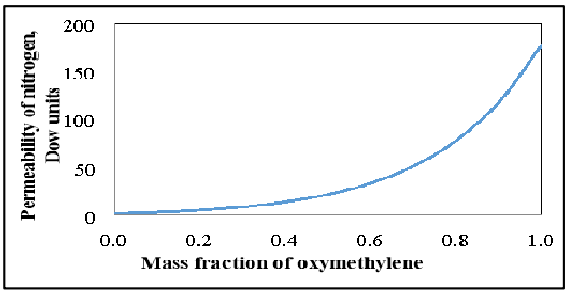

Figure 16. Change in permeability of nitrogen with mass fraction of polyoxymethylene

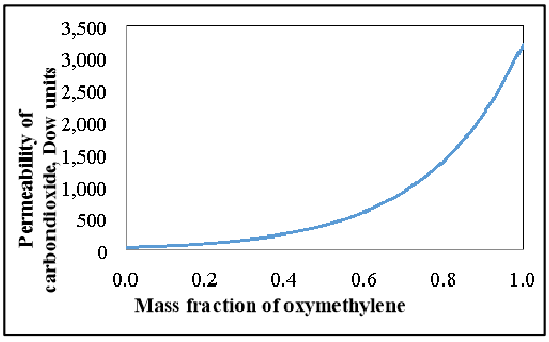

Figure 17. Change in permeability of carbon dioxide with mass fraction of polyoxymethylene

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RESEARCH ARTICLE

Trigonella foenum-graecum L. (Fenugreek) Extract to Block ADP Ribose Phosphatase Enzyme of COVID-19 for Prevention: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with PDB code 6LNV enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" revealed that Trigonelle present in *T. foenum-graecum* L. extract can efficiently combat "SARS-CoV-2 virus".

Keywords: Biovia, COVID-19, Discovery studio, Phytochemical, SARS-CoV-2, *T. foenum-graecum* L.

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" as been spread over 100 countries and becomes pandemic. [1], [2] Till now no specific drug for this virus has been developed. [3] Now integrated treatment of different drugs are used to treat the patients. Therefore in this context, plant based drug development is required to treat this disease. Many plants are known to cure different diseases. [4]Their phytochemicals will be low-cost but effective. *Trigonella foenum-graecum* L. belongs to family Fabaceae and commonly called as Fenugreek. It contains L-trytophan, coumarin, diosgenin, trigonelle etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" software tool (Dassault Systemes of France) was used for computational approaches to analyze the predictions for a large set of phytochemicals as the primary drug development process. Literature data revealed that *T. foenum-graecum* L. contains L-trytophan, coumarin, diosgenin, trigonelle etc. The phytochemicals present in these plant specimens has the capability to inhibit the PDB code 6LNV enzyme which can control the multiplication of COVID-19. Different enzymes of COVID-19 were searched and obtained from Brenda enzyme data

base. Molecular docking method has been used to identify the phytochemical from the plant extract that can deactivate the PDB code 6LNV enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

Molecular docking was carried out by opting the CDOCK method. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". Confirmations of ligands were obtained by "Molecular Dynamic methods". The drug was identified by taking the high positive value of -CDOCKER energy and the difference in between -CDOCKER and -CDOCKER interaction energy.

CONCLUSIONS

It was identified that the phytochemicals present in *T. foenum-graecum* L. can be used to check COVID-19 attack. Using "Discovery Studio module of Biovia software", it can be predicted that that trigonelle can act upon the PDB code 6LNV enzyme of the virus and can prevent from this viral infection.

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Table 1. Results of CDocking of phytochemicals PDB code 6LNV enzyme (receptor)

Sl No.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Lysine	23.637	24.2213	0.5843	
2	Coumarin	14.2044	17.5477	3.3433	Minimum inhibition of viral protein
3	Trigonelle	19.2485	18.6433	-0.6052	Maximum inhibition of viral protein
4	Scopoletin	18.0017	21.7889	3.7872	
5	Fenugreekine	Error		0	
6	Nicotin acid	15.9262	19.3515	3.4253	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) of SARS CoV-2 using *Aloe vera* Extract: An *In silico* Analysis

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ABSTRACT

Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase of NSP3 of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that6VXS-aloe emodin of *Aloe vera* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]*Their phytochemicals* will be low-cost but effective. *Aloe vera* belongs to family Asphodelaceae (Liliaceae). It contains 12 anthraquinones, which are phenolic compounds generally known as intestinal medicines. Aloin and emodin go about as analgesics, antibacterials and antivirals. It gives 4 plant steroids; cholesterol, campesterol, β-sisosterol and lupeol etc. This study identifies those phytochemicals which can cure COVID-19 attack.[5, 6]

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Aloe vera* contains 12 anthraquinones, which are phenolic compounds generally known as intestinal medicines. Aloin and emodin go about as analgesics, antibacterials and antivirals. It gives 4 plant steroids; cholesterol, campesterol, β-sisosterol and lupeoletc. It is known that plants belonging to this family are effective against viruses.

This work is focused on identification of the particular phytochemical responsible for inhibiting ADP ribose phosphatase of NSP3 of SARS-CoV-2and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract thatcan deactivate the ADP ribose phosphatase of NSP3 of SARS-CoV-2. The detailed method has been described elsewhere [7].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that 6VXS-aloe emodin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Aloe vera* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatAloe emodin can significantly interact with the viralADP ribose phosphatase of NSP3 of SARS-CoV-2.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase of NSP3 of SARS-CoV-2 (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Aloe- emodin	25.0075	29.7321	4.7246
2	Anthraquinone	13.6454	19.3660	5.7206
3	Cinnamic acid	17.0733	21.9162	4.8429
4	Salicylic acid	18.2504	24.6911	6.4407
5.	Aloin	FAILED	FAILED	FAILED
6.	Glucomannan	FAILED	FAILED	FAILED

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) of SARS CoV-2 using *Bacopa monnieri* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase of NSP3 of the virus of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated thatEpigeninofbacopamonnieri extractextractcan effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]*Their phytochemicals* will be low-cost but effective.
Bacopamonnieri belongs to family Scrophulariaceae. It contains bacosides, cucurbitacins, bacitracin A-D along with certain flavonoids, luteolin, and apigenin. This study identifies those phytochemicals which can cure COVID-19 attack.[5,6,7]

MATERIALS AND METHODS

"Biovia Discovery studio" module (DassaultSystemes of France) was used for analysis. Published works showed that bacopamonniericontains bacosides, cucurbitacins, bacitracin A-D along with certain flavonoids, luteolin, and apigenin. It is known that plants belonging to this family are effective against viruses. This work is focused on

identification of the particular phytochemical responsible for inhibiting ADP ribose phosphatase of NSP3 of the virusand controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate the ADP ribose phosphatase of NSP3 of the virus. The detailed method has been described elsewhere [8].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSIONS

It was identified that bacopamonnieri plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatEpigenin can significantly interact with the ADP ribose phosphatase of NSP3 of the virus.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase of NSP3 of the virus (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Epigenin	21.2447	26.4822	5.2375
2	Bacoside-A3	FAILED	FAILED	FAILED
3	Curcubetain-E	FAILED	FAILED	FAILED
4	D-mannitol	FAILED	FAILED	FAILED
5	(S)-Nicotine	1.29834	22.0478	20.7494

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Papain-Like Protease of SARS CoV-2 (6W9C) Enzyme using *Adhatoda vasica* Extract: An *In silico* Analysis

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ABSTRACT

In this work,the interaction of phytochemicalswith a specific enzyme of SARS CoV-2 is explored by molecular dockingusing"Biovia Discovery Studio". The outbreak of "Coronavirus disease 2019 (COVID-19)" is caused by a noble coronavirus named "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". Thisdiseasehas been listed as a pandemic by WHO in February 2020. The interaction between the phytochemicals present in plant extract of *Adhatoda vasika* is analyzed with "Papain-like protease of SARS CoV-2 (6W9C)" of SARS CoV-2 to discover the particularphytochemical accountable for the pre-emption of COVID-19. Higher positive values of "-CDocker energy and -CDocker interaction energy" confirmed that Kaempferol of*Adhatoda vasika* extract may show desirable activity against the "SARS-CoV-2 virus".

Keywords: Kaempferol, Biovia, Discovery Studio, COVID-19, phytochemical, 6W9C, SARS-CoV-2, *Adhatoda vasika*

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has spread quicklyall over the world creating dread among human civilization and has been stated as a pandemic by WHO.[1][2] However, there is no significant progress towards the treatment of it to date.[3] This situation needs an effective way to discover medicines with a suitable method against the virus. There are a large number of medicinal plants which contain such phytochemicals that may be effective towards various viral diseases.[4]These phytochemicals may active toward inhibiting the growth of the virus as well as cost-effective. To identify these phytochemicals molecular docking is one of the suitable ways, without any wet lab test which saves time, energy, chemicals, and manpower. Justicia adhatoda (*Adhatoda vasica*) belongs to family Acanthaceae. plant extract of Adhatodavasicais known to be effective against diseases like leprosy, heart troubles,

bronchitis, thirst, asthma, fever, blood disorders, vomiting, leucoderma, loss of memory, jaundice, mouth troubles, tumors, gonorrhea, sore-eye, and fever [5].

MATERIALS AND METHODS

"Biovia Discovery studio" module (DassaultSystemes of France) has been used for analysis. The plant is known to contain phytochemicals like Vasicine, Vasicinone, Peganine, Kaempferol, etc.[6, 7]. The plants which belong to this family are highly active against various viral diseases. This article is intended to focus on the exploration of the specific phytochemical/s responsible for preventing"Papain-like protease of SARS CoV-2 (6W9C)" of SARS CoV-2.
The information regarding the enzymes for COVID-19 is extracted from the "Brenda enzyme database." The method of Molecular docking has been employed to recognize the phytochemical responsible against preventing the enzyme, whichcan disable the "Papain-like protease of SARS CoV-2 (6W9C)". The method has been elaborated elsewhere [8].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". Fig. 1 displays the active site of6W9C enzyme which is indicated as light green color. The conformations of theligands were acquired by "Molecular Dynamic methods".The criteria for identification of a good drug are it must have high positive value of -CDOCKER energy, in addition to that, the minorvariance between -CDOCKER energy and -CDOCKER interaction energytodiscover the drug. Table 1 displays that Kaempferol is the keyphytochemical which can effectively inhibit COVID-19 disease.

CONCLUSIONS

This piece of work explored that *Adhatoda vasika* can inhibit COVID-19 attack. Using the "Discovery Studio module of Biovia software", it has beenexplored thatKaempferolcan significantly interact with "Papain-like protease of SARS CoV-2 (6W9C)" to deactivate the virus. The higher positive value of - C DOCKER energy (23.1593)and the low difference in - C DOCKER interaction energy and - C DOCKER energy(5.5817) makesKaempferola medicinally significant phytochemical of *Adhatoda vasika* towards the treatment of COVID-19.

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Table 1. Results of CDocking of phytochemicals with "Papain-like protease of SARS CoV-2 (6W9C)" (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Vasicine	-13.5794	34.8701	48.4495
2	Vasicinone	5.98834	20.8737	14.88536
3	Peganine	7.80199	23.0555	15.25351
4	Kaempferol	23.1593	28.741	5.5817

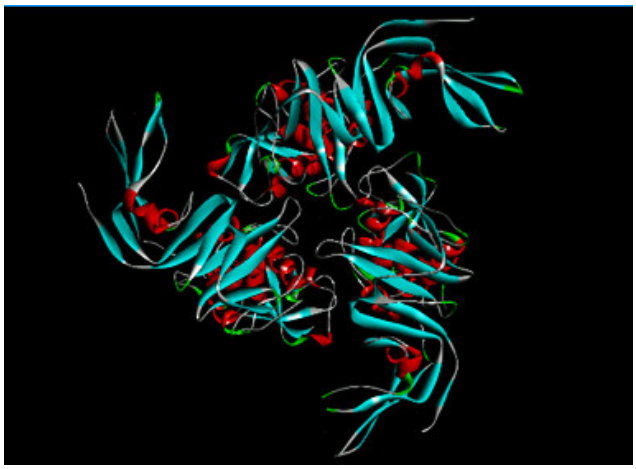

Figure 1. The active site of "Papain-like protease of SARS CoV-2 (6W9C)"enzyme.

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RESEARCH ARTICLE

Prevention of COVID-19 by Blocking "ADP Ribose Phosphatase of NSP3 (6W6Y)"of SARS CoV-2 using "*Aloe vera*" Extract: An *In silico* Analysis

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ABSTRACT

In this article, the molecular docking of phytochemicals with a specific enzyme of SARS CoV-2 of" was experimented using "Biovia Discovery Studio". "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" is responsible for the outbreak of "Coronavirus disease 2019 (COVID-19)" which has been declared as a pandemic by WHO. The interaction between the phytochemicals present in plant extract of *Aloe vera* is studied with "ADP ribose phosphatase of NSP3 (6W6Y)" of SARS CoV-2 to explore the specific chemical responsible for the prevention of COVID-19. Higher positive values of "-CDocker energy and -CDocker interaction energy" indicated that Aloe emodin of *Aloe vera* extract may work effectively against "SARS-CoV-2 virus".

Keywords: Phytochemical, Biovia, Discovery Studio, COVID-19, SARS-CoV-2,*Aloe vera*,Aloe emodin, 6W6Y.

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has spread rapidly throughout the entire world creating panic among the human population. It has been declared as a pandemic by the world health organization.[1][2] However, until now there is no established treatment. [3] Thisserious health concern needs to be tackled efficiently by identifying medicines against the virus. Numerous medicinal plants consisting of certain phytochemicals generally active against various viral diseases.[4]These phytochemicals are effective as well as low cost. "*Aloe vera* belongs to the family Asphodelaceae". It acts as an antioxidant and known to have antibacterial properties. The medicinal properties includethe burn healing, moderation of dental plaque, inhibition of wrinkles, relief from canker sores, and weakening of constipation [5, 6].

MATERIALS AND METHODS

"Biovia Discovery studio" module (DassaultSystemes of France) has been used for analysis. Various publications explain that the*Aloe vera* extract contains phytochemicals termed Aloe emodin, Babalocin, Anthraquinone, Glucomannan, Folic acid, etc.[7, 8]. The plants which belong to this family are highly active against various viral diseases. This article is intended to focus on the exploration of the specific phytochemical/s responsible for preventing"ADP ribose phosphatase of NSP3 (6W6Y)" of SARS CoV-2. The information regarding the enzymes for COVID-19 is extracted from the "Brenda enzyme database." The method of Molecular docking has been employed to recognize the phytochemical responsible against preventing the enzyme, whichcan disable the "ADP ribose phosphatase of NSP3 (6W6Y)". The method has been elaborated elsewhere [9].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". Fig. 1 shows the active site of the 6W6Y enzyme. It appears as light green color. The conformations of theligands wereacquired by "Molecular Dynamic methods".The criteria for identification of a good drug are it must have a high positive value of -CDOCKER energy, in addition to that, the minorvariance between -CDOCKER energy and -CDOCKER interaction energytodiscover the drug. Table 1 displays that Aloe emodin is the constituent phytochemicalthat can effectively inhibit COVID-19 disease.

CONCLUSIONS

This piece of work explored that*Aloe vera*can inhibit COVID-19 attack. Using the "Discovery Studio module of Biovia software", it has been identified thatboth Aloe emodin and Anthraquinonecan significantly interact with "ADP ribose phosphatase of NSP3 of COVID-19 (6W6Y)" to deactivate the virus. However, the higher positive value of - C DOCKER energy displayed by Aloe emodinmedicinal importance to *Aloe vera* towards the treatment of COVID-19.

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Table 1. Results of CDocking of phytochemicals with "ADP ribose phosphatase of NSP3 of COVID-19 (6W6Y)" (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Aloe emodin	21.2534	31.8024	10.549
2	Anthraquinone	14.7421	20.1924	5.4503
3	Folic acid	Failed	Failed	Failed
4	Glucomannan	Failed	Failed	Failed
5	Babalocin	Failed	Failed	Failed

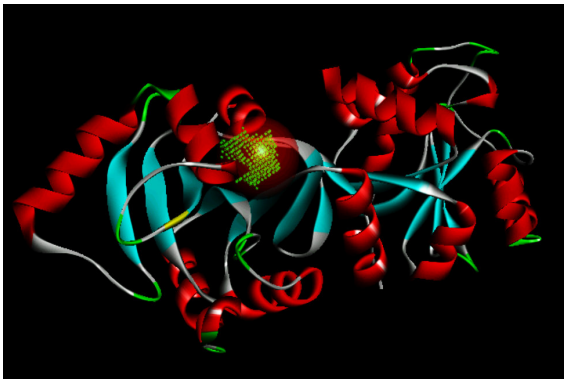

Figure 1. The active site of "ADP ribose phosphatase of NSP3 of COVID-19 (6W6Y)"enzyme.

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) using *Filipendula ulmaria* Extract: An *In silico* Analysis

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ABSTRACT

The outbreak of the novel coronavirus (2019-nCOV) with severe acute respiratory syndrome (SARS) has worsened the public health and economy.To overcome these obstacles researchers are trying to come up with a traditional vaccine or preventive drugs. This study focuses on identification ofphytochemicals from plant extract which has the capability to fight against COVID-19 by deactivating ADP ribose phosphatase of NSP3 (PDB: 6VXS) which is involved in replication of viral protein. Biovia Discovery Studio has been used for the study of molecular docking of phytochemicals with different enzyme. From Biovia Discovery Studio, -CDocker energy and -CDocker interaction energy was notedto know the strength of the interaction. High positive values are observed for different phytochemicals such as 2-hydroxycalcone, vaniline, 4-hydroxycalcone, L-ascorbic acid,therefore these phytochemicals can effectively deactivate the enzymatic metabolic activity thereby interrupting the metabolic pathway of ADP ribose phosphatase of NSP3 (PDB: 6VXS).

Keywords: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2.

INTRODUCTION

Near the end of December 2019, a novel coronavirus (2019-nCoV) with a unique characteristic of human-to-human transmission [1] and results in severe acute respiratory syndrome (SARS) has been originated in Wuhan province of China [2-3]. As per the global statistics, the mortality rate is doubled in just 7 days with this deadly virus. Globally more than 3 million people have been already confirmed with COVID-19 positive along with 274,488 death reports as on 10th May, 2020 (WHO reports). To battle this dangerous COVID-19, various traditional drugs like chloroquine, hydroxychloroquine, remdesivir, and so on, have been attempted and found with certain therapeutic impact in vitro. In any case, the clinical medication response isn't very empowering and toxicity stays an unavoidable issue causing severe effects. This motivated us to examine the restraint of COVID-19 protease by Indian herbal plants [4].

Filipendula ulmaria (meadowsweet) is a perpetual herb in the family *Rosaceae* that develops in sodden regions of Europe and Western Asia [5]. *F. ulmaria* is used in European medication for curing of different diseases because of its antipyretic, diuretic, pain relieving, and anti-inflammatory activity [6]. Reachers have studied the use of F. ulmaria in the curing of different diseases such asflu, rheumatism, urinary tract infections,pneumonia andhyperacidity. The use of F. ulmaria in healing wounds is also important [7]. The different constituents present in F. ulmaria such as three main classes of phenolic compounds: phenolic acids and their derivatives (salicylic acid, methyl salicylate, gallic acid, salicylaldehyde, ellagic acid,), flavonoid glycosides (apigenin, quercetin, kaempferol), flavonoids and tannins (rugosin A, B1, B2, D, E1 and E2) [8]. Due to presence of salicylic acid and its derivatives in F. ulmaria flowers and leaves, it showanti-inflammatory activity. This study focuses on exploring the possibility of using these phytochemicals in curing the disease caused by COVID-19. Further, the specific phytochemical is not identified for treatment of COVID-19. ADP ribose phosphatase of NSP3 (non-structural protein3) or 6VXS (PDB) belongs to the PLpro domain and basically helps in viral replication[9]. In this papper, This the phytochemical of *Filipendula ulmaria* are identified which helps to cureCOVID-19 caused by(SARS-CoV-2) by inhibiting the protien pathway.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Filipendula ulmaria*contains 2-hydroxycalcone, vaniline, 4-hydroxycalcone, L-ascorbic acid, spiraeoside, avicularin, salicin, rutin, etc.In earlier reports it was noticed that different plants belonging to *Rosaceae* family has potential to fight against microbes/viruses. This work is based on recognition of the specific phytochemical can cure COVID-19. Brenda enzyme database was used to identify and list different enzymes found in COVID-19. It has been found that ADP ribose phosphatase of NSP3 (protein database code 6VXS) is involved in replication of viral protein The detailed method has been described elsewhere.

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that 2-hydroxycalcone, vaniline, 4-hydroxycalcone and L-ascorbic acid. can effectively deactivate 6VXS, thereby interrupting the metabolic pathway ofADP ribose phosphatase of NSP3 of the virus.

CONCLUSIONS

It was observed that *Filipendula ulmaria* plant has medicinal action against COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. Using Discovery Studio module of Biovia software, molecular docking operation was performed to identify the phytochemicals2-hydroxycalcone, vaniline, 4-hydroxycalcone, L-ascorbic acid, spiraeoside, which can have a significant interaction with the 6VXS proteinof the virus. It was found that 2-hydroxycalcone and vanilinecan have strong interaction with the enzyme followed by 4-hydroxycalcone, and L-ascorbic acid successfully inhibiting the metabolic cycle of the microbe. Thus, this study could explain that the presence of 2-hydroxycalcone, vaniline, 4-hydroxycalcone, L-ascorbic acidcanprovide the medicinal values to *Filipendula ulmaria*against COVID-19 caused byADP ribose phosphatase of NSP3 (PDB: **6VXS**) which is involved in replication of viral protein.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase of NSP3 (PDB: 6VXS)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	2-hydroxycalcone	20.7389	29.6334	8.8945
2	4-hydroxycalcone	17.5385	28.9132	11.3747
3	L-ascorbic acid	9.3386	32.2158	22.8772
4	Vaniline	19.3159	23.4184	4.1025
5	Spiraeoside (Quercetin-4′-O-β-glucoside)	-2.67241	41.0751	43.7475
6	Avicularin	FAILED	FAILED	FAILED
7	Salicin	FAILED	FAILED	FAILED

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking nsp-9 RNA Binding Protein (6W4B) using *Adhatoda vasica* Extract: An *In silico* Analysis

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ABSTRACT

World Health organization on 11th February 2020 declared the name of epidemic disease which was first noticed in Wuhan, China in December 2019 as coronavirus disease (COVID 19). This study focuses on identification ofphytochemicals from plant extract which has the capability to fight against COVID-19 by deactivating nsp-9 RNA binding protein of COVID-19. Biovia Discovery Studio is software in which the molecular docking of the chemical constituentswas examined with the different enzyme. Based on - C DOCKER interaction energy and - C DOCKER energy, it was informed that which phytochemicals can be used to fight against COVID-19. It was noticed that different phytochemicalssuch as kaempferol, quercitin and peganinecan effectively deactivate the nsp-9 RNA binding protein (protein database code: 6W4B) due to high positive value of -C DOCKER and –CDOCKER interaction energywhich is involved in viral genomic RNA reproduction or on particularly for both, viral replication and virulence.

Keywords: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2.

INTRODUCTION

Near the end of December 2019, a novel coronavirus (2019-nCoV) with a unique characteristic of human-to-human transmission [1] has been originated in Wuhan province of China [2-3]. This infection has marked as dead-threatening to numerous people in China and spread to different nations in a very short period of time. To battle this dangerous COVID-19, various traditional drugs like chloroquine, hydroxychloroquine, remdesivir, and so on, have been attempted and found with certain therapeutic impact in vitro. In any case, the clinical medication response isn't very empowering and toxicity stays an unavoidable issue causing severe effects. This motivated us to examine the restraint of COVID-19 protease by Indian herbal plants [4]. Actually the therapeutic values of the herb are due to the one or more chemical compounds that participated in certain physiological action of the human body, these substances are called phyto-chemicals. Different phytochemicals which are obtained from different parts of plant such as seed, leaves, roots, flowers and fruits can be used in medical purpose[5]. The plants which is used in medical

purpose have many properties such as anti-diabetes action, anti-oxidant, anti-cancer and anti-inflammatory properties [6]. Therefore, many plants can be used as starting material for the preparation of pharmaceutical products which have no bad impact.

Various plants are used in the designing of drugs of modern medicinal system. It was observed that 25% of modern pharmaceutical drugs have designed using medical plants. Now a day it is very need of medical plants in research. Further, researchers have to check the quality, biological activity, safety and clinical efficacy of the numerous plants for its use in medical purposes. It is noticed that many developing scientific methods have been developed to improve the research so that different constituents and its properties can be identified. The beneficial effects of phytochemicals obtained from different plants are tested on doing the experiment animal models [7]. Generally,anti-inflammatory, anticancer, anti-bacterial and anti oxidant properties of phytochemicals have drawn special attention for researcher. Considering different plants, Vasaka or Malabar nut tree is one of the important medical plants. The prominent alkaloid found in Adhatoda leaves is the quinazoline alkaloid known asvasicine [8]. The leaves and foundations of Adhatoda contain the alkaloids l-vasicinone, deoxyvasicine, vasicinolone and vasicinol [9]. Apart from these, plant also contains peganine, Quercetin,kaempferol in their extract [10].In this paper, the different phytochemicals of *Adhatoda vasica* are identified which can be used to cure COVID-19 caused bynsp-9 RNA binding protein[11] by inhibiting the viralRNA production.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Adhatoda vasica* contains vasicine, vasicinone, peganine, Quercetin, kaempferol, etc. It has been well-known that different plants belonging to Acanthaceae family has potential to fight against microbes/viruses. In this study, the phytochemicals are recognized which can be used against COVID-19. Brenda enzyme database can be used to find out different enzymes associated with COVID-19. It has been found that nsp-9 RNA binding protein (protein database code: 6W4B) is involved in viral genomic RNA reproduction or on particularly for both, viral replication and virulence. The detailed method has been described elsewhere.

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". If high positive value of -CDOCKER energy are observed with small difference in –CDOCKER interaction energy and –CDOCKER energy for phytochemicals and enzyme then it was considered that the phytochemicals can fight against the microbial enzyme.The results indicated that kaempferolcan effectively deactivate the enzyme thereby interrupting the metabolic pathway of the nsp-9 RNA binding protein. From the results, high positive values for kaempferolwas found which shows that it can be used to cure COVID-19.Further, quercitin and peganinecan also deactivate the enzyme to a small extent due to small positive -CDocker energy and -CDocker interaction energy). Thus, the effective constituent preventing COVID-19 caused by nsp-9 RNA binding protein virus iskaempferol.

CONCLUSIONS

It was studied that *Adhatoda vasica* plant has the ability to fight against COVID-19. This study was carried out to find the phytochemical responsible for its medicinal action. Using Discovery Studio module of Biovia software, Molecular docking was examined using Discovery Studio module of Biovia softwareso that to the constituentkaempferol is identified which can be used to fight against COVID-19. It was found that kaempferolcan have strong interaction

with the enzyme followed by quercitin and peganine successfully inhibiting the metabolic cycle of the microbe. However vasicinone have negative – Cdocker energy which concluded that this constituent can not be used to cure corona virus. Further, it was noticed that the presence of kaempferol, quercitin and peganine canprovide the medicinal values to *Adhatoda vasica* against COVID-19 caused bynsp-9 RNA binding protein.

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Table 1. Results of C-Docking of phytochemicals with nsp-9 RNA binding protein(PDB: 6W4B)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Vasicine	-103.247	-11.7568	-91.4902
2	Vasicinone	-103.114	-11.3998	-91.7142
3	Quercitin	3.70648	16.1879	12.4814
4	Peganine	3.11654	18.6299	15.5133
5	Kaempferol	11.3134	17.3932	6.0798

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) using *Adhatoda vasica* (Vasak) Extract: An *In silico* Analysis

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ABSTRACT

The outbreak of the novel coronavirus (2019-nCOV) in Wuhan, China, has created a pandemic situation throughout the globe that worsens the public health and economy. Still now, no specific medicines or vaccines are available to combat this deadly virus. Therefore, researchers throughout the globe are working seriously to develop proper drugs to neutralize the negative impact of viral proteins.This study focuses on identification ofquercitinand kaempferol as effective phytochemicals of *Adhatoda vesica* to impart the inhibiting role in viral replication through binding with ADP ribose phosphatase of NSP3 of COVID-19.

Keywords: Phytochemical, Biovia, Vasak, Discovery studio, COVID-19.

INTRODUCTION

Near the end of December 2019, a novel coronavirus (2019-nCoV) with a unique characteristic of human-to-human transmission [1] and results in severe acute respiratory syndrome (SARS) has been originated in Wuhan province of China [2-3]. This infection has marked as dead-threatening to numerous people in China and spread to different nations in a very short period of time. On January 30, 2020, the Director-General of the World Health Organization declared that that the outbreak of 2019-nCoV constitutes a public health emergency of international concern and issued temporary recommendations under the *International Health Regulations* [4-5]. As per the global statistics, the mortality rate is doubled in just 7 days with this deadly virus. Globally more than 3 million people have been already confirmed with COVID-19 positive along with 274,488 death reports as on 10th May, 2020 (WHO reports). The Indian scenario of COVID-19 is also painful. More than 41, 000 people are enlisted with active cases and 2109 people have been already passed away. By the time, situation is getting worse with this viral infection and the mortality graph approaches to skyward. To battle this dangerous COVID-19, various traditional drugs like chloroquine, hydroxychloroquine, remdesivir, and so on, have been attempted and found with certain therapeutic impact in vitro

[8]. Actually, the therapeutic values of different medicinal plants are contributed by some chemical compounds, known as phyto-chemicals. Among different herbs, Vasaka or Malabar nut tree is indigenous to India and well known for its medicinal values. *AdhatodaVasica*Nees belonging to family Acanthaceae, is a small, evergreen shrub with dense branching and offering purple or white flowers. Vasica is most notable for its viability in treating respiratory conditions. The leaves of Vasica are shows strong impact on the respiratory framework. Vasica shows an antispasmodic and expectorant impact, and has been utilized for a considerable length of time with much accomplishment to treat asthma, chronic bronchitis, and other respiratory conditions. The huge pharmacological demand of Adhatoda towards bronchodilatory impact is accepted to be the consequence of its rich grouping of alkaloids [9]. The prominent alkaloid found in Adhatoda leaves is the quinazoline alkaloid known as vasicine [10].Adhatodavasica was also known to treat ulcers initiated by ethanol, pylorus, and aspirin. Apart from these, plant also contains peganine, Quercetin, kaempferol in their extract [11]. Among various viral proteins, papain-like protease (PLpro), 3C-like protease (3CLpro) and spike protein [12] are known to be more important. ADP ribose phosphatase of NSP3 (non-structural protein3) or 6VXS belongs to the PLpro domain and basically helps in viral replication. This study focuses on the identification of the active phytochemicals of *Adhatoda vasica* against novel Coronavirus [13] by inhibiting the viral transcription and replication.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Earlier reportedworks revealed that *Adhatoda vasica* contains vasicine, vasicinone, peganine, Quercetin, kaempferol, etc. The aim of this study was to reveal the active phytochemicals of *Adhatoda vasica* against 2019-nCoV. Online enzyme database source (Brenda) was used to find out the list of active enzymes/proteins, associated with the microbial life cycle. Among various proteins (structural and non-structural proteins), ADP ribose phosphatase of NSP3 (PDB Code:**6VWS**) was chosen for molecular docking which is known for its role in viral replication. The detailed method has been described elsewhere [14].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that quercitin of the *Adhatoda vasica* has the highest influence in deactivating 6VXS, thereby interrupting the viral replication.

CONCLUSIONS

The role of different phytochemicals of *Adhatoda vasica* plant against novel coronavirus (2019-nCOV) was explored via molecular docking (C-DOCK) technique in Biovia software. Among different phytochemicals, quercitin and kaempferol were found to provide significant interaction with ADP ribose phosphatase of NSP3 of COVID-19. On the other hand, other phytochemicals of *Adhatoda vasica* like vasicine, vasicinone, peganine were found to non-effective againstADP ribose phosphatase of NSP3 of COVID-19 as they shown negative values of "- C DOCKER ENERGY". Thus, the medicinal contribution of *AdhatodaVasica*againstCOVID-19is due to the presence of quercitin andkaempferol.

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Table 1.Results of CDocking of phytochemicals with ADP ribose phosphatase of NSP3 of COVID-19

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Vasicine	-1.4622	18.0087	19.4709
2	Vasicinone	-0.8565	13.6178	14.4743
3	Peganine	-1.4936	17.5796	19.0732
4	Quercitin	15.4280	24.5447	9.1167
5	Kaempferol	14.8936	26.6799	11.7863

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) using *Aloe vera* Extract: An *In silico* Analysis

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ABSTRACT

Therecent quick spread of RNA-based deadly virus put a severe threat to the world population via severe acute respiratory syndrome (SARS). The unavailability of specific curing routes to corona infection compels the researchers to find out the way of ayurvedic medication of novel Corona virus. The molecular docking via Biovia software may explore a rapid solution to find out the active phytochemicals to deactivate the ADP ribose phosphatase of NSP3 protein of novel Corona virus. Different phytochemicals of *Aloe barbadensis miller* likealoe-emodin salicylic acid, cinnamic acid and anthraquinone showed effective interaction with theADP ribose phosphatase of NSP3 of COVID-19, related toviral transcription and replication.

Keywords: Phytochemicals, *Aloe vera*,Biovia, Discovery studio, COVID-19.

INTRODUCTION

Near the end of December 2019, a novel coronavirus (2019-nCoV) with a unique characteristic of human-to-human transmission [1] and results in severe acute respiratory syndrome (SARS) has been originated in Wuhan province of China [2-3]. This infection has marked as dead-threatening to numerous people in China and spread to different nations in a very short period of time. On January 30, 2020, the Director-General of the World Health Organization declared that that the outbreak of 2019-nCoV constitutes a public health emergency of international concern and issued temporary recommendations under the *International Health Regulations* [4-5]. As per the global statistics, the mortality rate is doubled in just 7 days with this deadly virus. Globally more than 3 million people have been already confirmed with COVID-19 positive along with 274,488 death reports as on 10th May, 2020 (WHO reports). The Indian scenario of COVID-19 is also painful. More than 41, 000 people are enlisted with active cases and 2109 people have been already passed away. By the time, situation is getting worse with this viral infection and the mortality graph approaches to skyward. Instead of different chemical compounds like chloroquine, hydroxychloroquine, remdesivir, researchers are also motivating to explore medicinal herbs for the treatment of novel Coronavirus [8]. The medicinal

activities of certain herbals are associated with the presence of active compounds, known as phytochemicals. *Aloe vera* plant has been known and utilized for a prolonge time for its excellence, therapeutic and healthy skin properties. *Aloe vera* (*Aloe barbadensis miller*) has been utilized for restorative purposes in a few societies for centuries: Greece, Egypt, India, Mexico, Japan and China. It belongs to Asphodelaceae (Liliaceae) family, and is a shrubby or arborescent, perpetual, xerophytic, delicious, pea-green shading plant [9]. *Aloe vera* contains 75 possibly active phytochemicals , including vitamins (A, C and E), enzymes, sugars, minerals (calcium, copper, magnesium, manganese, potassium, sodium and zinc), saponins, salicylic acid etc [10, 11]. The most widely recognized polysaccharides of this plant are glucomannans [beta-(1,4)- acetylated mannan]. *Aloe vera* contains 12 anthraquinones, which are phenolic compounds generally known as intestinal medicines. Aloin and emodin go about as analgesics, antibacterials and antivirals. It gives 4 plant steroids; cholesterol, campesterol, β-sisosterol and lupeol. All these have anti-inflammatory activity and lupeol additionally has pain relieving properties. Among different viral protein of Coronavirus, papain-like protease (PLpro) is most studied because of its relation to the viral replication.ADP ribose phosphatase of NSP3 (non-structural protein3) or 6VXS (PDB) belongs to the PLpro domain and basically helps in viral replication. This study focuses on the identification of the phytochemical of *Aloe barbadensis miller* responsible to cure COVID-19 caused byADP ribose phosphatase of NSP3 [12]by inhibiting the life cycle of the virus.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis for molecular docking. Earlierliterature revealed that *Aloe barbadensis miller* contains aloin, aloe-emodin, anthraquinone, cinnamic acid, salicylic acid, glucomannan, etc as the active phytochemicals. This work illustrates the recognition of the active phytochemicals of *Aloe barbadensis miller*, might be probablefor curing COVID-19.Brenda is a online enzyme database, which was used to select and target the enzyme. In present manuscript, we have targeted the ADP ribose phosphatase of NSP3 of COVID-19 (PDB code:6VXS), associated with the viral replication. The complete docking procedure was illustrated in earlier document [13].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.Table 1, revealed that that aloe emodin, salicylic acid, cinnamic acid and anthraquinone are the active components which shows the positive " -C-DOCKER ENERGY" with the ADP ribose phosphatase of NSP3 of COVID-19, associated with the viral transcription and replication.

CONCLUSIONS

Molecular docking analysis through "discovery studio" of Biovia revealed that aloe-emodinsalicylic acid, cinnamic acid and anthraquinone are the key phytochemicals of *Aloe barbadensis miller* which showed effective interaction with theADP ribose phosphatase of NSP3 of COVID-19. Other phytochemicals of *Aloe barbadensis miller* like aloin and glucomannan were not shown any information during molecular docking towards deactivating the viral protein. It may be due to steric factors.

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Table 1. Results of C-Docking of phytochemicals with ADP ribose phosphatase of NSP3 of COVID-19

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Aloe-emodin	25.0075	29.7321	4.7246
2	Anthraquinone	13.6454	19.3660	5.7206
3	Cinnamic acid	17.0733	21.9162	4.8429
4	Salicylic acid	18.2504	24.6911	6.4407
5.	Aloin	FAILED	FAILED	FAILED
6.	Glucomannan	FAILED	FAILED	FAILED

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Papain-Like Protease of SARS CoV-2(6W9C) Enzyme using *Mucuna pruriens (Velvet bean)* Extract: An *In silico* Analysis

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ABSTRACT

Novel Coronavirus-2019 is a deadly virus with severe acute respiratory syndrome. This study deals with the recognition of phytochemicals from *Mucuna pruriens* which can fight against COVID-19 by deactivating 6W9C. Different phytochemicals of *Mucuna pruriens* likedopamine and bufotenine showed significant interaction with the Papain-like protease of SARS CoV-2 of COVID-19(6W9C) and therefore, may be used as COVID-19 preventive components.

Keywords: phytochemical, Biovia, Discovery Studio, COVID-19, SARS-CoV-2, *Mucana pruriens*, Dopamine, 6W9C.

INTRODUCTION

Novel Coronavirus (COVID-19) is a transmittable disease that has already created a pandemic situation within a very short period of time. This disease is declared as a pandemic on 11 March 2020 by world health organisation (WHO) [1, 2].The exploration of proper therapies against COVID-19 is the urgent need of current era. Different components of medicinal plantsincluding leaves, roots, bark, fruits, flowers, and seeds are generally utilized to extract the active phytochemicals [3].Among different medicinal herbs, *Mucana pruriens* and its extracts have been long used in tribal communities as a treatment for various diseases [4].It has significant use to treat diseases including Parkinson's diseasebecause ofpresence of L-dopa [5-7].This study explores the possibility of using these against COVID-19. This study reveals on the recognition of the phytochemicals of *Mucana prurient* sresponsible to cure COVID-19.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Reported works showed that*Mucana prurient* consists phytochemicals such as Dopamine, Bufotenine, behenic acid, phytic acid, linoleic acid, genistine, etc.[8,9]. This work is related on the recognition of active phytochemicals of *Mucana pruriens* against COVID-19. The selection of enzyme was performed on "Brenda enzyme database". It has been found thatpapain-like protease (protein database code: 6W9C) of novel Corona virus is involved in viral replication. The complete procedure has been described in the earlier literature [10].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".The active site of the enzyme is displayed in Figure 1. High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.Table 1 shows that 6W9C-Dopamine interaction has the highest positive value of -CDOCKER energy20.3518the value of the difference is 0.4915 between - C DOCKER interaction energy and - C DOCKER energy. Similarly,Bufotenine also showssatisfactory results with a lower difference (5.9241) but having -CDOCKER energy14.2236.Thus, this study explored thatDopaminecan effectively deactivate 6W9Cenzyme thereby interrupting the metabolic pathway of the virus. Higher positive values for Dopaminemakes it the most active phytochemical against6W9C enzyme of the virus. On the other hand, behenic acid, phytic acid, linoleic acid, genistine cannot deactivate the enzyme. Thus, the key phytochemicals preventing COVID-19 caused by 6W9C virus are dopamine and bufotenine.

CONCLUSIONS

The pharmacological activity of different phytochemicals of *Mucana pruriens* against COVID-19 was explored using the Discovery Studio module of Biovia software. Result showed that, among different phytochemicals, dopamine and bufotenine may deactivate the Papain-like protease of novel Corona virus.

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Table 1. Results of CDocking of phytochemicals(*Mucana pruriens*) with Papain-like protease of SARS CoV-2 (6W9C)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Dopamine	20.3518	19.8603	-0.4915
2	Bufotenine	14.2236	20.1477	5.9241
3	Behenic acid	FAILED	FAILED	FAILED
4	Genistine	-82.6411	-5.27716	77.36394
5	Linoleic acid	FAILED	FAILED	FAILED
6	Phytic acid	FAILED	FAILED	FAILED

Figure 1. The active site of the enzyme (6W9C)

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RESEARCH ARTICLE

Prevention of COVID-19 by Blocking ADP Ribose Phosphatase of NSP3 (6W6Y) of SARS CoV-2 using *Mucuna pruriens (Velvet bean)* Extract: An *In silico* Analysis

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ABSTRACT

This article exploresthe interaction of phytochemicals usingmolecular docking with a specific enzyme of SARS CoV-2 by "Biovia Discovery Studio". "Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" is responsible for the outbreak of "Coronavirus disease 2019 (COVID-19)" which has been declared as a pandemic by WHO. The interaction between the phytochemicals present in plant extract of Velvet bean is studied with "ADP ribose phosphatase of NSP3 (6W6Y)" of SARS CoV-2 to explore the specific phytochemical responsible for the prevention of COVID-19. Higher positive values of "-CDocker energy and -CDocker interaction energy" confirmed that Dopamine ofVelvet bean extract may show desirable activity against "SARS-CoV-2 virus".

Keywords: Dopamine, Biovia, Discovery Studio, COVID-19, phytochemical, 6W6Y, SARS-CoV-2,Velvet bean.

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has spread rapidly throughout the entire world creating panic among the human population and has been declared as a pandemic by WHO.[1, 2] However, todate no treatment is established.[3] Thishas created a serious health alarm that needs to be tackled efficiently by discovering medicines against the virus. Numerous medicinal plants consisting certain phytochemicals generally active against various viral diseases.[4] These phytochemicals are effective as well as lower in cost. *Mucana pruriens* belongs to family Fabaceae. The plant extract of *Mucana pruriens* is known to be used by tribal communities for the cure of various snakebites as a toxin moderator [5]. It has significant use to treat Parkinson's disease, as it is rich in L-dopa content [6, 7]. In addition, the seeds of this plant have the potential to assuage Parkinson's disease induced neurotoxocity[8].

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) has been used for analysis. The plant extract consists of phytochemicals named Dopamine, Bufotenine, Behenic acid, Phytic acid, Linoleic acid, etc [9, 10]. The plants which belong to this family are highly active against various viral diseases. This article is intended to focus on investigation of the specific phytochemical/s responsible for preventing"ADP ribose phosphatase of NSP3 (6W6Y)" of SARS CoV-2. The information regarding the enzymes for COVID-19 is extracted from s"Brenda enzyme database." The method of Molecular docking has been employed to recognize the phytochemical responsible against preventing the enzyme, that can disable the "ADP ribose phosphatase of NSP3 (6W6Y)". The method has been elaborated elsewhere [9].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". Fig. 1 Displays the active site of6W6Y enzyme which is indicated as light green color. The conformations of theligands were acquired by "Molecular Dynamic methods".The criteria for identification of a good drug are it must have high positive value of -CDOCKER energy, in addition to that minorvariance between -CDOCKER energy and -CDOCKER interaction energytodiscover the drug. Table 1 displays that Dopamine is the keyphytochemical which can effectively inhibit COVID-19 disease.

CONCLUSIONS

This piece of work explored that *Velvet bean* can inhibit COVID-19 attack. Using "Discovery Studio module of Biovia software", it has been identified that Dopamine can significantly interact with "ADP ribose phosphatase of NSP3 of COVID-19 (6W6Y)" to deactivate the virus. The higher positive value of - C DOCKER energy and the low difference in - C DOCKER interaction energy and - C DOCKER energy makes Dopaminea medicinally important phytochemical of *Velvet bean* towards the treatment of COVID-19.

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Table 1. Results of CDocking of phytochemicals with "ADP ribose phosphatase of NSP3 of COVID-19 (6W6Y)" (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Dopamine	17.6205	16.7135	-0.907
2	Bufotenine	11.6875	23.1651	11.4776
3	Behenic acid	Failed	Failed	Failed
4	Phytic acid	Failed	Failed	Failed
5	Linoleic acid	Failed	Failed	Failed

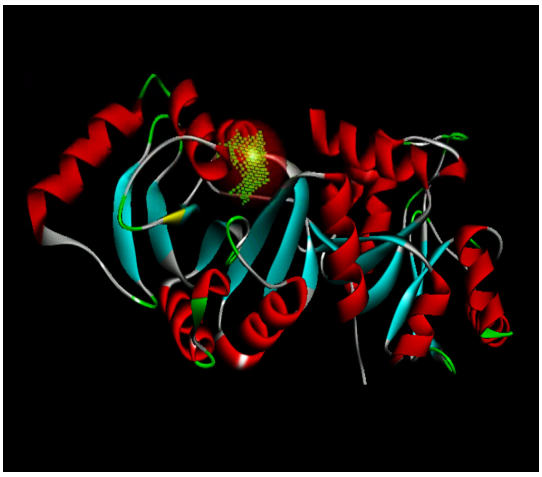

Figure 1. Active site of "ADP ribose phosphatase of NSP3 of COVID-19 (6W6Y)"enzyme.

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RESEARCH ARTICLE

In silico Analysis of Polyvinyl Alcohol and Polydichloroethylene Compatibility in a Blend

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ABSTRACT

A blend is formed withthe combination of two or more components. The compatibility of polyvinyl alcohol and Dichloroethylene was studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram, Blends Analysis-energy distribution, energy distribution and mixing energy.The results indicated that the pair can become compatible at both low and high temperature Phase diagram indicated that a single phase can be obtained above 500K which was the critical temperature. The coordination number was found to be 5.83+/-0.05.The highest number of configurations with respect to energy level was found to be 0.4kcal/mol. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend , in silico, polyvinyl alcohol, Dichloroethylene.

INTRODUCTION

Blends or composites are formed with combination of more than one component where components do retain their identity in the mixture. As it is very difficult to find multiple properties in a single material, it is advisableto combine different components thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property.Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance.. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside

buildings. All the above mentioned examples relied on laboratory experiments.Usually blends are prepared by trial and error method andthis technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs.

Among the various polymers, polyvinyl alcohol (PVA) is a promising material due to its high dielectric strength, easy film formation, adhesiveness and whose properties can be controlled by dopant concentrations [8, 9]. The film forming ability of PVA is widely used in packaging industry to form strong polymeric films. It is because of their high mechanical strength, environmental stability and easy processability [10]. On the other hand, PVA is non-toxic, semicrystalline, hydrophilic, biocompatible and easily soluble in water [11].This study is intended to identify the interaction of polyvinyl alcohol and Dichloroethylene to form blends.

MATERIALS AND METHODS

Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. Polyvinyl alcohol and Dichloroethylene were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. Polyvinyl alcohol was used as the base and Dichloroethylene was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed.

RESULTS AND DISCUSSION

In this work the use of polyvinyl alcohol and Dichloroethylene as potential components of a blend was analyzed using Biovia Materials Studio.

Free Energy of Mixing: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend. The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution.Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will lead to a homogeneous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyvinyl alcoholand poly Dichloroethylene with negative value of mixing energy, which may lead to form a perfect blend with a high effort.

Chi Parameter: The Flory–Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a low value of χ for chemically dissimilar polymers indicate good mixing.Figure 2 show that the value of x highest at the temperature50K and it's value lowest at temperature500K.At first the value of x decreases with increase in temperature then it slowly increases after that when we increase the temperature the value of x decreases to a minimum value.Thisagrees with the free energy of mixing for the blend.

Coordination Number: "The coordination number Z_{ij} is the number of molecules of type *j* that can be packed around a single molecule of type *i*". In this study the coordination number was found to be 5.83+/-0.05.

Phase Diagram: The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).
b. "Fragmented metastable regions existed between binodals and spinodals" , and
c." The two-phase separated regions of immiscibility are bordered by the spinodals."

Energy Distribution for Blend: The generation of different orientations using the pairs method may lead to configurations of varying energy levels. Figure 5 shows the plot of frequency (P(E)) against energy levels. This show that the curve is somewhat asymmetrical in nature,long chain and low energy tail.The number of configurations with energy higher than the peak value decreased significantly. The maximum frequency was observed for the energy level of around -2.00 kcal/mol.

Mixing Energy: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 6 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that the value of mixing energy increases with increase in temperature after some time at a particular temperature the value of mixing energy decreases with increase in temperature.The value of mixing energy varied between Temperatures 50K to 500K it is very much possible to mix the two components at any feasible temperature with least mixing energy value.

CONCLUSIONS

The possibility of use of polyvinyl alcohol and dichloroethylene to form a homogeneous blend was explored using Biovia Materials Studio. The coordination number was found to be 5.83+/-0.05.The maximum number of configurations with respect to energy level was found to be 0.4Kcal/mol.Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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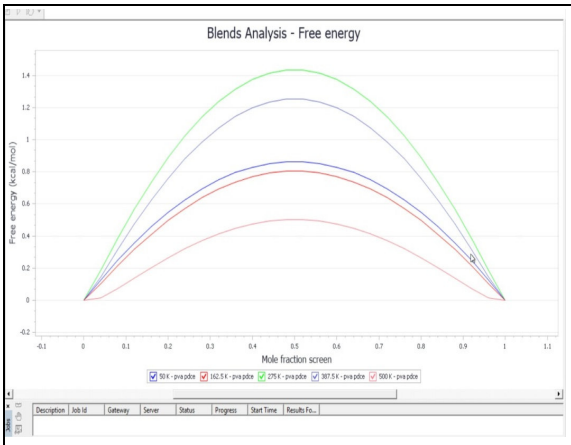

Figure 1. Free energy change with mole fraction of Dichloroethylene at different temperatures

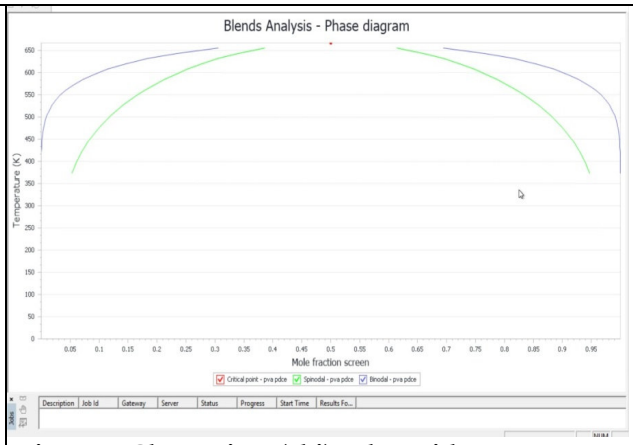

Figure 2. Change in χ (chi) value with temperature

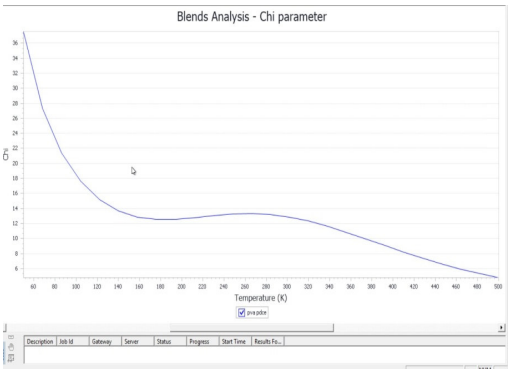

Figure 3. Phase diagram

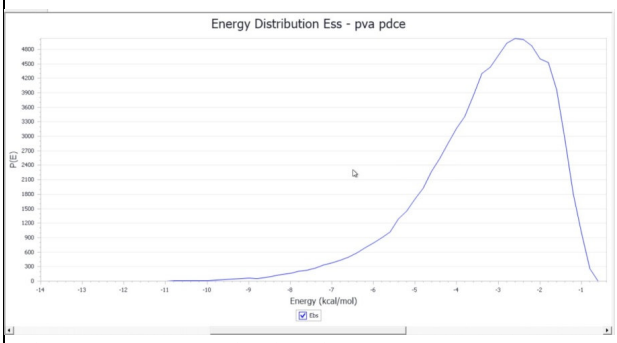

Figure 4. Energy distribution

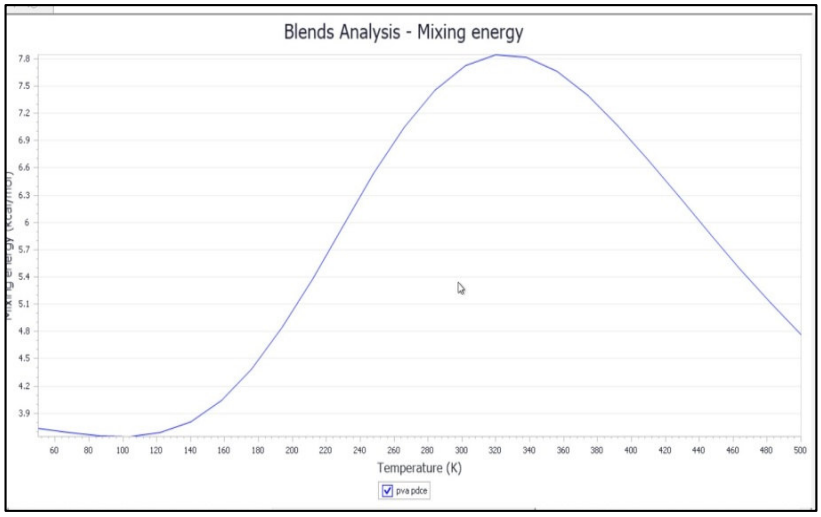

Figure 5. Mixing energy

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RESEARCH ARTICLE

In silico Analysis of Polyvinyl Alcohol and Polydichloroethylene Incorporated Compatibility in a Blend

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ABSTRACT

A blend is formed withthe combination of two or more components. The compatibility of polyvinyl alcohol and polydichloroethylene incorporated were studied to form a miscible blend using Biovia Materials Studio. The compatibility of the two components was demonstrated based on free energy of mixing, chi parameter, phase diagram and mixing energy. The results indicated that the pair can become compatible only at high temperature. Phase diagram indicated that a single phase can be obtained above 750 K which was the critical temperature. The coordination number was found to be 6.97 +/- 0.04. The highest number of configurations with respect to energy level was found to be -1.95kcal/mol. This study will not only help to determine pairs without performing laboratory experiments but also less time consuming and low cost process.

Keywords: Blend, *In silico*, polyvinyl alcohol, Polydichloroethylene incorporated.

INTRODUCTION

Blends or composites are formed with combination of more than one component where components do retain their identity in the mixture. As it is very difficult to find multiple properties in a single material, it is advisableto combine different components thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3].There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion.

Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.Usually blends are prepared by trial and error method andthis technique is a low cost and less time consuming method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs.

Among the various polymers, polyvinyl alcohol (PVA) is a promising material due to its high dielectric strength, easy film formation, adhesiveness and whose properties can be controlled by dopant concentrations [8, 9]. The film forming ability of PVA is widely used in packaging industry to form strong polymeric films. It is because of their high mechanical strength, environmental stability and easy processability [10]. On the other hand, PVA is non-toxic, semi-crystalline, hydrophilic, biocompatible and easily soluble in water [11].Researchers have found applications of glycopolymers (synthetic polymers containing pendant carbohydrate groups) in the separation and removal of toxins and bacteria, tumor cell recognition and glucose-responsive insulin delivery [12].

MATERIALS AND METHODS

Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. Polyvinyl alcohol and polydichloroethylene incorporated were prepared using the build menu of Materials Studio. The structure of the components were optimized using the components were used in blends->calculation menu of Materials studio. Polyvinyl alcohol was used as the base and Polydichloroethylene incorporated was used as screen. After calculation the blends->analysis menu of Materials studio was used to generate various data. The data were analyzed and the compatibility of the components to form a blend was analyzed.

RESULTS AND DISCUSSION

Free Energy of Mixing: A blend is said to be miscible if it is homogeneous. A negative value of free energy of mixing indicates that mixing is spontaneous and can lead to a homogeneous blend.The components can mix to form a miscible blend only if the entropic contribution to free energy exceeds the enthalpic contribution.Figure 1 shows that the free energy involved in mixing is always negative or less than zero for the temperatures studied. The free energy decreases with increase in temperature (upto 275 K) as evident from Eq. 1 and free energy increases with increase in temperature. The results indicated that the blend will not lead to a homogeneous mixture for the temperature range studied (50 to 500 K). The trend shows a very good compatibility between polyvinyl alcoholand poly Polydichloroethylene incorporated with negative value of mixing energy, which may lead to form a perfect blend with significantly less effort.

Chi Parameter: The Flory-Huggins χ parameter describes the excess free energy of mixing and helps to explain phase behavior for polymer blends and block copolymers. For polymers which are not chemically similar, a significant mismatch in cohesive energy density leads to a high χ value and, hence, a greater driving force for phase separation. Thus a low value of χ for chemically dissimilar polymers indicate good mixing.Figure 2 shows that the χ value is high for the temperature range studied (50 to 500 K) indicating demixing. The χ value decreased with increase in temperature.Thus at high temperature there is a possibility to form a miscible blend.This agrees with the free energy of mixing for the blend.

Coordination Number: "The coordination number Z_{ij} is the number of molecules of type *j* that can be packed around a single molecule of type i In this study the coordination number was found to be 6.97 +/- 0.04.

Phase Diagram: The compatibility of binary mixtures can be visualized by phase diagrams. Figure 3 shows the phase diagram for the two components of the blend. There are three regions of different degree of miscibility:

a. The single-phase miscible region existed above the critical temperature of around 750 K. This value supported the fact that a single phase blend can be formed at a high temperature (higher than 750 K).
b. "Fragmented metastable regions existed between binodals and spinodals", and
c. "The two-phase separated regions of immiscibility are bordered by the spinodals".

Energy Distribution for Blend: The generation of different orientations using the pairs method may lead to configurations of varying energy levels. Figure 5 shows the plot of frequency (P(E)) against energy levels. It shows that the distribution is somewhat asymmetrical and there is a long, low-energy tail. The number of configurations with energy higher than the peak value decreased significantly. The maximum frequency was observed for the energy level of around -2.00 kcal/mol.

Mixing Energy: A small value of mixing energy can favor the mixing process. Thus, the temperature at which the mixing energy is low can be chosen for mixing. Figure 6 shows that the mixing energy for the system was small for the temperature range studied. The graph indicated that an increase in temperature increased the mixing energy. It also shows that mixing energy gradually increases with increase intemperature with varying the temperature from 50 K to 500 K. So, it is very much possible to mix the two components at any feasible temperature with least mixing energy value.The formation of nonhomogeneous blend with polyvinyl alcohol as base might help formation of blend with high mechanical strength. This might have an application as packaging material and adsorbent.

CONCLUSIONS

The possibility of use of polyvinyl alcohol and Polydichloroethylene incorporated to form a homogeneous blend was explored using Biovia Materials Studio. The compatibility was analyzed based on free energy of mixing, chi parameter and mixing energy. The coordination number was found to be 6.97 +/- 0.04. The maximum number of configurations with respect to energy level was found to be -1.95 kcal/mol. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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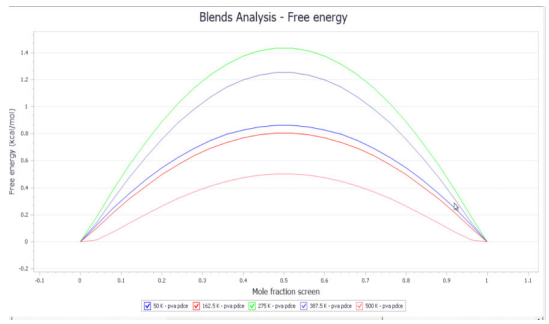

Figure 1. Free energy change with mole fraction of Polydichloroethylene incorporated at different temperature

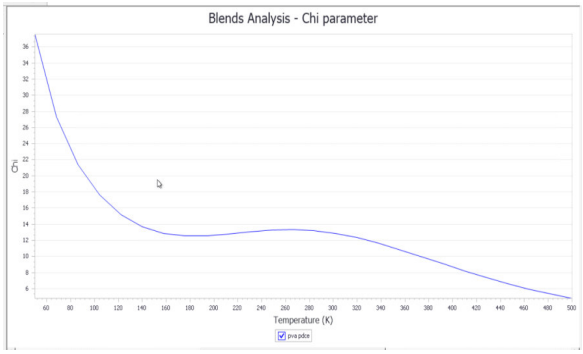

Figure 2. Change in χ (chi) value with temperature

Figure 3. Phase diagram

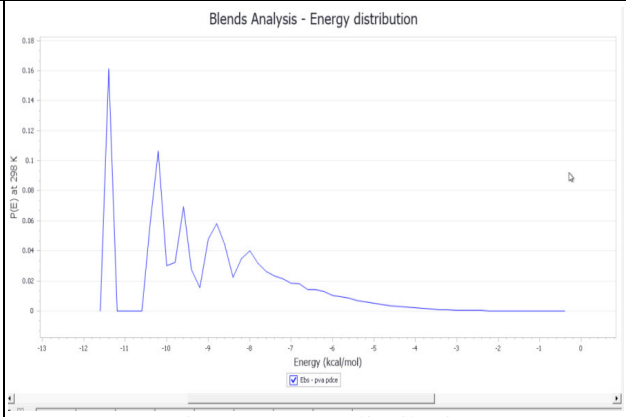

Figure 4. Energy distribution

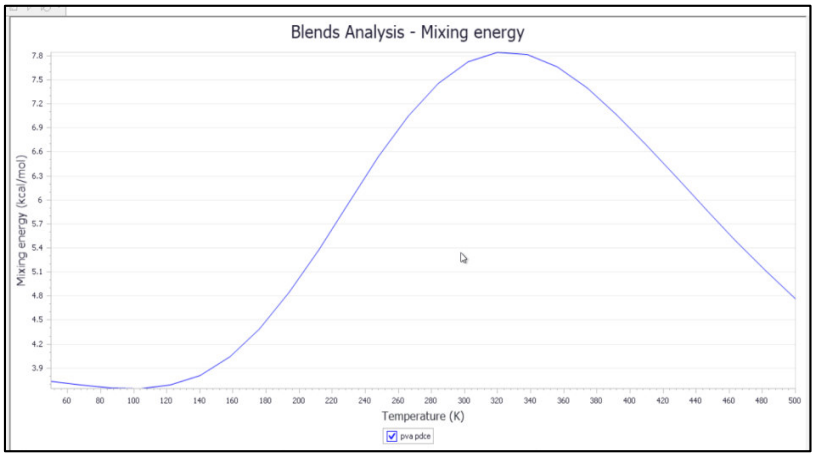

Figure 5. Mixing energy

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking (6M03) SARS-CoV-2 Enzyme using *Helichrysum chasmolycicum* Extract: An *In silico* Analysis

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ABSTRACT

Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PDB No. 6M03 of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy "indicated that Asteraceae of *Helichrysum chasmolycicum* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has danger the whole world. It has been signify as a epidemic [1], [2]. However, till now there is no established treatment [3]. There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4]. Their phytochemicals will be low-cost but effective. *Helichrysum chasmolycicum* belongs to family *Asteraceae*. It contains HEXADECANOIC ACID, 3,5-dihydroxy-3,4,7-trimethoxyflavone, KAEMPFEROL, APIGENIN, PALMITIC ACID etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Helichrysum chasmolycicum* contains HEXADECANOIC ACID, 3,5-dihydroxy-3,4,7-trimethoxyflavone, KAEMPFEROL , APIGENIN, PALMITIC ACID. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6M03 and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract,that can deactivate the PDB No. 6M03 viral protein. The detailed method has been described elsewhere [5,6].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSION

It was identified that *Helichrysum chasmolycicum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that PALMITIC ACID can significantly interact with the viral PDB NO. 6M03.

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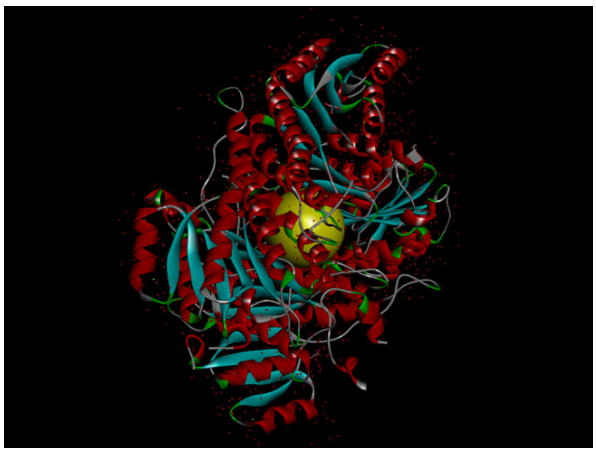

Figure 1. Active site of (SARS-CoV-2)enzyme

Table 1. Results of CDocking of phytochemicals with PDB NO. 6M03 (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	HEXADECANOIC ACID	37.7707	33.9444	-3.8263	
2	3,5-dihydroxy-3,4,7-trimethoxyflavone	20.7036	41.4785	20.7749	
3	KAEMPFEROL	29.1507	37.8341	8.6834	
4	APIGENIN	29.8714	36.3229	6.4515	
5	PALMITIC ACID	70.9459	63.3541	-7.5918	Maximum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6lvn Enzyme using *Acacia* Extract: an *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PDB NO. 6LVN of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy "indicated that DigalIic Acid of Acacia extract can effectively fight against"SARS-CoV-2 virus"

Keywords: phytochemicals, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" is an infectious disease caused by newly discovered coronavirus.[1][2], However, till now there is no vaccine nor any medicine specifically approved for the treatment of COVID-19.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective .*Acacia* belongs to family Fabaceae. It contains Gallic acid, Kaempferol, Digallic acid, Apigenin and Catechin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that Acacia contains Gallic acid, Kaempferol, Digallic acid, Apigenin and Catechin. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6LNV and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract that can deactivate the PDB No. 6LNV viral protein. The detailed method has been described elsewhere.

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Digallic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that Acacia plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that DigalIic Acid can significantly interact with the viral PDB NO. 6LNV.

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Table 1. Results of CDocking of phytochemicals with PDB NO. 6LNV (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Catechin	17.2704	25.435	8.1646	
2	Apigenin	10.7132	15.5728	4.8596	
3	DigalIic Acid	27.3652	19.92	7.4452	Maximum inhibition of viral protein
4	Ellagic Acid	FAILED			
5	Gallic Acid	21.9761	18.3891	3.5870	
6	Kaempferol	9.93466	14.5704	4.6358	Minimum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking 6W4B Enzyme using *Acacia* Extract: an *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PDB NO. 6W4B of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy "indicated that DigalIic Acid of Acacia extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemicals, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" caused by an infection with SARS-CoV-2.[1][2], There is currently no treatment specifically approved for COVID-19,and no cure for the infection[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [9].Their phytochemicals will be low-cost but effective .Acacia belongs to family Fabaceae. It contains Gallic acid, Kaempferol, Digallic acid, Epigenin, Catechin and Ellagic Acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that Acacia contains Gallic acid, Kaempferol, Digallic acid, Epigenin, Catechin and Ellagic Acid. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6W4B and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract that can deactivate the PDB No. 6W4B viral protein. The detailed method has been described elsewhere.

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Digallic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Acacia plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that DigalIic Acid can significantly interact with the viral PDB NO. 6W4B.

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1.Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV)". World Health Organization (WHO). Archived from the original on 31 January 2020. Retrieved 11 February 2020.
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Table 1. Results of CDocking of phytochemicals with PDB NO. 6W4B (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	CATECHIN	23.1586	30.2456	7.0870	
2	EPIGENIN	19.3234	25.4012	6.0778	
3	DIGALLIC ACID	35.131	28.3744	6.7566	Maximum inhibition of viral protein
4	ELLAGIC ACID	13.2638	22.1148	8.8510	Minimum inhibition of viral protein
5	GALLIC ACID	22.2054	19.2437	2.9617	
6	KAEMPFEROL	19.9763	24.7447	4.7684	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP ribose phosphatase of NSP3 (6W6Y) by using *Eclipta prostrata* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PDB No. 6w6y of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy "indicated that *Asteraceae* of *Eclipta prostrata* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has menace the whole human kind. It has been proclaim as a epidemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]*Their phytochemicals* will be low-cost but effective. *Eclipta prostrata* belongs to family *Asteraceae*. It contains heptadecane etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Eclipta prostrata* contains heptadecane. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6w6y and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract,that can deactivate the PDB No. 6w6y viral protein. The detailed method has been described elsewhere [5,6].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSION

It was identified that *Eclipta prostrata* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that heptadecane can significantly interact with the viral PDB NO. 6W6Y.

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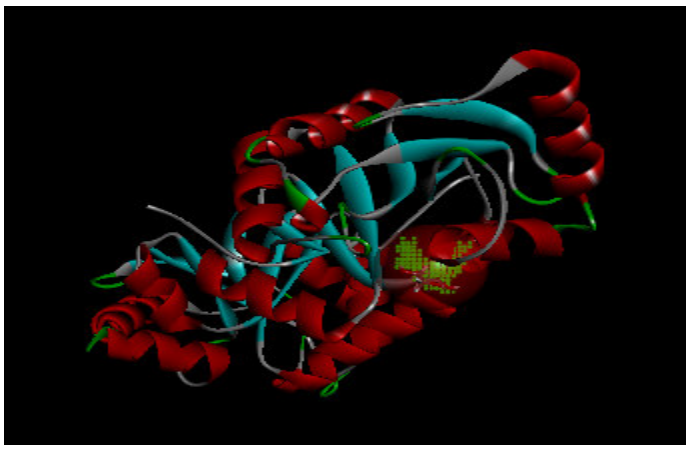

Figure 1. Active site of (COVID-19) enzyme

Table 1. Results of CDocking of phytochemicals with PDB NO. 6w6y (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Heptadecane	25.4401	24.1332	-1.3069

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking ADP Ribose Phosphatase of NSP3 (6VXS) of using *Trigonella foenum - graecum* Extract: An *In-silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PDB No. 6VXS of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy "indicated that Trigonelline of *Trigonella Foenum*-Graecum extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemicals, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" is a disease caused by SARS-Cov-2 that can trigger respiratory tract infection.[1][2], At this time, there are no specific vaccines or treatment for COVID-19 .[6]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[9]Their phytochemicals will be low-cost but effective.*Trigonella foenum-graecum* belongs to family Fabaceae. It contains Lysine,Sapogenins ,Trigonelline, Coumarin and Nicotinic Acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Trigonella Foenum*-Graecum contains Lysine,Sapogenins ,Trigonelline, Coumarin and Nicotinic Acid. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6VXS and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the PDB No. 6VXS viral protein. The detailed method has been described elsewhere.

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy".The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.
Table 1 shows that Trigonelline is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Trigonella foenum-graecum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Trigonelline can significantly interact with the viral PDB NO. 6VXS.

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Table 1. Results of CDocking of phytochemicals with PDB NO. 6VXS (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Lysine	24.2644	27.7391	3.4747	
2	Coumarin	14.6119	18.3165	3.7046	Minimum inhibition of viral protein
3	Trigonelline	25.658	24.8741	0.7839	Maximum inhibition of viral protein
4	Sapogenins	16.3381	23.4088	7.0707	
5	Nicotinic Acid	16.2384	19.7583	3.5199	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking Nsp9 RNA Binding Protein of SARS CoV-2 (6W4B) Enzyme using *Allium sativum* Extract: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PDB No. 6W4B of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy "indicated that Amaryllidaceae of *Allium sativum* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threat the whole human kind. It has been demonstrate as a epidemic [1][2]. However, till now there is no established treatment [3]. There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Allium sativum* belongs to family Amaryllidaceae. It contains ferulic acid, Caffeicacid, Coumaric acid, Sinapic acid, Vanilic acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Allium sativum* contains ferulic acid, Caffeicacid, Coumaric acid, Sinapic acid, Vanilic acid. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6W4B and controlling of COVID-19. Brenda enzyme database was

used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract,that can deactivate the PDB No. 6W4B viral protein. The detailed method has been described elsewhere [5,6].

RESULTS AND DISCUSSION

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CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSION

It was identified that *Allium sativum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Caffeic acid can significantly interact with the viral PDB NO. 6W4B.

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Table 1. Results of CDocking of phytochemicals with PDB NO. 6W4B (receptor)

SL . NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	ferulic acid	18.9853	21.8066	2.8213	
2	Caffeic acid	19.9917	20.7511	0.7594	Maximum inhibition of viral protein
3	Coumaric acid	18.7974	20.5886	1.7912	Minimum inhibition of viral protein
4	Sinapic acid	-213.203	-76.4474	136.7556	
5	Vanilic acid	19.3633	24.2401	4.8768	

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RESEARCH ARTICLE

COVID-19 Prevention by Blocking NSP15 Endoribonuclease (6VWW) from SARS CoV-2 of using *Ficus religiosa* Extract: An *In-silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "NSP15 Endoribonuclease of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Bergaptol of *Ficus religiosa* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has scared the the people globally. It has killed many people globally. Thus, has been declared as pandemic by WHO [1][2].However, the people working on this fails to discover any medicines till now [3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases[4,5].*Their phytochemicals* will be low-cost but effective.*Ficus religiosa* belongs to family Moraceae. The leaves of the plants contain Glucose, Asteriod and Mennos, Phenolic while its bark is rich in Vitamin K, tainen and Phaetosteroline. etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Ficus religiosa* contains Glucose, Asteriod and Mennos, Phenolic while its bark is rich in Vitamin K, tainen and Phaetosterolineetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting NSP15 Endoribonucleaseand controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking

method has been used to identify the phytochemical from the plant extract thatcan deactivate the NSP15 Endoribonuclease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Heptadecane is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Ficus religiosa leaves* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Bergaptol can significantly interact with the viralNSP15 Endoribonuclease.

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Table 1. Results of CDocking of phytochemicals with NSP15 Endoribonuclease (Receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	REMARKS
1	Lanosterol	-82.6435	34.3813	48.2622	
2	Beta-sitosterolglucoside	-53.6586	50.7329	2.9257	
3	Bergapten	8.0972	18.1749	10.0777	
4	Bergaptol	13.4735	18.6356	5.1621	Maximum inhibition of viral protein
5	stigmasterol	-56.1569	42.6584	13.4985	

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RESEARCH ARTICLE

COVID-19 Prevention using *Bacopa monnieri* L. Extract by Blocking COVID-19 Main Protease in Apo form (SARS-CoV-2 Main Protease) Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "main protease of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Luteolin of *Bacopa monnieri* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is most infectious disease in current situation. Its become pandemic and affecting Human race day by day[1][2],till now there is no proper treatment available to inhibit its activity[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases[4].*Their phytochemicals* will be low-cost but effective.*Bacopa monnieri* belongs to family plantaginaceae. It contains apigenin, luteolin, nicotine, D.monnitol etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Bacopa monnieri* contains apigenin, luteolin, nicotine, D.monnitol etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting main protease and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the main protease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Luteolin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Bacopa monnieri* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Luteolin can significantly interact with the viralmain protease.

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Table 1. Results of CDocking of phytochemicals with main protease (receptor)

SL .NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Luteolin	21.2948	24.9445	3.6497	Maximum inhibition of viral protein
2	Apigenin	20.9862	26.5621	5.5759	
3	(S)-nicotine	-0. 991833	19.3516	20.343433	
4	D. Mannitol	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Bacopa monnieri* (Water Hyssop) L. Extract by Blocking 2019- nCoV HR2 Domain (SARS-CoV-2 S2 Subunit) Enzyme: An *In silico* Analysis

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ABSTRACT

The COVID -19 (Corona virus 2019) is a communicable disease transmitted by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),the genus of Betacorona virus.This causes illness like sore throat,fever,dry cough,tiredness,shortness in breath,chest pain with some other respiratory complexities and in serious cases it causes loss of speech , difficulty in breathing ,proceed to pneumonia and later death.This epidemic affecting millions of people is creating a matter of shiver & shock worldwide and slowly turning pandemic from epidemic. The disease day by day is mushrooming up and taking a lot of lives, which is now a great matter of concern. The researchers, scientists and health experts are now in a hurry to invent a drug to overcome this epidemic. However,the main aim of this study is to extract plant phytochemicals and use them in designing drugs rather than using any synthetic chemicals,which will be overrated and time consuming and non guaranteed having many more side effects.Phytochemicals are biologically active plant chemicals found in different parts of the plant like leaf, fruits, root and flowers. It has been studied that the *Bacopa monnieri* L. *(Water hyssop*) plant extract is expected to cure the so called CV19 or COVID -19 caused by (SARS-CoV-2). The virus contains (2019-NCOV HR2 DOMAIN)SARS-coV-2 S2 subunit enzyme which is reported to be very crucial for the survival of the organism.The molecular docking of the phytochemicals with the microbial enzyme was studied using Biovia Discovery Studio. The strength of the interaction was evaluated based on -CDocker energy and -CDocker interaction energy. High positive values for both the parameters indicated that out of different phytochemicals luteolincan effectively deactivate the enzymatic metabolic activity thereby interrupting the life cycle of (SARS-CoV-2) virus.

Keywords: Phytochemical, BIOVIA, Discovery studio, COVID-19, SARS-CoV-2, *Bacopa monnieri* L.

INTRODUCTION

In December 2019, a novel coronavirus called SARS-CoV-2 has resulted in the outbreak of a respiratory illness known as COVID-19. It's a communicable disease resulting in the ongoing 2019–20 coronavirus pandemic with serious fatal implications for countries with ageing populations. The World Health Organization (WHO) accredited the 2019–20 coronavirus outbreak a Public Health Emergency of International Concern (PHEIC) on 30 January 2020, and a pandemic on 11 March 2020[1][2].Some of the first cases of the epidemic were reported in December 2019 at Wuhan, the capital of China's Hubei province, which has since escalated globally and turned pandemic[3][4]. Since then, the virus has spread to nearly every country, leading the World Health Organization (WHO) to declare a pandemic.The new coronavirus has been responsible for millions of infections globally, causing hundreds of thousands of deaths. The United States has seen the highest number of these deaths.

The first people with COVID-19 had links to an animal and seafood market. This suggests that animals initially transmitted the virus to humans. Then, people with no connections to the market developed the disease, confirming that humans can pass the virus to each other[5].Unfortunately any kind of preventive or molecular drugs or vaccines couldn't been developed yet due to continuous mutationaccording to geographic regions of the virus[6].However, rather than vaccinations, where attenuated antigenic materials are used to stimulate an individual's immune system,Anti-viral targeting may be approached (which is known as' targeted therapy'), where antiviral drug is designed to identify the viral proteins, or parts of proteins, can be disabled. Among different sources of natural products, plants have been a source of novel chemical substance, which serves as starting materials for a number of old and new pharmaceutical products(7).

Research is needed in the field of medicinal plants are huge, but are balanced by the potential health benefits and the enormous size of the market. Research into the quality, safety, biological activity, and clinical efficacy of the numerous plants in common usage is required. Newly fledgling scientific techniques and approaches have been used in the growing area of medicinal plant research, for the investigation of constituents and determination of biological activity of medicinal plants & herbs. Evidence for the benificial effects of selected plants is generally based on experiments demonstrating a biological activity in a relevant in vitro bioassay or experiments using animal models. Plants that demonstrated anticancer, antioxidant, anti-inflammatory, immunostimulatory, and antimicrobial properties have received research attention.(8)*Bacopa monnieri* L.(*Waterhyssop)plant* belongs to family plantaginaceae. The leaves extract of this plant is used to cure diseases like leprosy, lupus, varicoseulcers, eczema, psoriasis, diarrhea, fever, amenorrhea etc.The plant is seen at southern and Eastern India,Australia,Europe,Africa,Asia,and North & South America.*Bacopa monnieri* L.*plant* contain phytochemicals like apigenin, luteolin,nicotine, D. Mannitol etc. There is high possibility that these phytochemicals play a very major role in curing COVID-19. However, there is no report identifying the specific phytochemical responsible to cure CV19. Coronaviruses typically affect the respiratory tracts of birds and mammals, including humans.Most recently, authorities identified a new coronavirus outbreak in China that has now reached other countries. The virus is called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and it can cause COVID-19.Scientists found evidence of human coronaviruses in the 1960s, in the noses of people with the common cold.Human coronaviruses that are particularly prevalent include 229E, NL63, OC43, and HKU1.

The name "coronavirus" comes from the crown-like projections on their surfaces. "Corona" in Latin means "halo" or "crown."Coronaviruses belong to the subfamily Coronavirinae in the family Coronaviridae.Doctors currently recognize seven types of coronavirus that can infect humans.Common types include:-229E (alpha coronavirus), NL63 (alpha coronavirus), OC43 (beta coronavirus), HKU1 (beta coronavirus). Rarer strains that cause more severe illnesses include MERS-CoV, which causes the disease MERS, and SARS-CoV, the virus responsible for SARS.In 2019, a new strain, called SARS-CoV-2, started circulating, causing the disease COVID-19.(9)(10).Coronavirus disease 2019 (COVID-19) is a communicable disease infested by severe acute respiratory syndrome coronavirus 2 (SARS-

CoV-2).[11] Genetic analysis has revealed that the coronavirus genetically clusters with the genus Betacoronavirus, in subgenus Sarbecovirus (lineage B) together with two bat-derived strains. It is 96% identical to the whole genome level of other bat coronavirus samples (BatCov RaTG13)[12][13].Those infected with the virus may be asymptomatic or develop flu-like symptoms, including fever, cough, fatigue, and shortness of breath, tiredness, restlessness etc. Emergency symptoms include difficulty breathing, persistent chest pain or pressure, confusion, difficulty waking, and bluish face or lips. Immediate medical attention is advised to the patient, if these symptoms are seen. Symptoms like nausea, vomiting, and diarrhea have been observed in varying percentages [14][15]. It spreads like a cold or flu through the expelled airborne nasopharyngeal droplets from a person with infection of COVID-19 or through close contact. When inhaled or came in contact with eyes, nose or mouth, the virus can settle down in the lungs, where it begins to grow which can be life-threatening later. However, it is possible to control the disease by inhibiting the metabolic pathway of the microorganism. This study focuses on the identification of the phytochemical of *Bacopa monnieri* L. *plant* , which may be responsible to cure COVID-19 caused by(SARS-CoV-2)by inhibiting the protien pathway.

MATERIALS AND METHODS

Software used

Discovery studio module of BIOVIA software (Dassault Systemes of France) is used for analysing the entire study. The software utilizes machine learning techniques to predict the level of molecular interaction between the ligand and enzyme.

List of phytochemicals

The phytochemicals are non-nutritive chemical compounds produced by plants, generally to help them thrive or thwart competitors , predators, or pathogens. Phytochemical is a term that refers to a variety of plant-derived compounds with therapeutic acivities such as anticarcinogenic ,antimutagenic ,anti-inflammatory,& antioxidant properties.They are the secondary metabolites produced from plants which has the potential against the threats like bacteria,virus,fungi etc. to protect the plant itself. The phytochemicals are present in different parts of the plants like ;root, fruits, flowers,leaves and bark.When these parts are consumed by human they act like the divine weapons against the diseases and also build strong immunity. Some phytochemicals are still using as poison and traditional medicines in various parts of the country. Several researches and studies have been showed that *Bacopa monnieri L. contains phytochemicals like Apigenin*, Luteolin, Nicotine, D.mannitol etc. It has been already proved that Bacopa monnieri L. plant belongs to Plantaginaceae family ,Lamiales order and is an angiosperm. The plant is otherwise named as water hyssop, waterhyssop, brahmi, thyme-leafed gratiola, herb of grace, and Indian pennywort. It's is a perennial, creeping herb native to the wetlands of southern and Eastern India, Australia, Europe, Africa, Asia, and North and South America. It has already been established that the plant has potential against CV19. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-1 or CV19.

Enzyme found in(SARS-CoV-2)

It has been proved that COVID-19 can cause as a result of (SARS-CoV-2), severe acute respiratory syndrome coronavirus- 2 infestation. Various metabolic cycles have been seen in the viral life cycle for its survival. These metabolic cycles are regulated by different enzymes. Brenda enzyme database was used to identify and list different enzymes found in (SARS-CAOv-2). It has been found that (SARS-coV-2 S2 subunit) enzyme (protein database code 6LVN) is most likely involved with RNA synthesis of virus, which is found in extracellular matrix in order to survival of the microbe i.e:CV19.

Molecular docking

The Discovery studio module of Biovia software was used for identifying molecular interaction and performs molecular docking. This method has been used to identify the phytochemical from the plant extract that act as a ligand and form a strong covalent bond with the viral protein to successfully inhibit the microbe. The BIOVIA discovery studio is used to identify the interaction between the enzyme and the ligand & perform the molecular docking of Biovia software was used for identifying molecular interaction and perform molecular docking. In this process firstly, the sdf files for the phytochemicals found in the *Bacopa monnieri* L. plant were downloaded from the website (PUBCHEM). The protein database code of the enzyme was identified from the website (RCSB).The active site of the enzyme was identified via "receptor cavity" protocol found under "receptor-ligand interaction" option. Molecular docking was done using the CDocker protocol of BIOVIA software under "receptor-ligand interaction". The enzyme molecule was treated as the receptor molecule while the phytochemical was treated as the ligand. The "-CDOCKER_ENERGY" and "-CDOCKER_INTERACTION_ENERGY" were used as indicator for the quality of the molecular docking. The highest positive value of those indicators represented a good interaction between the ligand and the receptor. Hence, the interactions with high values may indicate the major phytochemical responsible for curing the disease.

RESULTS AND DISCUSSION

Fig. 1 shows the active site of the (SARS- cov-2 S2 subunit) enzyme. The active site appears as light green color. CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy of the result. The ligand conformations were obtained by Molecular Dynamic(MD) methods.Based on the internal ligand strain energy and receptor-ligand interaction energy, -CDOCKER energy was calculated. The energy of the non-bonded interaction that exists in between the protein and the ligand is signified by -CDOCKER. The criteria for best interaction between the ligand & the enzyme was chosen based on ;

a) high positive value of -CDOCKER energy &
b)small difference between -CDOCKER energy and -CDOCKER interaction energy.

Table 1 ;shows that (luteolin)-(SARS-coV-2 S2 subunit) interaction has the highest positive value of -CDOCKER energy, which is (14.28375) and minimum value of the difference ,that is (4.82375) between - C DOCKER interaction energy and - C DOCKER energy followed by apigenin. Thus, the result indicates that the phytochemical luteolin can effectively deactivate (SARS-coV-2S2subunit) enzyme thereby interrupting the RNA synthesis of the virus CV19. Higher positive values for (luteolin) indicated that it was the most active ingredient against (SARS-CoV-2) virus. Elseways, Nicotine can deactivate the enzyme to a small extent (negative -CDocker energy but positive -CDocker interaction energy). Therefore, the key phytochemicals preventing COVID-19 caused by (SARS-CoV-2) virus are luteolin and apigenin respectively.

CONCLUSION

Beforehand,it was proved that the plant ,*Bacopa monnieri L.* was curative against CV19. COVID-19 is caused by (SARS-CoV-2). This study was done to give the theoretical basis of this above observation. Using Discovery studio module of BIOVIA software, molecular docking operation was performed for the identification of the phytochemicals like; luteolin,apigenin, nicotine, D.mannitol etc.which can have a compelling interaction with the viral enzyme(SARS-CoV-2S2subunit) of the microbe. It was found that luteolin can form strong bond with the enzyme followed by apigenin, is successfully inhibiting the lipid metabolic cycle of the microbe. D.mannitol was found to be less effective in deactivating the enzyme of the microbe. Therefore, this study can explain that the

presence of luteolin, apigenin provided the medicinal values to *Bacopa monnieri* L. against COVID-19 caused by(SARS-CoV-2).

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Table 1:- Results of CDocking of phytochemicals with (SARS-coV-2S2subunit) enzyme

SL.NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	luteolin	14.28375	17.7017	3.41795
2	apigenin	9.03785	13.8616	4.82375
3	(S) nicotine	-5. 35258	15.1041	20.45678
4	D.mannitol	Failed	Failed	Failed

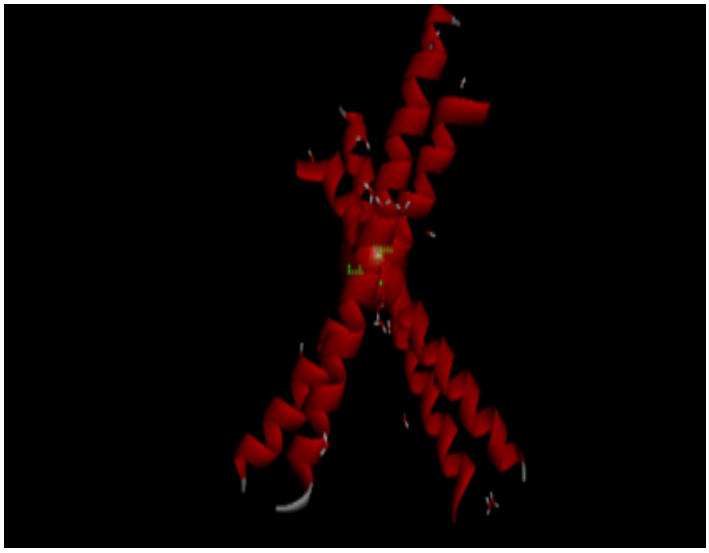

Figure 1:- Active site of (SARS-coV-2 S2 subunit) enzyme

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RESEARCH ARTICLE

COVID-19 Prevention using *Bacopa monnieri* L. Extract by Blocking Nsp9 RNA Binding the Protein of SARS CoV-2 Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PDB No. 6W4B of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Apigenin of Bacopa monnieri L extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" is an infectious disease produced by severe acute respiratory syndrome. The whole world is terrible to the pandemic desease COVID–19[1][2]., However, till now there is no established treatment[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4].Their phytochemicals will be low-cost but effective. *Bacopa monnieri* L belongs to family Plantaginaceae. It contains phytochemicals like apigenin, luteolin, D.mannitol,(S)-nicotine etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Bacopa monnieri* L contains phytochemicals like apigenin, luteolin, D.mannitol,(S)-nicotine etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6W4B and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the

phytochemical from the plant extract that can deactivate the PDB No. 6W4B viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Apigenin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Bacopa monnieri* L plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Apigenin can significantly interact with the viral PDB No. 6W4B.

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Table 1. Results of CDocking of phytochemicals with PDB No. 6W4B (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Apigenin	14.1645	20.2617	6.0972	Maxium inhibition of viral protein
2	Luteolin	6.2971	16.6104	10.3133	
3	D. Monnitol	Failed	Failed	Failed	
4	(S).nicotine	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Bacopa monnieri* L. Extract by Blocking (Bestrophin-2 Ca+- Unbound State) (250nM Ca 2+) Enzyme: An I*n silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Bestrophin-2 of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Luteolin of Bacopa monnieriL extract can effectively fight against "SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has threatened the whole world. It has been declared as a pandemic [1][2].However, till now there is no established treatment[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4].Their phytochemicals will be low-cost but effective. *Bacopa monnieri* L. belongs to family plantaginaceae. It contains phytochemicals like apigenin, luteolin, D. Mannitol, (S)-nicotine etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that Bacopa monnieriL contains phytochemicals like apigenin, luteolin, D. Mannitol, (S)-nicotine etc.. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Bestrophin-2 and controlling of

COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Bestrophin-2 viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.Table 1 shows that Luteolin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Bacopa monnieri* L plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Luteolin can significantly interact with the viral Bestrophin-2

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Table 1. Results of CDocking of phytochemicals with Bestrophin-2 (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Apigenin	17.6914	24.1106	6.4192	
2	Luteolin	20.6034	24.7092	4.1058	Maximum inhibition of viral protein
3	D. Mannitol	Failed	Failed	Failed	
4	Nicotine	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Bacopa monnieri* L. Extract by Blocking NSP15 Endoribonuclease Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory protein syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with NSP 15 Endoribonuclease Enzyme was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated thatLuteolin of Bacopa Monnieri extractcan effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has very critical problem to the whole world.The researchers try to find the vaccine of this disease but they are unable to get till now[1][2], However, till now there is no established treatment[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4]. Their phytochemicals will be low-cost but effective. *Bacopa Monnieri* belongs to family plantaginaceae It contains phytochemicals like apigenin,lutolin, nicotine,D.mannitol etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that Bacopa Monnieri containphytochemicals like apigenin, lutolin, nicotine,D.mannitol etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting NSP 15 Endoribonuclease Enzyme and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the viralprotein NSP-15 Endoribonuclease Enzymeviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Luteolin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Bacopa monnieri* plantcan prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Luteolin and nicotine can significantly interact with the NSP-15 Endoribonuclease Enzyme.

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Table 1. Results of CDocking of phytochemicals with NSP-15-Endoribonuclease Enzyme(receptor)

SL. NO.	LIGAND	-CDOCKER ENERGY	-CDOCKER INTERACTION ENERGY	Difference between-CDOCKER interaction energy and-CDOCKER energy	Remark
1	Luteolin	24.0781	27.4769	3.3988	Maximum inhibition of viral protein
2	Apigenin	20.9814	26.3184	5.3988	
3	(S)-nicotine	-3.52151	16.9191	20.4442	Minimum inhibition of viral protein
4	D.monnitol	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Capsicum annuum* (Chilli Pepper) Extract by Blocking Strctural protein HR2 Domain (6LVN) Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with Strctural protein HR2 Domain (6LVN) Enzyme was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Heptadecane of *Capsicum annuum* (chilli pepper) extract can effectively fight against "SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Capsicum annuum* (chilli pepper) belongs to family Solanaceae. It is used to lymph node swelling and boils, as reliever for flu and asthma. The fruit have been used as diuretic, stomachic,hemorrhoids and antoanginal.. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Capsicum annuum* (chilli pepper) contains . It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Strctural protein HR2 Domain (6LVN) Enzymeand controlling of COVID-19. Brenda enzyme database was used to list

different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate theStrctural protein HR2 Domain (6LVN) Enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSION

It was identified that *Capsicum annuum* (chilli pepper) plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that heptadecane can significantly interact with the viral Strctural protein HR2 Domain (6LVN) Enzyme .

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5. Debasmita Das, Sunanya Das, Mukundjee, Pandey, Dipankar Bhattacharyay. "In silico Analysis of Phytochemicals from Mucuna pruriens (L.) DC against Mycobacterium tuberculosis Causing Tuberculosis" , European Journal of Medicinal Plants, 2020

Table 1. Results of CDocking of phytochemicals with Strctural protein HR2 Domain (6LVN) Enzyme (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remark
1	Quercetin	11.5858	13.78	2.1942	
2	Rhamnetin	13.785	22.4875	8.7025	
3	Mynicetin	12.9417	14.1295	1.1878	
4	Linalool	-15.3876	14.8746	-0.513	
5	Kaempferol	17.0647	13.3634	3.7013	Maximum inhibition of viral

					protein
6	Apigenin	9.03785	13.8618	4.82395	
7	Capsaicin	-211.369	-77.3917	-77.7607	
8	Beta- mycrene	-16.7451	13.7269	-3.0182	
9	Rutin	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Capsicum annuum* Extract by Blocking Papain-Like Protease of SARS CoV-2 : An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Protease of SARS CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Quercetin of *Capsicum annuum* extract can effectively fight against "SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective.*Capsicum annuum* belongs to family Solanaceae. It contains Quercetin, Alpha-terpineol, apigenin, beta-carotene, beta-pinene, camphene, capsaicin, linalool, luteolin,mycrene, myrecetin, rutin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Capsicum annuum* contains Quercetin, Alpha-terpineol, apigenin, beta-carotene, beta-pinene, camphene, capsaicin, linalool, luteolin,mycrene, myrecetin, rutin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting protease and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract that can deactivate the protease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Capsicum annuum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral protease structure.

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Table 1. Results of CDocking of phytochemicals with Papain-like protease structure of CoV-2 (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Alpha-terpineol	-6.3509	22.0324	28.3833	
2	Apigenin	25.52	34.31	8.79	
3	Camphene	-47.16	17.21	64.37	
4	Capsaicin	21.1611	35.3315	14.17	

5	Linalool	-5.97972	24.137	30.1	
6	Luteolin	29.9609	37.39	7.43	
7	Quercetin	31.5442	34.8942	3.35	Maximum inhibition of viral protein
8	Rutin	FAILED	FAILED	NA	
9	1,8-cineole	FAILED	FAILED	NA	

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RESEARCH ARTICLE

COVID-19 Prevention using *Capsicum annuum* (Capsicum) Extract by Blocking Protease (6M03) Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Protease of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Capsicum annuum* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no proper vaccin.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Capsicum annuum* belongs to family Solanaceae. It contains Quercetin, Luteolin, Apigenin, Gallic Acid, Myricetin, Kaempferol, Vanillin, Eugenol, Nicotinic Acid, Camphene etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Capsicum annuum* contains Quercetin, Luteolin, Apigenin, Gallic Acid, Myricetin, Kaempferol, Vanillin, Eugenol, Nicotinic Acid, Camphene etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Protease and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract that can deactivate the Protease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Capsicum annuum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral Protease.

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Table 1. Results of CDocking of phytochemicals with Protease (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	26.7445	29.4942	2.7497	Maximum inhibition of viral protein
2	Luteolin	21.2948	24.9445	3.6497	
3	Apigenin	20.9862	26.5621	5.5759	

4	Gallic Acid	19.8199	16.4905	-3.3294	
5	Myricetin	19.5732	22.1435	2.5703	
6	Kaempferol	19.227	23.6424	4.4154	
7	Vanillin	14.5247	17.7653	3.2406	
8	Eugenol	9.8973	19.3507	9.4534	
9	Nicotinic Acid	9.86256	12.1471	2.28454	
10	Camphene	-51.2335	13.1844	64.4179	

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RESEARCH ARTICLE

COVID-19 Prevention using *Capsicum* Extract by Blocking Crystal Structure of NSP15 Endoribonuclease Enzyme (6VWW): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "NSP15 Endoribonuclease of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Myricetin of *Capsicume* xtract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. Capsicum belongs to family Solanaceae. It contains Apigenin, camphene, capsaicin, luteolin, linalool, myricetin, quercetin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (DassaultSystemes of France) was used for analysis. Published works showed that *Capsicum* contains Apigenin, camphene, capsaicin, luteolin, linalool, myricetin, quercetinetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting NSP15 Endoribonuclease and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate the NSP15 Endoribonuclease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Myricetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that Capsicum plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Myricetin can significantly interact with the viral NSP15 Endoribonuclease.

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Table 1. Results of CDocking of phytochemicals with NSP15 Endoribonuclease (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Myricetin	27.3984	28.7175	1.3191	Maximum inhibition of viral protein
2	Luteolin	23.1562	25.7803	2.6241	
3	Quercetin	21.1329	23.8976	2.7647	
4	Apigenin	15.8298	20.4086	4.5788	
5	Capsaicin	14.0295	27.8969	13.8674	
6	Linalool	-13.617	17.561	31.178	

7	Camphene	-52.3302	12.0844	64.4146	Minimum inhibition of viral protein
8	1,8-cineole	Failed	Failed	Failed	
9	Alpha-terpineol	Failed	Failed	Failed	
10	Beta-carotene	Failed	Failed	Failed	
11	Beta-pinene	Failed	Failed	Failed	
12	Rutin	Failed	Failed	Failed	
13	Myrcene	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Capsicum* Extract by Blocking SARS-CoV-2 Nucleocapsid Protein: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Nucleocapsid Protein of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Myricetin of *Capsicum* plant extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Capsicum* belongs to Solanaceae family. It contains 1,8-cineole, α-terpineol, apigenin, β-carotene, β-pinene, camphene, capsaicin, linalool, luteolin, myrcene, myricetin, quercetin, rutinetc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (DassaultSystemes of France) was used for analysis. Published works showed that *Capsicum* plantcontains 1,8-cineole, α-terpineol, apigenin, β-carotene, β-pinene, camphene, capsaicin, linalool, luteolin, myrcene, myricetin, quercetin, rutin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Nucleocapsid and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in

COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate the Nucleocapsidviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Myricetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSION

It was identified that *Capsicum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Myricetin can significantly interact with the viral Nucleocapsid.

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Table 1. Results of CDocking of phytochemicals with Nucleocapsid (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Myricetin	27.0413	29.5263	2.485	Maximum inhibition of viral protein
2	Quercetin	25.4733	28.3794	2.9061	
3	Luteolin	24.9651	28.0482	3.0831	

4	Capsaicin	24.018	38.7477	14.7297	
5	Apigenin	20.2965	25.0024	4.7059	
6	Linalool	-13.0146	16.5625	29.5771	
7	Camphene	-52.4446	11.8579	64.3025	Minimum inhibition of viral protein
8	1,8-cineole	Failed	Failed	Failed	
9	α-terpineol	Failed	Failed	Failed	
10	β-carotene	Failed	Failed	Failed	
11	β-pinene	Failed	Failed	Failed	
12	Myrcene	Failed	Failed	Failed	
13	Rutin	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Champa* Extract by Blocking Papain-Like Protease of SARS CoV-2: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with PDB No. 6W9C of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of Champa extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" is a most saviour viral transmitted pandemic disease which threaten the whole world [1][2]. However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Champa* belongs to family Magnoiliaceae. It contains phytochemicals like Alpha Cadinol, Alpha Humelene, Beta Caryophyllene, Beta Selinene, Camphor sulphonic acid, Docosanic Acid, Gallic Acid, Farnesol, Gamma Cadinene, Nerolidol, Oleic Acid, Quercetin, Stigmasterol etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Champa* consists of phytochemicals like Alpha Cadinol, Alpha Humelene, Beta Caryophyllene, Beta Selinene, Camphor sulphonic acid, Docosanic Acid, Gallic Acid, Farnesol, Gamma Cadinene, Nerolidol, Oleic Acid, Quercetin, Stigmasterol etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting PDB No. 6W9C and controlling of

COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the PDB No. 6W9C viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Champa plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral PDB No. 6W9C.

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Table 1. Results of CDocking of phytochemicals with PDB No. 6W9C (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Beta Caryophyllene	-21.77	20.5353	42.3053	
2	Iso-quercetin	11.5193	41.6965	30.1782	
3	Gamma Cadinene	-24.24	20.77	45.01	

4		-25.30	24.95	50.25	
5	Beta-selinene	-17.89	21.85	39.74	
6	Farnesol	-43.74	25.41	69.15	
7	Quercetin	31.5442	34.8941	3.3499	**Minimum inhibition of viral protein**
8	Gallic acid	29.9926	27.2057	2.7869	
9	Camphor sulphonic acid	FAILED	FAILED	NA	
10	Docosanic Acid	FAILED	FAILED	NA	
11	Stigmasterol	FAILED	FAILED	NA	
12	Oleic Acid	FAILED	FAILED	NA	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cinnamomum verum* Extract by Blocking Nps 9 RNA Binding Protein Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Nps 9 RNA binding protein Enzyme" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Gossyptin of *Cinnamomum verum* extract can effectively fight against "SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has in danger of extinction the complete world. It has been affirmed as a virulent disease [1][2]., However, till now there is no established treatment[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4].Their phytochemicals will be low-cost but effective.*Cinnamomum verum* belongs to family Lauraceae. It contains phytochemicals like Cinnamic Acid, Quercetin, Vanillin, Coumarinic acid, Eugenol, Nicotine, 9,12- Octadecadienoic Acid, Beta- caryophyllene, Codeine, Curcumin, Gossypetin, Proanthocyanidin, Sucrose etc.. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Cinnamomum verum* contains phytochemicals like Cinnamic Acid, Quercetin, Vanillin, Coumarinic acid, Eugenol, Nicotine, 9,12- Octadecadienoic Acid, Beta- caryophyllene, Codeine, Curcumin, Gossypetin, Proanthocyanidin, Sucrose etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Nps 9 RNA binding

protein Enzyme and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Nps 9 RNA binding protein Enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSION

It was identified that Cinnamomum verum plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Gossyptin can significantly interact with the viral Nps 9 RNA binding protein Enzyme.

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Table 1. Results of CDocking of phytochemicals with Nps 9 RNA binding protein Enzyme (receptor)

SL. NO.	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Gossyptin	30.0579	29.4436	0.6143	Maximum inhibition of viral protein

2.	curcumin	25.0669	34.4527	9.3858	
3.	Cinnamic Acid	12.7699	14.3203	1.5504	
4.	Eugenol	4.82461	14.3289	9.50429	
5.	Vanillin	11.7233	14.957	3.2337	
6.	sucrose	-14.6835	32.1585	46.842	
7.	Quercetin	FAILED	FAILED	FAILED	
8.	Coumarinic acid	FAILED	FAILED	FAILED	
9.	Nicotine	FAILED	FAILED	FAILED	
10.	9,12-Octadecadienoic Acid	FAILED	FAILED	FAILED	
11.	Beta- caryophyllene	FAILED	FAILED	FAILED	
12.	Codeine	FAILED	FAILED	FAILED	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cinnamomum verum* Extract by Blocking Structural Protein HR2 Domain: An *In silico* Analysis

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ABSTRACT

COVID-19 is an infectious disease infected by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). The disease shows symptoms such as a , fever, cough and in more severe cases, difficulty breathing. Now a time this disease can affect a lot of people in every day world wide. Scientists all over the world are doing research on how to get rid from such diseases by looking traditional vaccine or preventive drugs. However, this study objective to derive medicines from plant phytochemicals rather than synthesizing new chemicals which proved to be more expensive and unsafe compared to their organic counterpart. Phytochemicals are non-nutritive bioactive compounds extracted from plants. It has been identified that plant *Cinnamomum verum* extract is expected to cure COVID-19, which is caused by SARS-CoV-2. The said virus contains structural protein HR2 Domain which is expected to be valuable for the survival of the virus SARS-CoV-2. The molecular docking of the phytochemicals with the microbial structural protein was studied using BIOVIA Discovery Studio. The strength of the interaction was evaluated based on -CDocker energy and -CDocker interaction energy. High positive values indicated that out of different phytochemicals Quercetin and Gossypetin expected that can effectively deactivate the structural part of virus SARS-CoV-2.

Keywords : Phytochemical, BIOVIA, Discovery studio, COVID-19, SARS-CoV-2, structural protein HR2 Domain , *Cinnamomum verum*

INTRODUCTION

COVID-19 is a transmittable disease that is spreading rapidly from one person to another across the world resulting in the ongoing 2019–20 coronavirus pandemic with serious fatal implications for countries with ageing populations. The World Health Organization (WHO) accredited the 2019–20 coronavirus outbreak a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020 [1, 2]. This fatal disease was first reported in December 2019 at Wuhan, China, which has since increase rapidly world wide [3, 4]. According to the

statistics, So far we have received the report, it is known that it doubles its number every 7 days globally. It is a matter of great misfortune that till today the scientist of any country could not developed any kind of preventive or molecular drugs or vaccine yet due to continuous mutation according to geographic regions in the virus [5]. Since the old ages, this practice has been written in the texts of different traditional books of many countries or in the history of different countries, that there are many plant products having anti-viral and other medicinal properties, nature has been a source of medicinal factors for thousands of years [6]. The medicinal value of the plant is shown in its chemical substances, these substances are called phytochemicals, which can be used for curative purpose. Plants based medicinal constituents can be derived from any plant parts like seeds leaves, roots, flowers and fruits [7]. There are many medicinal plants and their phyto-extracts that have a lot of medicinal value such properties like anti-oxidant , anti-diabetes, anti-inflammatory, anti-cancer , anti-microbial, action etc [8]. Newly appear scientific techniques and approaches with advance technology now there are so many who want to research over Medicinal plants have been used in the growing area of medicinal research, for the investigation and determination of biological, Chemical activity of medicinal plants [9]. Plants that demonstrated anticancer, antioxidant, anti-microbial and immune-stimulatory properties have received research attention. *Cinnamon* belongs to family Lauraceae. *Cinnamon* bark extracthas been used as anti-inflammatory, antitermitic, nematicidal, mosquito larvicidal, insecticidal, anti-mycoticand anticancer agent [10]. The plant is a small evergreen tree native to Sri Lanka. *Cinnamomum verum* is known to contain phytochemicals like Cinnamic Acid, Quercetin, Vanillin, Coumarinic acid, Eugenol, Nicotine, 9,12-Octadecadienoic Acid, Beta- caryophyllene, Codeine, Curcumin, Gossyptin, Proanthocyanidin, Sucrose etc. There is high possibility that these phytochemicals play a major role in curing COVID-19. However, there is no report previously to identifying the specific phytochemical responsible to cure COVID - 19. Coronavirus disease 2019 (COVID-19) is a transmittable disease instigated by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [11]. Genetic analysis has revealed that the coronavirus genetically clusters with the genus Betacoronavirus, in subgenus Sarbecovirus (lineage B) together with two bat-derived strains. It is 96% identical at the whole genome level to other bat coronavirus samples (BatCov RaTG13). [12, 13] Those infected with the virus may be asymptomatic or develop flu-like symptoms, including fever, cough and shortness of breath. Emergency symptoms include difficulty breathing, persistent chest pain or pressure, confusion, difficulty waking, and bluish face or lips; immediate medical attention is advised if these symptoms are present. Symptoms such as nausea, vomiting, and diarrhea have been observed in varying percentages [14, 15]. It spreads much like a cold or the flu through the expelled airborne droplets from a person with infectious COVID-19 or through close/surface contact. When inhaled or came in contact with eyes, nose or mouth, the virus can settle in the lungs, where it begins to grow which can be life-threatening. However, it is possible to control the disease by inhibiting the protein pathway of the microorganism. It has been seen that Structural protein HR2 Domain which resides in the extracellular matrix of the virus is associated with the viral stucture synthesis [16]. By inhibiting the binding of the protein deactivating of the virus may be achieved.

This study focuses on the identification of the phytochemical of *Cinnamomum verum* responsible to cure COVID-19 caused by (SARS-CoV-2) by inhibiting the structural protien.

MATERIALS AND METHODS

Software used

Discovery studio module of BIOVIA was used for analysis. The software utilizes machine learning techniques to predict the level of molecular interaction

Methodology:

List of phytochemicals: Phytochemicals are extracted from plants as metabolites. The potential threats to plants include bacteria, viruses, fungi etc. When these plant's parts are consumed by humans these phytochemicals fight off threats to health so some phytochemicals used as traditional medicine. *Cinnamomum verum* contains phytochemicals like Cinnamic Acid, Quercetin, Vanillin, Coumarinic acid, Eugenol, Nicotine, 9,12- Octadecadienoic Acid, Beta-

caryophyllene, Codeine, Curcumin, Gossyptin, Proanthocyanidin, Sucrose etc. It has been assumed that *Cinnamomum verum* plant belonging to Lauraceae family has potential to help controlling COVID-19. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-19.

Protein found in (SARS-CoV-2): It has been reported that COVID-19 can cause as a result of (SARS-CoV-2) infestation.Various metabolic cycles have been seen in the viral life cycle for its survival. These metabolic cycles are regulated by different enzymes. Enzyme database was used to identify and list different enzymes found in (SARS-CoV-2). It has been found that Structural protein HR2 Domain (PDB code 6LVN) is most likely involved with viral structure formation which is found in extracellular matrix in order to survive.

Molecular docking: Molecular docking method has been used to identify the phytochemical from the plant extract, that act as a ligand and form a strong covalent bond with the bacterial protein to successfully inhibit the microbe. The Discovery studio module of BIOVIA software was used for identifying molecular interaction and perform molecular docking. In this process first the SDF files for the metabolites found in the *Cinnamon* plant were downloaded from the website Pub-Chem. The protein database code of the protein was identified from the website BRENDA and RCSB. The ligand binding site of the structural protein was identified through "receptor cavity" process found under "receptor-ligand interaction" menu. Molecular docking was done using the CDocker protocol of BIOVIA software under "receptor-ligand interaction". The protein molecule was treated as the receptor molecule and the phytochemical was act as the ligand. The "-CDOCKER_ENERGY" and "-CDOCKER_INTERACTION_ENERGY" were taken as sign for the quality of molecular docking. The high positive value of those indicators represented a strong interaction between the ligand and the receptor. Thus, the interactions with high positive values might indicate the specific phytochemical responsible for curing the infection.

RESULTS AND DISCUSSION

Fig. 1 represents the active site of the Structural protein HR2 Domain. It appears as yellow or light green color. CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy. The ligand conformations were obtained by Molecular Dynamic methods.

The value of -CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the nonbonded interaction that exists between the protein and the ligand.The criteria for best interaction was chosen based on a) high positive value of -CDOCKER energy and b) small difference between -CDOCKER energy and -CDOCKER interaction energy [16].

Table 1 represents that Quercetin and Structural protein HR2 Domain interaction has the highest positive value of -CDOCKER energy(16.82) and minimum value of the difference (3.1091) between - C DOCKER interaction energy and - C DOCKER energy followed by Vanillin, Coumarinic acid, Eugenol. Thus, the results indicated that Quercetin can effectively deactivate Structural protein HR2 Domain thereby interrupting the spick protein structure synthesis. Higher positive values for Quercetin indicated that it was the most active ingredient against (SARS-CoV-2) virus closely followed by Gossypetin, Vanillin, Cinnamic acid, Eugenol. On the other hand, Nicotine can deactivate the protein to a small extent because of unstable bonding. Thus, the key phytochemicals preventing COVID-19 caused by SARS-CoV-2 virus is Quercetin.

CONCLUSIONS

It was previously known that *Cinnamomum verum* plant has medicinal action against COVID-19. COVID-19 is caused by (SARS-CoV-2). This study was carried out to provide the theoretical basis of this observation. Using Discovery studio module of Biovia software, molecular docking operation was performed to identify the phytochemical (Quercetin, Vanillin, Cinnamic acid, Eugenol, Nicotine, 9,12- Octadecadienoic Acid, Beta- caryophyllene, Proanthocyanidin, etc), which can have a significant interaction with the major Structural protein HR2 Domain of the virus. It was found that Quercetin, can form strong bond with the enzyme followed by, Vanillin, Coumarinic acid, Eugenol. On the other hand Nicotine can deactivate the protein to a small extent while other phytochemicals failed to

dock with the protein. Thus, this study could explain that the presence of Quercetin provided the medicinal values to *Cinnamomum verum* against COVID-19 caused by SARS-CoV-2.

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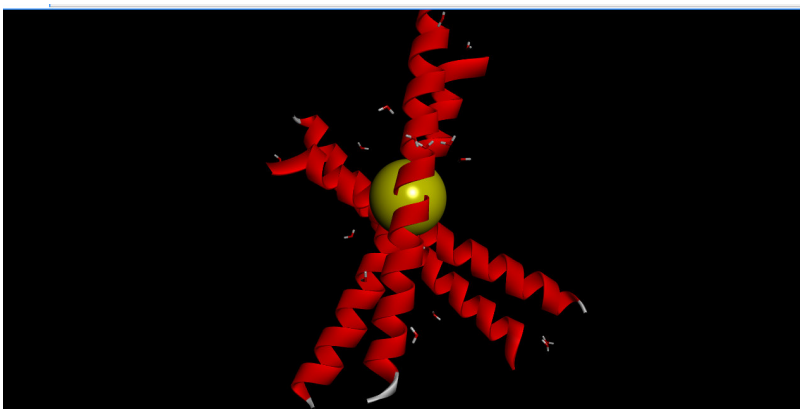

Figure 1. Active site of (Structural protein HR2 Domain)

Table 1. Results of CDocking of phytochemicals with Structural protein HR2 Domain

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Quercetin	16.82	19.9291	3.1091
2	Gossypetin	15.3187	15.5728	0.2541
3	Vanillin	12.1918	15.7596	3.5678
4	Cinnamic acid	9.80696	11.6933	1.88634
5	Eugenol	4.91076	14.5411	9.63034
6	Nicotine	-4. 5079	15.7942	20. 3021
7	9,12- Octadecadienoic Acid	FAILD	NA	NA
8	Beta- caryophyllene	FAILD	NA	NA
9	Proanthocyanidin	FAILD	NA	NA

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RESEARCH ARTICLE

COVID-19 Prevention using *Cinnamomum verum* L. Extract by Blocking SARS- CoV-2 Main Protease with Unliganded Active Site (2019- nCoV, Coronavirus Disease 2019, COVID-19): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "main protease of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Gossyptin of *Cinnamomum verum* L extract can effectively fight against "SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. Cinnamomum verum L belongs to family Lalauracea. It contains photochemical Beta-caryophyllene, cinnamic acid, codeine, curcumin, eugenal, gossyptin, nicotine, proanthocyanibin A2, quercetin, sucrose, vanillin, etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that cinnamomum Verum L contains Beta-caryophyllene, cinnamic acid, codeine, curcumin, eugenal, gossyptin, nicotine, proanthocyanibin A2, quercetin, sucrose, vanillin, etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting protease and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the protease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Gossiping is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Cinnamomum verum L plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Gossyptin can significantly interact with the viral protease.

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Table 1. Results of CDocking of phytochemicals with protease (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Gossyptin	11.2553	11.0641	0.1912	Maximum inhibition of viral protein
2	Cinnamic acid	11.2137	13.6262	2.4125	
3	Quercetin	7.64282	10.2481	2.60528	
4	Vanillin	5.88698	8.95011	3.06313	
5	Eugenol	-1. 21806	8.34884	9.5669	
6	Nicotine	-11. 1196	9.30871	20. 42831	
7	Beta-caryophyllene	-32. 1822	10.2574	42.4396	
8	Codeine	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cinnamomum verum* Extract by Blocking Nsp9 RNA Binding Protein Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with 'Nsp9 RNA binding protein enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Phloretic acid of *Cinnamon* plant extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world due to seriously ill and develop difficulty breathing. It has been declared as a harmful disease in mammals as well as in birds[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective.

Cinnamon belongs to family Lauraceae. It contain phytochemicals like Cinnamic Acid, Quercetin, Vanillin, Coumarinic acid, Eugenol, Nicotine, 9,12- Octadecadienoic Acid, Beta-caryophyllene, Codeine, Curcumin, Gossyptin, Proanthocyanidin, Sucrose, etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Cinnamon* contains Cinnamic Acid, Quercetin, Vanillin, Coumarinic acid, Eugenol, Nicotine, 9,12-Octadecadienoic Acid, Beta-caryophyllene, Codeine, Curcumin, Gossyptin, Proanthocyanidin, Sucrose, etc. It is

known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting the bacterial protein and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the phytochemicals from the plant extract, that act as a ligand and form a strong covalent bond with the bacterial viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

Table 1 shows that Cinnamic Acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cinnamomum verum* plant plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Cinnamic Acid can significantly interact with the viral enzyme Nsp9 RNA binding protein of the microbe.

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Table 1. Results of CDocking of phytochemicals with (Nsp9 RNA binding protein (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Cinnamic Acid	19.0329	21.216	2.1831	Maximum inhibition of viral protein
2	Quercetin	17.9809	22.3797	4.3988	
3	Vanillin	15.536	19.298	3.762	
4	Coumarinic acid	14.9804	22.9455	7.9651	
5	Eugenol	11.9843	22.7254	10.7411	
6	Nicotine	-0.0300726	23.6963	23.7263726	Minimum inhibition of viral protein
7	9,12- Octadecadienoic Acid	FAILED	FAILED	FAILED	
8	Beta-caryophyllene	FAILED	FAILED	FAILED	
9	Codeine	FAILED	FAILED	FAILED	
10	Curcumin	FAILED	FAILED	FAILED	
11	Gossyptin	FAILED	FAILED	FAILED	
12	Proanthocyanidin	FAILED	FAILED	FAILED	
13	Sucrose	FAILED	FAILED	FAILED	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cinnamomum verum* Extract by Papain-Like Protease of SARS CoV-2: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Papain-like Proteaseof SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Gossyptin of *Cinnamomum verum* extract can effectively fight against"SARS-CoV-2 virus".

Keywords : Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2, *Cinnamomum verum*

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has scared the the people globally. It has killed many people globally. Thus, has been declared as pandemic by WHO [1][2].However, the people working on this fails to discover any medicines till now [6].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases[9].Their phytochemicals will be low-cost but effective.
Cinnamomumverumbelongs to family Lauraceae. *Cinnamon* bark extracthas been used as anti-inflammatory, antitermitic, nematicidal, mosquito larvicidal, insecticidal, antimycoticand anticancer agent. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Cinnamomum verum* bark extract has been used as anti-inflammatory, antitermitic, nematicidal, mosquito larvicidal, insecticidal, antimycotic and anticancer agentetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Papain-like Proteaseand controlling of COVID-19. Brenda enzyme database was used to list different

enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract thatcan deactivate the Papain-like Proteaseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Heptadecane is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cinnamomum verum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Gossyptin can significantly interact with the viral Papain-like Protease.

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Table 1. Results of CDocking of phytochemicals with Papain-like Protease(Receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Cinnamic Acid	18.2459	20.2016	1.9557	
2	Quercetin	31.5442	34.8941	3.3499	
3	Vanillin	18.9666	22.8268	3.8602	
4	Coumarinic acid	19.2099	21.6965	2.4866	
5	Gossyptin	34.1452	33.0254	1.1198	Maximum inhibition of viral protein
6	Eugenol	11.5363	21.0124	9.4761	
7	Nicotine	1.439	21.3123	19.8733	
8	Beta- caryophyllene	-21.77	20.5353	42.3053	
9	Sucrose	-4.5147	46.2192	50.7339	
10	Curcumin	31.1427	38.9292	7.7865	
11	9,12- Octadecadienoic Acid	FAILED	FAILED	FAILED	
12	Proanthocyanidin	FAILED	FAILED	FAILED	
13	Codeine	FAILED	FAILED	FAILED	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cinnamon* Extract by Blocking ADP Ribose Phosphatase of NSP3 Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase of NSP3 of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Gossyptin of *Cinnamon* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a transmissible disease with serious fatal disease [1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective.

Cinnamon belongs to family LauraceaeIt contains Catechin, Beta caryophyllene, Cinnaminic acid, Codeine, Curcumin, Eugenol, Gossyptin, Nicotine, Proanthocyanidin A2, Quercetin, Sucrose, Vanillinetc.This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.

Published works showed that CINNAMONcontains Catechin, Beta caryophyllene, Cinnaminic acid, Codeine, Curcumin, Eugenol, Gossyptin, Nicotine, Proanthocyanidin A2, Quercetin, Sucrose, Vanillinetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting ADP ribose phosphatase of NSP3and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate theADP ribose phosphatase of NSP3viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Gossyptinis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that CINNAMONplant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatGossyptincan significantly interact with the viralADP ribose phosphatase of NSP3.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase of NSP3 (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Catechin	failed	NA	NA	
2	Beta caryophyllene	-18.9642	23.8049	42.7691	
3	Cinnaminic acid	24.6093	26.2458	1.6365	
4	Codeine	FAILED	NA	NA	
5	Curcumin	FAILED	NA	NA	
6	Eugenol	20.0117	29.4863	9.4746	Maximum inhibition of viral protein
7	Gossyptin	47.3628	46.4538	0.909	
8	Nicotine	9.42953	30.0351	20.60557	
9	Proanthocyanidin A2	FAILED	NA	NA	
10	Quercetin	42.0864	45.5796	3.4932	
11	Sucrose	-9.84368	54.9451	64.78878	
12	Vanillin	27.3931	30.5529	3.1598	

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RESEARCH ARTICLE

COVID-19 Prevention using *Clove* Extract by Blocking SARS-Cov-2 Main Protease with Unliganded Active Site Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "SARS-Cov-2main protease" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Rhamnetin of *Clove* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has a great negative impact on the whole world. The pandemic term has already been added with the disease [1][2].Till now there is no proper established treatment for the disease [3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective .

Clove belongs to family myrtaceae. It contains rhamnetin, myricetin, gallic acid, kaempferol, bita caryophyllene, vanilla, euganol, compesterol 3 beta-d -glucoside, oleanoid acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.

Published works showed that Clovecontains rhamnetin, myricetin, gallic acid, kaempferol, bita caryophyllene, vanilla, euganol, compesterol 3 beta-d -glucoside, oleanoid acidetc. It is known that plants belonging to this family

are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting SARS-Cov-2main protease and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the SARS-Cov-2main protease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Rhamnetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Clove plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatRhamnetin can significantly interact with the viralSARS-Cov-2main protease.

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Table 1. Results of CDocking of phytochemicals with SARS-Cov-2main protease (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Rhamnetin	35.0319	40.7472	5.4153	Maximum inhibition of viral protein
2	Myricetin	33.4677	35.7694	2.3	
3	Gallic acid	28.9433	26.8748	2.0685	
4	Kaempferol	26.5394	30.6694	4.1355	
5	Beta- caryophyllene	19.7229	23.4882	3.7653	
6	Vanillin	16.7433	20.0137	3.2704	
7	Eugenol	14.5118	23.8261	9.3143	
8	Compesterol 3-beta-d -glucoside			Failed	
9	Stigmasterol			Failed	
10	Oleanoid acid			Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cocoa* Extract by Blocking ADP Ribose Phosphatase of NSP3 Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Cocoa* extract can effectively fight against"SARS-CoV-2 virus".

Keywords : phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has the lethal effect on human society. The disease has clearly declared as a pandemic one.[1][2], Proper treatment mechanism for the disease has not been developed yet[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4].Their phytochemicals will be low-cost but effective.

Cocoabelongs to family Malvaceae. It contains caffeine, chlorogenic acid, Ferulic acid, phenylactic acid, phloretic acid, quercetin, procyandine, syringic acid, theobromine, vanillicaci and vitexinetc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.

Published works showed that Cocoacontains caffeine, chlorogenic acid, Ferulic acid, phenylactic acid, phloretic acid, quercetin, procyandine, syringic acid, theobromine, vanillicaci and vitexin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting ADP ribose phosphataseand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the ADP ribose phosphataseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetinis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Cocoacan prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetincan significantly interact with the viralADP ribose phosphatase.

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Table 1. Results of C Docking of phytochemicals with ADP ribose phosphatase(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Caffeine	24.4652	33.1522	8.687	
2	Chlorogenic acid	26.5368	48.0345	21.4977	
3	Ferulic acid	28.1379	31.5238	3.3859	
4	Hyperin	FAILED	NA	NA	
5	IsoQuercetin	FAILED	NA	NA	
6	IsoOrientin	-1.02645	42.3316	43.35805	
7	Isovitexin	FAILED	NA	NA	
8	Luteolin	39.3043	43.0319	3.7276	
9	Naringenin	FAILED	NA	NA	
10	p-Coumaric acid	30.2916	29.9014	0.5499	
11	Phenyl Acetic Acid	28.2216	28.3612	0.1396	
12	Phloretic acid	29.7417	30.4999	0.7578	
13	Quercetin	42.0864	45.5796	3.4932	Maximum inhibition of viral protein
14	Pro cyanidin	FAILED	NA	NA	
15	Syringic acid	27.9228	33.5604	5.6376	
16	Theobromine	25.1602	30.7189	5.5587	
17	Vanillic acid	29.5785	31.2962	1.7177	
18	Vitexin	FAILED	NA	NA	

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RESEARCH ARTICLE

COVID-19 Prevention using *Coconut* Extract by Blocking Structural Protein HR2 Domain (6lvn): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "non-structural protein 9 of -nCoV HR2 Domain Enzyme was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Nicotinic acid of Coconut extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"one of the dangerous desease. Which has affected many people. It has been declared as a pandemic.[1][2], However, till now the researchers find no vaccine for it.[6]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[9] Their phytochemicals will be low-cost but effective .

Coconut belongs to family *Arecaceae*. It contains Nicotinic acid,Biotin, Catechins, Folic acid,Leuconantho cyanidinsand Riboflavin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Coconut* contains Nicotinic acid,Biotin, Catechins, Folic acid,Leuconantho cyanidinsand Riboflavin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting -nCoV HR2 Domain Enzyme and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the -nCoV HR2 Domain Enzyme viral protein. The detailed method has been described elsewhere [].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Nicotinic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Coconut plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Nicotinic acid can significantly interact with the -nCoV HR2 Domain Enzyme.

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Table 1. Results of CDocking of phytochemicals with -nCoV HR2 Domain Enzyme

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Nicotinic acid	8.22195	11.5957	-3.37375	Maximum inhibition of viral protein
2	Biotin	Failed	Failed	Failed	
3	Catechins	Failed	Failed	Failed	
4	Folic acid	Failed	Failed	Failed	
5	Leuconantho cyanidins	Failed	Failed	Failed	
6	Riboflavin	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cocos nucifera* (Coconut) Extract by Blocking the Crystal Structure of COVID-19 Main Protease in Enzyme (6M03): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "protease in apo form of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Nicotonic acid of coconut extract can effectively fight against "SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. Coconut belongs to family Arecaceae. *Cocos nucifera* extract is used to cure disease like diarrhea. Its oil is used to treat skin and teeth diseases . it is also used in different medicines and making cosmetics. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that coconut contains Biotin , Catechins, Folic acid, Leucoantho cyanidine, Nicotonic acid, Riboflavin obtain from Cocos nucifera etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting protease in apo form and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19.

Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the protease in apo form viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSIONS

It was identified that coconut plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Nicotonic acid can significantly interact with the viral protease in apo form.

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Table 1 shows that Nicotonic acid is the phytochemical that can really prevent COVID-19 attack.

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Nicotonic acid	9.86256	12.1471	2.28454
2	Biotin	Failed	Failed	Failed
3	Catechins	Failed	Failed	Failed
4	Folic acids	Failed	Failed	Failed
5	Leucoantho cyanidine	Failed	Failed	Failed
6	Riboflavin	Failed	Failed	Failed

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RESEARCH ARTICLE

COVID-19 Prevention using *Cocos nucifera* Extract by Blocking Main Protease Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Main Protease"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Nicotinic acid of *Cocos nucifera* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has become the most threatened viral disease to the whole world. This disease is now apandemic.[1][2], Although a lot of works are going on but till date the proper medication is unknown [3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4].Their phytochemicals will be low-cost but effective . *Cocos nucifera* belongs to family Arecaceae. It contains riboflavin, nicotinic acid, leucoanthocyanidins, catechins, biotin, folic acidetc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Cocos nucifera* contains riboflavin, nicotinic acid, leucoanthocyanidins, catechins, biotin, folic acidetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Main Proteaseand controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Main Proteaseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Nicotinic acidis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cocos nucifera* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatNicotinic acid can significantly interact with the viralMain Protease.

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Table 1. Results of CDocking of phytochemicals with Main Protease(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Nicotinic acid	13.9016	17.5288	3.6272	Maximum inhibition of viral protein
2	Riboflavin	11.8707	39.008	27.1373	
3	Leucoanthocyanidins	Failed	Failed	Failed	
4	Catechins	Failed	Failed	Failed	
5	Biotin	Failed	Failed	Failed	
6	Folic acid	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cocos nucifera* (Coconut Plant) Extract by Blocking Nucleocapsid Protein N-terminal RNA Domain (6M3M): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Nucleocapsid of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Riboflavin of *Cocos nucifera* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is an infectious disease. [1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Cocos nucifera* belongs to family arecaceae. It contains biotin, catechins, folic acid, leucoantho cyanidins, nicotinic acid, riboflavin, pantothenic acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Cocos nucifera* contains biotin, catechins, folic acid, leucoantho cyanidins, nicotinic acid, riboflavin, pantothenic acid etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Nucleocapsid and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Nucleocapsid viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Riboflavin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cocos nucifera* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Riboflavin can significantly interact with the viral Nucleocapsid.

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Table 1. Results of CDocking of phytochemicals with Nucleocapsid (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Riboflavin	13.0926	32.8597	19.7671	Maximum inhibition of viral protein
2	Nicotinic acid	10.482	12.5569	2.0749	
3	Biotin	FAILED	FAILED	NA	
4	Folic Acid	FAILED	FAILED	NA	
5	Pantothenic Acid	FAILED	FAILED	NA	
6	Catechins	FAILED	FAILED	NA	

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RESEARCH ARTICLE

COVID-19 Prevention using *Coffea arabica* (Coffee) Extract by Blocking structure of SARS CoV-2 nucleocapsid protein N-terminal RNA binding Domain (6M3M): An In Silico Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "-nCoV HR2 Domain Enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Heptadecane of *Coffea Arabica* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective.

Coffea Arabica belongs to family Rubiaceae. It contains Kafestol and Triglycerides etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Coffea Arabica* contains Kafestol and Triglycerides etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting -nCoV HR2 Domain Enzyme and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the -nCoV HR2 Domain Enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Heptadecane is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Coffea Arabica* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatheptadecane can significantly interact with the viral -nCoV HR2 Domain Enzyme.

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Table 1. Results of CDocking of phytochemicals with -nCoV HR2 Domain Enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Cafestol	-41.0443	24.9511	65.9954	
2	Triglycerides	Failed	Failed	Failed	
3	Caffein	Failed	Failed	Failed	
4	Chlorogenic acid	Failed	Failed	Failed	Minimum inhibition of viral protein

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RESEARCH ARTICLE

COVID-19 Prevention using *Commiphora wightii* Extract by Blocking NSP15 Endoribonuclease (6VWW) Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "NSP15 Endoribonuclease (6VWW)of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Commiphora wightii* extract can effectively fight against"SARS-CoV-2 virus".

Key words : phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a transmissible disease with serious fatal implications for countries with ageing populations.1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Commiphora wightii* belongs to family Burseraceae. It contains Quercetin, Eugenol, Alpha-pinene, Linalool, Alpha-terpineol, D-limonene, Geraniol, Bornylacetate, Progesterone, Z-guggulsterone [11,12].This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *CommiphoraWightii*contains Quercetin, Eugenol, Alpha-pinene, Linalool, Alpha-terpineol, D-limonene, Geraniol, Bornylacetate, Progesterone, Z-guggulsteroneetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting NSP15 Endoribonuclease (6VWW)and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate the NSP15 Endoribonuclease (6VWW)viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Commiphora wightii* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetincan significantly interact with the viralNSP15 Endoribonuclease (6VWW).

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Table 1. Results of CDocking of phytochemicals with NSP15 Endoribonuclease (6VWW)(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	DIFFERENCE BETWEEN - C DOCKER INTERACTION ENERGY AND – C DOCKER ENERGY	Remarks
1	Quercetin	21.1329	23.8976	2.7647	Maximum inhibition of viral protein
2	Eugenol	6.6301	16.2032	9.5731	
3	Alpha-pinene	-12.5163	12.4414	24.9577	
4	Linalool	-13.617	17.561	31.178	
5	Alpha-terpineol	-13.5084	15.0944	28.6028	
6	D-limonene	-24.799	13.6314	38.4303	
7	Geraniol	-28.9901	15.7409	44.731	
8	Bornyl acetate	Failed	Failed	Failed	
9	Progesterone	Failed	Failed	Failed	
10	Z-guggulsterone	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Commiphora wightii* (Mukul Myrrh Tree) Extract By Blocking Structural Protein HR2 Domain (6lvn): An *In silico* Analysis

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ABSTRACT

Corona virus disease 2019 (COVID-19) is an infectious disease produced by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).The disease causes respiratory illness (like the flu) with symptoms such as fever, cough, and fatigue, while other symptoms include sputum production, headache, haemoptysis, diarrhea, dyspnea. It has been a source of fear and anguish worldwide as an ongoing epidemic which is ensuing thousands of death and affecting millions of people every day. To overcome these pandemic situation researchers are trying to come up with a traditional vaccine rather than the synthetic drugs. This is because derive medicines from plant extract containing phytochemicals are proved to be less expensive and safe compared to synthetic chemicals. Corona virus disease 2019 (COVID-19) is an infectious disease produced by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and spread by social gathering. Phytochemicals are non-nutritive compounds obtained from plants. It has been found that plant *Commiphora wightii* extract is expected to cure COVID-19, which is caused by SARS-CoV-2. The said virus contains structural protein HR2 Domain which is reported to be very crucial for the survival and metabolism of the organism. The molecular docking of the phytochemicals with the microbial structural protein was studied using Biovia Discovery Studio. The strength of the interaction was evaluated based on -CDocker energy and -CDocker interaction energy. High positive values for both the parameters indicated that out of different phytochemicals Quercetin and **Eugenol** can effectively deactivate the structural part of virus SARS-CoV-2.

Key words : Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

The novel corona virus 2019 currently designated as COVID 2019 is in the limelight since the beginning of New Year 2020. Corona viruses are enveloped positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope; hence the name

corona virus[2]. Though human corona viruses have been recognized for many years but COVID 2019 was a new strain and its wide global spread sparkled panic among the common public [1]. In December 2019, patients with unexplained pneumonia have been found in Wuhan City, Hubei Province, China. The disease caused by SARS CoV-2. SARS CoV-2 is a new β-corona virus, and its gene sequence is most similar to that of viruses isolated from bats, [3] but there is likely an unknown intermediate host .The incubation period of SARS CoV-2 infection 1 to 14 days, generally 3 to 7 days. The most common symptoms at onset of COVID-19 illness are fever, cough, and fatigue, while other symptoms include sputum production, headache, haemoptysis, diarrhea, dyspnea, and lymphopenia [4][5][6][7]. At present, it has been found that patients with SARS CoV-2 infection are the main source of infection, and the transmission effect of asymptomatic patients should not be underestimated. According to the current data, the main routes of transmission are respiratory droplet transmission and contact transmission. So, it was concluded that the COVID-19 is not a super-hot spreading virus (spread by one patient to many others), but rather likely spread due to many patients getting infected at various locations throughout the hospital through unknown mechanisms [8] .Unfortunately any kind of preventive or molecular drugs or vaccine couldn't been developed yet due to continuous mutation according to geographic regions in the virus [9]. However, rather than vaccinations, where attenuated antigenic materials are used to stimulate an individual's immune system, Anti-viral targeting may be approached where antiviral drug is designed to identify viral proteins, or parts of proteins, that can be disabled.

Medicinal plants are the integral part of the variety of cultures has been used over many centuries [10]. The Ayurveda empowered the system of freedom and long life. Now – a- days many synthetic drugs have side effects. For eliminating these types of problems medicines are manufactured which has fully botanical origin. If plants show medicinal properties and they can regulate the physiology of human only because of the substances called phytochemicals. These phytochemicals are secondary chemicals which has role in producing biologically active compound which protects the plants from different predators. Various parts of this plant such as the leaves, roots, seed, bark, fruit, flowers and immature pods has medicinal properties [11].Various plants and their phytocompounds has antiepileptic, anti-viral, anti-malarial, antifertility, nephroprotective, immune modulator, immune stimulatory properties, anti-inflammatory activity, anti diabetic effect [12].The different natural product extracted from plants are safe and cost effective.

Medicinal plants are the chief source of many drugs prescribed today in modern medicinal system. About 25% of modern pharmaceutical drugs have ethno botanical origins. Research needs in the field of medicinal plants are huge, which will be beneficial in therapeutic as well as in economic status. Research should be done on numerous plants for knowing its quality, safety, biological activity, and clinical efficacy. Recently new technologies and research have implemented for manufacturing the medicines having botanical origin for making a healthy world. For knowing the beneficial effects and biological activities of selected plants generally experiments has done on the basis of in vitro bioassay or experiments using animal models [13]. Now –a- days the main attention of research is to demonstrate anticancer, antioxidant, anti-inflammatory, immune stimulatory, and antimicrobial property of plants.

Commiphora wightii belongs to family Burseraceae. *Commiphora wightii* gum resin extract is used to cure disease like treat menorrhagia, anemia, leucorrhoea, rheumatism, nervous diseases, bone-fractures, obesity, disorder of lipid metabolism and peptic ulcer [14][15]. *Commiphora wightii* is known to contain phytochemicals like quercetin, alpha-pinene, alpha-terpinol, eugenol, D-limonene, geraniol, linalool, progesterone [16]. There is high possibility that these phytochemicals play a major role in curing wound healing [17]. However, there is no report identifying the specific phytochemical responsible to cure COVID - 19. This study focuses on the identification of the phytochemical of *Commiphora wightii* responsible to cure COVID-19 caused by (SARS-CoV-2) by inhibiting the structural protein.

MATERIALS AND METHODS

Software used

Discovery studio module of Biovia software (Dassault Systems of France) was used for this research work. The level of molecular interaction determine by the machine learning techniques of BIOVIA software.

Methodology

List of phytochemicals

Phytochemicals are produced by plants as secondary metabolites to protect them from predators include bacteria, viruses, fungi etc. When these plants or their parts are consumed by humans these phytochemicals fight against the agents which are threats to the human health. This work is stressed on identification of the particular phytochemical responsible for inhibiting and decreasing the effect of COVID -19.

Structural protein found in SARS-CoV-2

It has been reported that COVID-19 can cause as a result of respiratory infestation. Various metabolic cycles have been exhibited by the viral life cycle for its survival and metabolism. Different enzymes regulates these metabolic cycles. . The list different enzymes in COVID -19 were identified by utilization of BRENDA database. The three-dimensional X-ray crystallographic structures of enzymes in COVID-19 were finding by using PDB structural protein data base (RCSB PDB). It has been found that structural protein HR2 Domain (protein database code 6LVN) is involved in protein metabolism and very crucial for survival and regulation of metabolism of the particular microbe.

Molecular docking

Molecular docking is a key tool in structural molecular biology and computer-assisted drug design. This method has been used to find the phytochemical from the plant extract that act as a ligand and form a strong covalent bond with the viral protein of that particular microbe that need them for survival and then the phytochemicals successfully inhibit the life cycle of viral protein . The Discovery studio module of BIOVIA software was utilizes for identification of molecular interaction and performs molecular docking. At first three dimensional structures of phytochemicals of *Commiphora wightii* were retrieved from PubChem database *(https://pub-chem.ncbi.nlm.nih.gov/)* in sdf format. Then three-dimensional X-ray crystallographic structures of structural protein HR2 Domain were downloaded from the Protein Data Bank *(http://www.rcsb.org/ pdb/home/home.do)*, and used to dock with the identified phytocompounds. The active site of the enzyme was identified via "receptor cavity" protocol found under"receptor-ligand interaction" menu. Molecular docking was performed between the structures of prepared by SARS-CoV-2 target proteins and those of phytocompounds of *Commiphora wightii* by 'CDOCKER' protocol of Discovery studio module of BIOVIA software; this is known as "receptor- ligand interaction". The protein molecule was considered as the receptor molecule and the phytochemical was considered as the ligand. The "-CDOCKER_ENERGY" and "-CDOCKER_INTERACTION_ENERGY" were explain the quality of molecular docking. A good interaction between the ligand and the receptor was indicated by higher positive value. Thus, the capability phytochemical of controlling the disease might showed by the interaction of ligand and receptor with higher positive values.

RESULTS AND DISCUSSION

Fig. 1 shows the active site of the structure of the 2019-nCoV HR2 Domain Enzyme. A light green color appears in the active site of viral protein. CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy. The ligand conformations were obtained by Molecular Dynamic methods.

-CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the non bonded interaction that exists between the protein and the

ligand. The best molecular interaction was explained by two criteria such as a) high positive value of -CDOCKER energy and b) small difference between -CDOCKER energy and -CDOCKER interaction energy [18]. Table 1 show that Quercetin interaction has the highest positive value of -CDOCKER energy (11.5858) and minimum value of the difference (2.1942) between - C DOCKER interaction energy and - C DOCKER energy followed by Eugenol. Thus, the results explained that Quercetin and eugenol could effectively inhibit and interact with the structural protein HR2 Domain thereby interrupting the metabolic pathway of the virus. Higher positive values for Quercetin indicated that it was the most active secondary metabolites against COVID -19 viruses. The other phytocompounds such as alpha-pinene, alpha-terpineol, D-limonene, linalool, geraniol could inhibit the structural protein to a small extent (negative -CDocker energy but positive -CDocker interaction energy).Progesterone could not inhibit and bind with structural protein HR2 Domain. Thus, the most diseases curing phytochemicals preventing COVID-19 caused by SARS-CoV-2 virus were Quercetin and Eugenol.

CONCLUSIONS

It was previously known that *Commiphora wightii* plant has therapeutic action against COVID-19. COVID-19 is caused by SARS-CoV-2. This study was carried out to provide the theoretical basis of this analysis. Discovery studio module of Biovia software, has used for molecular docking operation to find the phytochemical Quercetin and Eugenol, which can have a strong molecular interaction with the vital structural protein HR2 Domain of the microbe. It was found that Quercetin and Eugenol can form strong bond with the structural protein successfully inhibiting the formation of structure of the microbe. Alpha pinene, alpha-terpineol, D- limonene, limonool, geraniol were found to be not much effective in deactivating the structural protein of the microbe. The progesterone could not deactivate viral protein. Thus, this study could explain that the Quercetin and Eugenol were the most important therapeutic ingredients against COVID-19 caused by SARS-CoV-2.

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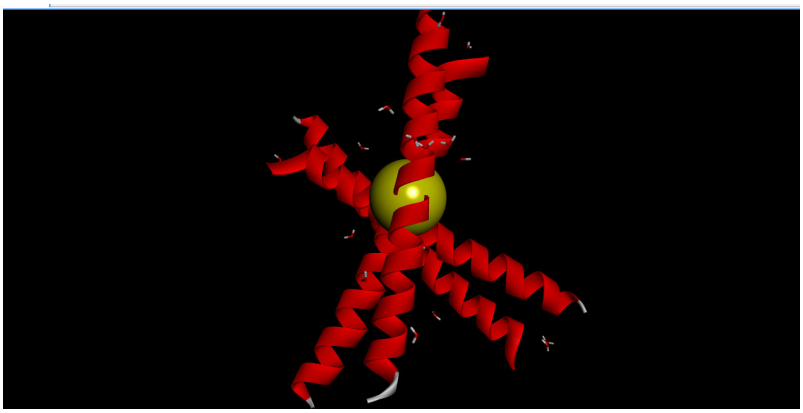

Figure 1. Active site of structural protein HR2 Domain.

Table 1. Results of CDocking of phytochemicals with structure of the 2019-nCoV HR2 Domain Enzyme

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Quercetin	11.5858	13.7800	2.1942
2	Eugenol	4.91067	14.54110	9.63033
3	Alpha-pinene	-12.8891	11.9804	24.8695
4	Linalool	-14.4458	14.2966	28.7424
5	Alpha-terpineol	-13.9703	15.0424	29.0127
6	D-limonene	-28.0489	10.2067	38.2556
7	Geraniol	-27.9037	17.7432	45.6469
8	Progesterone	Failed	Failed	Failed

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RESEARCH ARTICLE

COVID-19 Prevention using *Commiphora wightii* Extract by Blocking SARS-Cov-2 Main Protease with Unliganded Active Site (6Y84) Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "SARS Cov-2 main protease" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Commiphora wightii* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is the most effective diseaseto the whole world. It has been declared as a pandemic.[1][2], However, till presentno proper medicine has been prepared for it.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective .*Commiphora wightii* belongs to family Burseraceae. It contains Geraniol, Quercetin, Eugenol, D-Limonene, Alpha-Terpineol, Progesterone, Z-guggulsterone, Bornylacetate, Alpha-Pinene and Linalooletc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS:

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Commiphora wightii* contains Geraniol, Quercetin, Eugenol, D-Limonene, Alpha-Terpineol, Progesterone, Z-guggulsterone, Bornylacetate, Alpha-Pinene and Linalool etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting SARS Cov-2 main proteaseand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the SARS Cov-2 main proteaseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetinis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Commiphora wightii* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetin can significantly interact with the viralSARS Cov-2 main protease.

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Table 1. Results of CDocking of phytochemicals with SARS Cov-2 main protease(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	30.2178	38.1902	7.9724	Maximum inhibition of viral protein
2	Eugenol	14.5118	23.8261	9.3143	
3	Alpha-Terpineol	-4.63606	23.9765	28.61256	
4	Linalool	-5.14219	25.463	30.60519	
5	Alpha-Pinene	-8.38594	16.461	24.84694	
6	D-Limonene	-19.1929	19.1273	38.3202	
7	Progesterone	-21.0368	33.9782	55.015	
8	Geraniol	-21.5378	25.1402	46.678	
9	Z-guggulsterone	-37.858	30.4573	68.3153	
10	Bornyl acetate	failed	failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Commiphora wightii* Extract by Blocking Structural Nucleocapsid Protein N-terminal RNA Binding Domain (6M3M): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "structural nucleocapsid protein of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Commiphora wightii* extract can effectively fight against"SARS-CoV-2 virus".

Keywords: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Commiphora wightii* belongs to family Burseraceae. It contains Quercetin,Eugenol,Linalool,Alpha-terpineol,Alpha-pinene,D-limonene,Progesterone,Geraniol,Z-gugglesterone etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Commiphora wightii* contains Quercetin, Eugenol,Linalool, Alpha-terpineol, Alpha-pinene, D-limonene, Progesterone, Geraniol, Z-guggl esterone etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting structural nucleocapsid

proteinand controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate the structural nucleocapsid proteinviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that commiphorawightii plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetin can significantly interact with the viralstructural nucleocapsid protein.

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Table 1. Results of CDocking of phytochemicals with structural nucleocapsid protein (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	25.4733	28.3794	2.9061	Maximum inhibition of viral protein
2	Eugenol	5.94869	16.382	10.43331	
3	Linalool	-13.0146	16.5625	29.5771	
4	Alpha-terpineol	-13.2758	14.7926	28.0684	
5	Alpha-pinene	-13.4502	11.4153	24.8655	
6	D-limonene	-25.6076	12.8819	38.7477	
7	Progesterone	-26.3664	28.9443	55.3107	
8	Geraniol	-26.5484	16.5054	43.0538	
9	Z-gugglesterone	-39.4932	27.3857	66.8789	Minimum inhibition of viral protein
10	Bornyl acetate	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Michelia Champa ca* L. Extract by Blocking Nsp[15] RNA Binding Protein Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Nsp[15] RNA binding protein enzyme" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Gallic Acid of *Michelia Champa ca* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)", has become the live threating disease for humankind[1][2],Lot of works on the medicine of the disease has been performed but still no remarkable achievement scientists have[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Michelia Champa ca* belongs to family Magnoliaceae. It contains phytochemicals like Gallic Acid, Quercetin, Alpha cadinol, Alpha humelene, Alpha selinene, Beta caryophyllene, Beta selinene, Camphor sulfonic acid, Docosanoic acid, Farnesol , Gamma cadinene, Nerolidol, Oleic acid, Stigmasterol etc.This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Michelia Champa ca* contains Gallic Acid, Quercetin, Alpha cadinol, Alpha humelene, Alpha selinene, Beta caryophyllene, Beta selinene, Camphor sulfonic acid, Docosanoic acid, Farnesol , Gamma cadinene, Nerolidol, Oleic acid, Stigmasterol etc.. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Nsp[15] RNA binding protein enzymeand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Nsp^{15} RNA binding viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Gallic Acidis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Michelia Champa ca* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Gallic Acid can significantly interact with the viral Nsp^{15} RNA binding protein enzyme.

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Table 1. Results of CDocking of phytochemicals with Nsp[15] RNA binding protein enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Gallic Acid	20.1811	16.0931	4.008	Maximum inhibition of viral protein
2	Beta selinene	-20.507	19.4637	39.9707	
3	Alpha humelene	-56.057	17.5305	73.5875	
4	Beta caryophyllene	-21.963	20.3394	42.3024	
5	Gamma cadinene	-24.8532	20.0489	44.9021	
6	Nerolidol	-29.6734	22.9992	52.6726	
7	Alpha cadinol	FAILED	FAILED	FAILED	
8	Alpha selinene	FAILED	FAILED	FAILED	
9	Docosanoic acid	FAILED	FAILED	FAILED	
10	Farnesol	FAILED	FAILED	FAILED	
11	Oleic acid	FAILED	FAILED	FAILED	
12	Stigmasterol	FAILED	FAILED	FAILED	

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RESEARCH ARTICLE

COVID-19 Prevention using *Michelia Champa ca* L. Extract by Blocking Nsp9 RNA Binding Protein Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with microbial enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin can of *Michelia Champa ca* L. plant extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world due to infections range from mild to deadly. It has been declared as a fast growing global pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Champa* flower plant belongs to family Magnoliaceae. It contains phytochemicals like Gallic Acid, Quercetin, Alpha cadinol, Alpha humelene, Alpha selinene, Beta-caryophyllene, Beta selinene, Camphor sulfonic acid, Docosanoic acid, Farnesol , Gamma cadinene, Nerolidol, Oleic acid, Stigmasterol, etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Michelia Champa ca* L. contains Gallic Acid, Quercetin, Alpha cadinol, Alpha humelene, Alpha selinene, Beta-caryophyllene, Beta selinene, Camphor sulfonic acid, Docosanoic acid, Farnesol , Gamma cadinene, Nerolidol, Oleic acid, Stigmasterol, etc . It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting microbial enzyme and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Nsp9 RNA binding protein thereby interrupting the viral RNA synthesis. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Michelia Champa ca L.* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral enzyme (Nsp9 RNA binding protein)of the microbe.

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Table 1. Results of CDocking of phytochemicals with Nsp9 RNA binding protein (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Gallic Acid	24.3895	21.7008	-2.6887	Minimum inhibition of viral protein
2	Quercetin	17.9809	22.3797	4.3988	Maximum inhibition of viral protein

3	Alpha cadinol	FAILED	FAILED	FAILED	
4	Alpha humelene	FAILED	FAILED	FAILED	
5	Alpha selinene	FAILED	FAILED	FAILED	
6	Beta-caryophyllene	FAILED	FAILED	FAILED	
7	Beta selinene	FAILED	FAILED	FAILED	
8	Camphor sulfonic acid	FAILED	FAILED	FAILED	
9	Docosanoic acid	FAILED	FAILED	FAILED	
10	Farnesol	FAILED	FAILED	FAILED	
11	Gamma cadinene	FAILED	FAILED	FAILED	
12	Nerolidol	FAILED	FAILED	FAILED	
13	Oleic acid	FAILED	FAILED	FAILED	
14	Stigmasterol	FAILED	FAILED	FAILED	

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RESEARCH ARTICLE

COVID-19 Prevention using *Michelia Champaca* L. Extract by Blocking SARS-Cov-2 Main Protease Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with protease Enzyme was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Gallic acid of *Michelia Champa ca* extract can effectively fight against "SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has endangered the entire world. It has been confirmed as a deadly disease.[1][2], However, till now there is no established treatment.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Michelia Champa ca* belongs to family Sterculiaceae. It contains Beta-caryophyllene, beta-selinene,farnesol,gamma-cadinene,nerolidol,eugenol,gallicetc, quercetin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Michelia Champa ca* contains Beta-caryophyllene, beta-selinene,farnesol,gamma-cadinene,nerolidol,eugenol,gallicetc, quercetin etc.. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting protease Enzyme and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the protease Enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSIONS

It was identified that *Michelia Champa ca* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Gallic acid can significantly interact with the viral protease Enzyme.

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Table 1. Results of CDocking of phytochemicals with protease Enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Gallic acid	13.9109	12.0759	1.835	Maximum inhibition of viral protein
2	Quercetin	7.64282	10.2481	2.60528	
3	Eugenol	-1. 21806	8.34884	9.5669	

4	Beta-selinene	-29. 289	10.3821	39.6711	
5	Beta-caryophyllene	-32. 1822	10.2574	42.4396	
6	(-)-gamma-cadinene	-36. 9196	8.02721	44. 26876	
7	Nerolidol	-43. 6565	8.27006	51.92656	
8	Farnesol	-55. 8006	9.46816	65.26876	

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RESEARCH ARTICLE

COVID-19 Prevention using *Michelia champaca* by Blocking ADP Ribose Phosphatase of NSP3 Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Gallic acid of *Michelia Champa ca* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is the disease defining the crisis of global health. Now the disease has been announced as a pandemic.[1][2], Treatment of the disease has not been discovered yet [3]There is a quick need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective . *Michelia Champa ca* belongs to family Magnoliaceae. It contains Farnesol, Gallic acid, b-cadinene, Nerolidol ,Beta-salinene, Oleic acid, Stigmasterol, Docosanoicetc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Michelia Champa ca* contains Farnesol, Gallic acid, b-cadinene, Nerolidol ,Beta-salinene, Oleic acid, Stigmasterol, Docosanoicetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting ADP ribose phosphatase and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the ADP ribose phosphataseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Gallic acidis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Michelia Champa ca* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatGallic acid can significantly interact with the viralADP ribose phosphatase.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	DIFFERENCEBETWEEN-C DOCKER INTERACTIONENERGYAND - C DOCKER ENERGY	Remarks
1	Gallic acid	27.1432	27.4455	0.3023	Maximum inhibition of viral protein
2	Beta-salinene	-21.2435	18.961	40.2045	
3	Gamma-cadinene	-28.631	20.1715	48.8025	
4	Nerolidol	-29.888	22.9953	52.5833	
5	Farnesol	-48.14	26.8317	74.9717	
6	Alpha-cadinol	Failed	NA	NA	
7	Alpha-humelene	Falied	NA	NA	
8	Oleic acid	Failed	NA	NA	
9	Stigmasterol	Failed	NA	NA	
10	Docosanoic	Failed	NA	NA	

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RESEARCH ARTICLE

COVID-19 Prevention using *Plumeria rubra* (*Champa* Flower) Extract by Blocking Structural Protein HR2 Domain (6LVN): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "structural protein HR2 Domain(6LVN) of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Gallic acids of *Plumeria rubra* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a pandemic diseases as recommended by WHO, most of the countries of the world getting affected day by day[1][2], discovery of an effective medicine against it is a great challenge to the researchers of the world. [3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective.*Plumeria rubra* belongs to family Apocynaceae. It contains phytochemicals like Galllic acids, Quercetin, Nerolidol, Alpha cadinol, Camphor sulphuric acid, Olic acid, alpha selinene, Gamma cadinene etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS & METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that Plumeria rubracontains phytochemicals like Galllic acids, Quercetin, Nerolidol, Alpha cadinol, Camphor sulphuric acid, Olic acid, alpha selinene, Gamma cadineneetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting structural protein HR2 Domain(6LVN) and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the structural protein HR2 Domain(6LVN) viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Gallic acids is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Plumeria rubra* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Gallic acids can significantly interact with the viral structural protein HR2 Domain(6LVN) .

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Table 1. Results of CDocking of phytochemicals with structural protein HR2 Domain (6LVN) (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Gallic acids	18.1064	13.7393	4.3671	Maximum inhibition of viral protein
2	Quercetin	11.5858	13.78	2.1942	
3	Nerolidol	-41.9765	9.29574	51.27224	
4	Alpha cadinol	Failed	Failed	Failed	
5	Camphor sulphuric acid	Failed	Failed	Failed	
6	Olic acid	Failed	Failed	Failed	
7	alpha selinene	Failed	Failed	Failed	
8	Gamma cadinene	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Plumeria rubra* Extract by Blocking ADP Ribose Phosphatase of NSP3 Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated thatQuercetinof *Plumeria rubra* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has now become one of the most terrific disease to the whole world. The tag of pandemism has already been added to it.[1][2], The curing technique of the disease is still a mystery[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases[4].Their phytochemicals will be low-cost but effective . *Plumeria rubra* belongs to family Apocynaceae. It contains Galllic acids, Quercetin, Nerolidol, Alpha cadinol, Camphor sulphuric acid, Olic acid, alpha selinene, Gamma cadineneetc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Plumeria rubra*contains Galllic acids, Quercetin, Nerolidol, Alpha cadinol, Camphor sulphuric acid, Olic acid, alpha selinene, Gamma cadinene etcIt is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting ADP ribose phosphataseand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the ADP ribose phosphataseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetinis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Plumeria rubra* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetincan significantly interact with the viralADP ribose phosphatase.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Alpha Cadinol	FAILED	NA	NA	
2	Alpha Humelene	-45.6697	24.6404	70.3101	
3	Alpha Selinene	FAILED	NA	NA	
4	Beta Caryophyllene	-18.9642	23.8049	42.7691	
5	Beta Selinene	-13.7696	28.5465	42.3161	
6	Camphor sulphonic acid	FAILED	NA	NA	
7	Docosanic Acid	FAILED	NA	NA	
8	Farnesol	-33.3112	34.2852	67.5964	
9	Gallic Acid	36.3442	32.6755	3.6687	
10	Gamma Cadinene	-21.1048	24.5563	45.6611	
11	Nerolidol	-18.2276	35.1584	53.386	
12	Oleic Acid	FAILED	NA	NA	
13	Quercetin	42.0864	45.5796	3.4932	Maximum inhibition of viral protein
14	Stigmasterol	FAILED	NA	NA	

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RESEARCH ARTICLE

COVID-19 Prevention using *Syzygium aromaticum*_(Clove) Extract by Blocking Viral Protein NSP-15-Endoribonuclease (6VWW) : An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory protein syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with viral protein NSP-15-Endoribonuclease (6VWW) was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Myricetin of *Syzygium aromaticum* extractcan effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has very dangerous for whole world.The researchers try to find the vaccine of this disease but they are unable to get till now[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Syzygium aromaticum* belongs to family myrtaceae. It contains Beta- caryophyllene,eugenol,Gallic acid,kaempferol, Myricetin quercetin,vanillin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Syzygium aromaticum* containbeta-caryophyllene, eugenol, Gallic acid,kaempferol, Myricetin, quercetin, vanillin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting viral protein NSP-15-Endoribonuclease (6VWW) and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the viral protein NSP-15-Endoribonuclease (6VWW) viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Myricetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Syzygium aromaticum* plantcan prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Myricetin and Rhamnetin can significantly interact with the viralprotein NSP-15-Endoribonuclease (6VWW).

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Table 1. Results of CDocking of phytochemicals with viral protein NSP-15-Endoribonuclease (receptor)

SL NO	LIGAND	-C DOCKER ENERGY	-C DOCKER INTERACTION ENERGY	Difference between-CDOCKERinteraction energy and -C DOCKER energy	Remark
1	Myricetin	27.0413	29.5263	2.485	Maximum inhibition of viral protein
2	Vanillin	13.4349	16.7968	3.3619	
3	GallicAcid	18.9185	15.1424	3.7761	
4	Rhamnetin	21.5095	27.4628	5.9533	
5	Kaempferol	19.8813	27.4993	7.618	
6	Eugenol	5.94869	16.382	10.43331	
7	β-Caryophyllene	-25.0454	17.1463	42.1917	Minimum inhibition of viral protein
8	Stigmasterol	Failed	Failed	Failed	
9	Oleanoidacid	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Syzygium aromaticum* (Clove) Extract by Blocking Structural Protein HR2 Domain (6LVN): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "structural protein HR2 Domain of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that *Syzygium aromaticum* (clove) Extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" caused by the SARS-CoV-2 has threatened the whole world [1][2], However, till now there is no established treatment.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Syzgium aromaticum* belongs from Myrtaceae family and generally it is also known as cloves. It is a dried flower bud (NCBI). Clove in particular has attracted the attention due to the potent antioxidant and antimicrobial activities standing out among the other spices. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Syzygium aromaticum* contains phytochemicals like Eugenol, Gallic acid, Kaempferol, Myricetin, Rhamnetin, Vanillin, Stigmasterol, Oleanoid acid, Beta-Caryophyllene, Compesterol 3- beta-d-glucoside. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting structural protein HR2 Domain of SARS-CoV-2 and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract that can deactivate the structural protein HR2 Domain of SARS-CoV-2 viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSIONS

It was identified that *Syzygium aromaticum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Gallic acids can significantly interact with the structural protein HR2 Domain of SARS-CoV-2.

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Table 1 shows that Gallic acid is the phytochemical that can really prevent COVID-19 attack.

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	DIFFERENCE BETWEEN -CDOCKER INTERACTION ENERGY AND –CDOCKER ENERGY
1	Gallic acids	18.3272	14.8785	3.4487
2	Rhamnetin	13.758	22.4875	8.7295
3	Myricetin	12.9417	14.1295	1.1878
4	Vanillin	12.235	15.7387	3.5037
5	Kaempferol	10.892	15.2245	4.3325
6	Eugenol	4.91076	14.5411	9.63034
7	Stigmasterol	Failed	Failed	Failed
8	Oleanoid acid	Failed	Failed	Failed
9	Compesterol 3-beta-d-glucoside	Failed	Failed	Failed
10	Beta-caryophyllene	Failed	Failed	Failed

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RESEARCH ARTICLE

COVID-19 Prevention using *Syzygium aromaticum* (Clove) Extract by Blocking the Protease Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "protease enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Myricetin of clove extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has threatened the whole world. It has been declared as a pandemic.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. Clove belongs to family Myrtaceae. *Syzygium aromaticum* leaves extract is used to cure disease like cancer, to treat toothache, colic, cough, asthma, intestinal flatulence, fever reduction.. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that clove contains *Syzygium aromaticum* contains phytochemicals like beta-Carophyllene, Eugenol,Gallic acid, Kaempferol, Quercetin, Myricetin,Rhamnetin &Vanillin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting protease enzymeand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the protease enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug.

CONCLUSIONS

It was identified that clove plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that myricetin can significantly interact with the viral protease enzyme.

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Table 1 shows that Myricetin is the phytochemical that can really prevent COVID-19 attack.

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Myricetin	19.5732	22.1435	2.5703
2	Beta-Caryophyllene	22.7097	19.8602	2.8495
3	vanillin	14.5247	17.7653	3.2406
4	Gallic acid	19.8199	16.4905	3.3294
5	Kaempferol	19.227	23.6424	4.4154
6	Rhamnetin	16.5698	22.8884	6.3186
7	Eugenol	9.8973	19.8199	9.8973
8	Compesterol 3-beta-d-glucoside	Failed	Failed	Failed
9	Oleanoic acid	Failed	Failed	Failed
10	Stigmasterol	Failed	Failed	Failed

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RESEARCH ARTICLE

COVID-19 Prevention using the *Obroma cacao* L. Extract by Blocking Papain-Like Protease of SARS CoV-2: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "PROTIASE of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Cacao* L extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)" is an an infectious malady transmitted through contact, air water etc.WHO has declared it as pandemic.[1][2], However, till now there is no established treatment.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Cacao* L belongs to family Malvaceae. It contains phytochemicals likeCaffeine, Luteoline, P-coumarinic acid, Phloretic acid, Quercetin, Chlorogenic acid, Iso-orientin, Isovitexines, M-Coumaric Acid-1,2,3-13C3, Phenylacetic acid, Vanillic acid, Syringin acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Cacao* L contains phytochemicals likeCaffeine, Luteoline, P-coumarinic acid, Phloretic acid, Quercetin, Chlorogenic acid, Iso-orientin, Isovitexines, M-Coumaric Acid-1,2,3-13C3, Phenylacetic acid, Vanillic acid, Syringin acid It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Protiase and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Protiase viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cacao* L plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral PROTIASE.

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Table 1. Results of CDocking of phytochemicals with PROTIASE (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Caffeine	12.62	20.61	7.99	
2	Chlorogenic acid	22.34	35.86	13.52	
3	Iso-orientin	21.53	50.66	29.13	
4	Isoquercetin	4.44	40.69	36.25	
5	Isovitexines	14.58	43.10	28.52	

6	P-coumaric acid	28.66	29.97	1.31	
7	Phenylacetic acid	19.27	19.42	0.15	
8	Phloretic acid	28.097	26.8005	1.2965	
9	Quercetin	31.5442	34.8941	3.3499	Maximun ninhibition of Viral Protein
10	Syringic acid	19.73	25.10	5.37	
11	Vanillic acid	21.90	24.91	3.01	
12	vitexin	22.1181	50.3151	28.1969	
13	Procyadin D	FAILED	FAILED	N/A	
14	Procyadin C1	FAILED	FAILED	N/A	

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RESEARCH ARTICLE

COVID-19 Prevention using *Theobroma cacao* (*Cocoa* Tree) Extract By Blocking Structural Protein HR2 Domain (6lvn): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "-nCoV HR2 Domain of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Phloretic acid of *Cocoa* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is an infectious disease. [1][2], At this time there is no specific vaccines or treatment for COVID-19.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *COCOA* belongs to family Malvaceae. It contains phytochemicals like Galllic acids, Ferulic acids, Luteolin, Vanilic acid, Phenylatic acid, Syringic acid, Caffeine, P-Coumaric acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Cocoa* contains Galllic acids, Ferulic acids, Luteolin, Vanilic acid, Phenylatic acid, Syringic acid, Caffeine, P-Coumaric acid etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting -nCoV HR2 Domain and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the -nCoV HR2 Domain viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Phloretic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cocoa* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Phloretic acid can significantly interact with the viral -nCoV HR2 Domain.

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Table 1. Results of CDocking of phytochemicals with -nCoV HR2 (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Phloretic acid	16.3888	15.0235	1.3653	Maximum inhibition of viral protein
2	Ferulic acids	13.928	17.2004	4.0439	
3	Luteolin	13.1565	16.0984	2.9419	
4	Vanilic acid	12.9284	14.2951	1.7164	
5	Phenylatic acid	12.5787	12.5699	0.0088	
6	Syringic acid	8.33446	14.2081	5.87364	
7	Caffeine	8.22602	16.2716	8.04558	
8	P-Coumaric acid	9.40832	10.7824	1.37408	

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RESEARCH ARTICLE

COVID-19 Prevention using *Theobroma cacao* Extract by Blocking Nsp15 RNA Binding Protein Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Nsp15 RNA binding protein Enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Procyanidin B4-3-O-gallate of *Theobroma cacao* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is become pandemic in the present situation. Human race are in a threatened condition for this virus. [1][2], presently no treatment available to the researchers. It's make a great challenge to the scientists [3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Theobroma cacao* belongs to family Malvaceae. It contains Caffenine, Chlorogenic acid , Ferulic acid, Hyperine-quercetin-3-O-Galactoside, iso-orientin, isoquercetin, isovitexines, luteolin, naringenin, 0-Coumaric acid, p-Coumaric acid, phenylacetic acid, Procyanidin B4-3-O-gallate, prunin-naringenin-7-O-glucoside,quercetin, syringic acid ,Theobromine , Vanillic aciid, vitexinetc. etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Theobroma cacao* contains Caffenine, Chlorogenic acid , Ferulic acid, Hyperine-quercetin-3-O-Galactoside, iso-orientin, isoquercetin, isovitexines, luteolin, naringenin, 0-Coumaric acid, p-Coumaric acid, phenylacetic acid, Procyanidin B4-3-O-gallate, prunin-naringenin-7-O-glucoside,quercetin, syringic acid Theobromine , Vanillic aciid, vitexinetc.etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Nsp15 RNA binding protein Enzymeand controlling of

COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Nsp15 RNA binding protein Enzyme.The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Procyanidin B4-3-O-gallate is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Theobroma cacao* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatProcyanidin B4-3-O-gallate can significantly interact with the viralNsp15 RNA binding protein Enzyme.

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Table 1. Results of CDocking of phytochemicals with Nsp15 RNA binding protein Enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
S1	Procyanidin B4-3-O-gallate	49.6829	61.9244	12.2415	Maximum inhibition of viral protein
2	Procyanidin B4	34.1931	51.2314	17.0383	
3	Procyanidin	37.35	56.5249	19.1749	
4	Procyanidin B3	34.1056	52.6046	18.499	

5	Procyanidin D	34.8277	48.2121	13.3844	
6	Iso-Orientin	16.8578	38.6229	21.7651	
7	Iso-Quercetin	8.544477	42.0724	33.527923	
8	Syringic acid	14.8026	19.7562	5.6736	
9	Chlorogenic acid	21.2123	38.4287	17.2164	
10	Iso-vitexine	13.0093	36.673	23.6637	
11	Hyperine quercetin 3-galactoside	14.751	41.0945	26.3435	
12	Luteolin	23.9531	27.3491	3.396	
13	Naringenin	18.4644	24.6201	6.1557	
14	vitexin	15.0355	40.0125	24.977	
15	Phloretic acid	20.3268	18.5591	1.7677	
16	Theobromine	11.4816	16.9827	5.5011	
17	O-Coumaric acid	9.15799	16.6507	7.49271	
18	P-Coumaric acid	21.6549	22.0772	0.4223	
V19	Phenyl acetic acid	13.6467	13.5591	0.0876	
20	Quercetin	27.1534	30.2261	3.0727	
21	Caffine	FAILED	FAILED	FAILED	
22	Ferulic	FAILED	FAILED	FAILED	
23	Orientic	FAILED	FAILED	FAILED	
24	Procyanidin B1	FAILED	FAILED	FAILED	
25	Procyanidin C1	FAILED	FAILED	FAILED	
26	Prunine-_Naringenin-7-O-glucoside	FAILED	FAILED	FAILED	
27	Quercetin-3-O-arabiniside	FAILED	FAILED	FAILED	

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RESEARCH ARTICLE

COVID-19 Prevention using *Theobroma Cacao* Extract By Blocking ADP Ribose Phosphates of NSP3 Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with microbial enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Phloretic acid of *Theobroma cacao* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has dark the whole world. It has been declared as a pandemic due to infectious disease.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Cocoa* belongs to family Malvaceae or Mallows. It contains phytochemicals like Caffenine, Chlorogenic acid , Ferulic acid, iso-orientin, isoquercetin, isovitexines, luteolin, naringenin, 0-Coumaric acid, p-Coumaric acid, phenylacetic acid, Procyanidin B4-3-O-gallate, prunin-naringenin-7-O-glucoside,quercetin,syringic acid ,Theobromine , Vanillic aciid, Isovitexin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Theobroma cacao* contains Caffenine, Chlorogenic acid , Ferulic acid, , iso-orientin, isoquercetin, isovitexines, luteolin, naringenin, 0-Coumaric acid, p-Coumaric acid, phenylacetic acid, Procyanidin B4-3-O-gallate, prunin-naringenin-7-O-glucoside,quercetin, syringic acid ,Theobromine , Vanillic aciid, vitexin etc. It is known that plants

belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-19.Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the microbial enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Phloretic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Theobroma cacao* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Phloretic acid can significantly interact with the viral metabolic cycle of the microbe.

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Table 1. Results of CDocking of phytochemicals with NSP3 ADP Ribose Phosphates protein enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	DIFFERENCE BETWEEN -C DOCKER INTERACTION ENERGY AND -C DOCKER ENERGY	Remarks
S1	Phenylacetic acid	22.1541	22.5257	0.3716	
2	Phloretic acid	23.0877	23.4262	0.3385	Maximum inhibition of viral protein
3	P-coumaric acid	25.5978	27.4221	1.8243	
4	Vanillic acid	20.6619	25.5048	4.8429	
5	Theobromine	13.3988	19.2642	5.8654	
6	Luteolin	24.5307	29.8973	5.3666	
7	Syringic acid	21.5352	28.0965	6.5613	
8	Prunin	-46.328	10.3064	56.6344	Minimum inhibition of viral protein
9	Procyanidin D	Failed	NA	NA	
10	Procyanidin C1	Failed	NA	NA	

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RESEARCH ARTICLE

COVID-19 Prevention using *Theobroma cacao* L. Extract by Blocking SARS-CoV-2 Main Protease Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)".The molecular docking of the phytochemicals with "main protiaseof SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated thatp-Coumarinic acid of *Theobroma cacao* leaf extract can effectively fight against"SARS-CoV-2 virus".

Key words: Phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has scared the the people globally. It has killed many people globally. Thus, has been declared as pandemic by WHO [1][2].However, the people working on this fails to discover any medicines till now [6].There is a need to identify medicines against the virus. There are a number of medicinal plantstreating various diseases [9].Their phytochemicals will be low-cost but effective. *Theobroma cacao* belongs to family malvaceae. *Theobroma cacao* is known to contain phytochemicals likeCaffeine, Luteoline, P-coumarinic acid, Phloretic acid, Quercetin, Chlorogenic acid, Iso-orientin, Isovitexines, M-Coumaric Acid-1,2,3-13C3, Phenylacetic acid, Vanillic acid, Syringin acid etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Theobroma cacao* contains phytochemicals like Caffeine, Luteoline, P-coumarinic acid, Phloretic acid, Quercetin, Chlorogenic acid, Iso-orientin, Isovitexines, M-Coumaric Acid-1,2,3-13C3, Phenylacetic acid, Vanillic acid, Syringin acid etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting main protease of SARS CoV-19and

controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract thatcan deactivate the main protease of SARS CoV-19viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Heptadecane is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Theobroma cacao* leaves can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatp-Coumarinic acidcan significantly interact with the viralmain protease of SARS CoV-19.

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Table 1. Results of CDocking of phytochemicals with main protease of SARS CoV-19(Receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	P-Coumarinic acid	10.8599	10.7271	0.1328	Maximum inhibition of viral protein
2	Phloretic acid	7.7141	6.46434	1.24976	
3	Quercetin	7.64282	10.2481	2.60528	
4	Luteoline	6.8315	10.0497	3.2182	
5	Caffenine	-0.349591	7.87358	8.223171	

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RESEARCH ARTICLE

COVID-19 Prevention using *Cocos nucifera* Extract By Blocking NSP15 Endoribonuclease (6VWW) Enzyme: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "NSP15 Endoribonuclease (6VWW)of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Nicotinic acid of *Cocos nucifera* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a transmissible disease with serious fatal implications for countries with ageing populations.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases. [4] Their phytochemicals will be low-cost but effective. *Cocos nucifera* belongs to family *Arecaceae*. It contains Nicotinic acid, Riboflavin, Biotin, Catechins, Folic acid and Leucoanthocyanidins etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Cocos nucifera* contains Nicotinic acid, Riboflavin, Biotin, Catechins, Folic acid and Leucoanthocyanidins etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting NSP15 Endoribonuclease (6VWW) and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, thatcan deactivate the NSP15 Endoribonuclease (6VWW) viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows thatNicotinic acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cocos nucifera* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatNicotinic acid can significantly interact with the viralNSP15 Endoribonuclease (6VWW).

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Table 1. Results of CDocking of phytochemicals with NSP15 Endoribonuclease (6VWW)(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Nicotinic acid	10.3536	14.0281	3.6745	Maximum inhibition of viral protein
2	Riboflavin	6.99033	34.5746	27.58427	
3	Biotin	Failed	Failed	Failed	
4	Catechins	Failed	Failed	Failed	
5	Folic acid	Failed	Failed	Failed	
6	Leucoanthocyanidins	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Commiphora wightii* (Commiphora) Extract By Blocking the SARS-CoV-2 Protease Enzyme (6M03): An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Protease Enzyme of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Commiphora wightii* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a very deadly deasease.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Commiphora wightii* belongs to family Burseraceae. It contains Alpha-pinene, Alpha-terpineol,Bornyl acetate, d-limonene, Eugenol, Geraniol, Linalool, Progesterone, Quercetin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Commiphorawightii* contains Alpha-pinene, Alpha-terpineol,Bornyl acetate, d-limonene, Eugenol, Geraniol, Linalool, Progesterone, Quercetin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Protease Enzyme and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Protease Enzyme viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Commiphora wightii* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral Protease Enzyme.

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Table 1. Results of CDocking of phytochemicals with Protease Enzyme (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	26.7445	29.4942	2.7497	Maximum inhibition of viral protein
2	Eugenol	9.8973	19.3507	9.4534	
3	Alpha- pinene	-8.39711	16.6948	25.09191	

4	Alpha terpinole	-12.2075	17.3353	29.5428	
5	Linalool	-14.4329	16.8727	31.3056	
6	Geraniol	-23.3239	24.8478	48.1717	
7	D-limonene	-25.2386	13.5546	38.7932	
8	Bornyl acetate	Failed	Failed	Failed	
9	Progesterone	Failed	Failed	Failed	
10	Z-guggulsterona	Failed	Failed	Failed	

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RESEARCH ARTICLE

COVID-19 Prevention using *Theobroma Cacao* Extract by Blocking Nsp9 RNA Binding Protein Enzyme: An *In silico* Analysis

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ABSTRACT

Coronavirus sickness 2019 (COVID-19) is an irresistible ailment created by extreme intense respiratory condition coronavirus 2 (SARS-CoV-2).The malady causes respiratory ailment (like this season's flu virus) with manifestations, for example, a hack, fever, and in progressively serious cases, trouble relaxing. It has been a wellspring of dread and anguish worldwide as a progressing pestilence which is resulting a huge number of deaths and influencing millions if individuals consistently. To beat these obstructions analysts are attempting to concoct a conventional immunization or preventive medications. Be that as it may, this investigation expectations to get meds from plant remove containing phytochemicals instead of incorporating new synthetics which end up being progressively costly and dangerous contrasted with their natural partner. Phytochemicals are non-nutritive mixes got from plants. It has been normal that plant remove based medications may fix COVID-19, which is brought about by (SARS-CoV-2). The said infection contains Nsp9 RNA restricting proteinenzyme which is accounted for to be extremely pivotal for the endurance of the living being. In this study *Theobroma cacao* plant separate is taken as ligands which will tie with the viral protein.The sub-atomic docking of the phytochemicals with the microbial compound was contemplated utilizing Biovia Discovery Studio. The quality of the cooperation was assessed dependent on - CDocker vitality and - CDocker collaboration vitality. High positive qualities for both the parameters demonstrated that out of various phytochemicals Phloretic corrosive can successfully deactivate the enzymatic metabolic movement subsequently intruding on the existence pattern of (SARS-CoV-2) infection.

Key words: *Theobroma cacao*, immunization, docking, ligands

INTRODUCTION

Coronavirus malady 2019 (COVID-19) is a transmittable ailment bringing about the progressing 2019–20 coronavirus pandemic with genuine lethal ramifications for nations with maturing populaces. The World Health Organization

(WHO) certify the 2019–20 coronavirus flare-up a Public Health Emergency of International Concern (PHEIC) on 30 January 2020, and a pandemic on 11 March 2020.[1][2] Some of the primary instances of the pestilence were accounted for in December 2019 at Wuhan, the capital of China's Hubei area, which has since heightened globally.[3][4] According to the insights, the development rate, at which the quantity of passings is multiplied, is just 7 days all inclusive. While 4600+ passings including everyday schedule according to the time the article being composed, sending the mortality diagram skyward. The all out number of affirmed cases has since contacted the 1 million imprint with 72000+ cases being accounted for every day. In any case, the all out number of COVID-19 cases isn't known.As World Health Organization (WHO) clarifies an affirmed case is "an individual with research center affirmation of COVID-19 infection".The complete number of affirmed cases are lower than the quantity of absolute cases on the grounds that not every person is tried. Not all cases have a "research facility affirmation", testing is the thing that has the effect between the quantity of affirmed and all out cases and furthermore in light of the fact that for some of them, the illness has finished and they have either recuperated or kicked the bucket from it. [5]. Shockingly any sort of preventive or atomic medications or immunization couldn't been grown at this point because of ceaseless mutationaccording to geographic areas in the virus.[6] However, instead of inoculations, where weakened antigenic materials are utilized to invigorate a person's resistant system,Anti-viral focusing on might be moved toward where antiviral medication is intended to distinguish viral proteins, or parts of proteins, that can be incapacitated.

Nature has been a wellspring of restorative specialists for a large number of years and a great number of present day drugs have been gotten from normal source [7]. The restorative estimation of the plants lies in some compound substances that produce a clear physiological activity on the human body, these substances are called phytochemicals, which can be utilized for remedial reason. Plants based restorative constituents can be gotten from any piece of plant like bark, leaves, blossoms, roots, organic products, and seeds.[8] Various therapeutic plants and their phytoextracts have indicated various therapeutic properties like enemy of oxidant , mitigating , hostile to malignant growth , against microbial, hostile to diabetes activity etc.[9]Among various wellsprings of normal items, plants have been a wellspring of novel concoction substance, which fills in as beginning materials for various old and new pharmaceutical items while ending up being protected and savvy .

Therapeutic plants are the establishment of numerous medications recommended today in present day restorative framework. About 25% of current pharmaceutical medications have herbal starting points. Research needs in the field of therapeutic plants are immense, yet are adjusted by the potential medical advantages and the huge size of the market. Investigation into the quality, security, natural movement, and clinical adequacy of the various plants in like manner utilization is required. Recently developing logical methods and approaches have been utilized in the developing region of therapeutic plant look into, for the examination of constituents and assurance of organic action of restorative plants. Proof for the advantageous impacts of chosen plants is commonly founded on tests showing an organic action in an important in vitro bioassay or examinations utilizing creature models.[10] Plants that exhibited anticancer, cancer prevention agent, mitigating, immunostimulatory, and antimicrobial properties have gotten look into consideration.

Cocoa plant has a place with family Malvaceae. *Theobroma cacao* leaves separate is utilized to fix sickness like asthma, shortcoming, loose bowels, breaks, loss of craving, jungle fever, parasites, pneumonia, hack, colic and poisoning.The plant is an evergreen tree whichnatively has a place with the profound tropical areas of Mesoamerica. Its seeds, *Cocoa* beans, are utilized to make chocolate alcohol, *Cocoa* solids, *Cocoa* margarine and chocolate.[11] *Theobroma cacao* is known to contain phytochemicals likePhloretic corrosive, Phenyl acidic corrosive, Quercetin, P-Coumaric corrosive, Ferulic Acid, Vanillic Acid, Theobromine, Caffine, Luteolin, Naringenin, Syringic corrosive, Hyperine quercetin 3-galactoside, Iso-vitexine, Chlorogenic corrosive, Vitexin, Procyanidin B4-3-O-gallate, Iso-Orientin, O-Coumaric corrosive, Procyanidin B3, Procyanidin B4, Procyanidin, Iso-Quercetin, Procyanidin D, Orientic, Procyanidin B1, Procyanidin C1, Prunine, Naringenin-7-O-glucoside, Quercetin-3-O-arabiniside and so on. There is high chance that

these phytochemicals assume a significant job in restoring COVID - 19. Be that as it may, there is no report recognizing the particular phytochemical dependable to fix COVID - 19.

Coronavirus ailment 2019 (COVID-19) is a transmittable illness affected by extreme intense respiratory condition coronavirus 2 (SARS-CoV-2).[12] Genetic examination has uncovered that the coronavirus hereditarily bunches with the family Betacoronavirus, in subgenus Sarbecovirus (ancestry B) along with two bat-determined strains. It is 96% indistinguishable at the entire genome level to other bat coronavirus tests (BatCov RaTG13).[13][14] Those tainted with the infection might be asymptomatic or create influenza like manifestations, including fever, hack, exhaustion, and brevity of breath.Emergency side effects incorporate trouble breathing, diligent chest torment or weight, disarray, trouble waking, and pale blue face or lips; prompt clinical consideration is exhorted if these indications are available. Side effects, for example, sickness, retching, and loose bowels have been seen in differing rates [15][16]. It spreads a lot of like a cold or seasonal influenza through the removed airborne beads from an individual with irresistible COVID-19 or through close/surface contact. Wheninhaled or interacted with eyes, nose or mouth, the infection can settle in the lungs, where it starts to develop which can be life-threatening.However, it is conceivable to control the malady by hindering the protein pathway of the microorganism. It has been seen that Nsp9 RNA restricting protein which dwells in the extracellular framework of the infection is related with the viral RNA synthesis.[17] By repressing the authoritative of the chemical deactivating of the infection might be accomplished

MATERIALS AND METHODS

Software used

Discovery studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques to predict the level of molecular interaction

Methodology

List of phytochemicals: Phytochemicals are produced by plants as secondary metabolites to protect them from predators. The potential threats to plants include bacteria, viruses, fungi etc. When these plants or their parts are consumed by humans these phytochemicals fight off threats to health. Some phytochemicals have been used as poisons and others as traditional medicine.

It has already been established that *Syzygium aromaticum* plant belonging to myrtaceae family has potential to help controlling COVID-19. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of COVID-19. It has been accounted for that COVID-19 can cause because of respiratory infestation.Various metabolic cycles have been found in the viral life cycle for its endurance. These metabolic cycles are managed by various chemicals. Brenda catalyst database was utilized to recognize and list various chemicals found in CoVID-19. It has been discovered that protease chemical (protein database code 6M03) is associated with request to endure.

Enzyme found in SARS CoV-2:: Molecular docking technique has been utilized to distinguish the phytochemical from the plant separate, that go about as a ligand and structure a solid covalent security with the bacterial protein to effectively restrain the organism. The Discovery studio module of Biovia programming was utilized for recognizing sub-atomic cooperation and perform sub-atomic docking. In this procedure first the sdf records for the phytochemicals found in the *Syzygium aromaticum* plant were downloaded from the site. The protein database code of the enzymewas distinguished from the site. The dynamic site of the compound was recognized by means of "receptor hole" convention found under "receptor-ligand collaboration" menu. Sub-atomic docking was finished utilizing the CDocker convention of Biovia programming under "receptor-ligand connection". The compound atom

was treated as the receptor particle and the phytochemical was treated as the ligand. The "- CDOCKER_ENERGY" and "- CDOCKER_INTERACTION_ENERGY" were utilized as marker for the nature of sub-atomic docking. The high positive estimation of those markers introduced a decent collaboration between the ligand and the receptor. In this manner, the communications with high qualities may demonstrate the significant phytochemical answerable for relieving the ailment.

RESULTS AND DISCUSSION

Fig. 1 shows the activesite of the Protease enzyme. It appears as light green color. CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy. The ligand conformations were obtained by Molecular Dynamic methods.

-CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the nonbonded interaction that exists between the protein and the ligand.The criteria for best interaction was chosen based on a) high positive value of -CDOCKER energy and b)small difference between -CDOCKER energy and -CDOCKER interaction energy.

Table 1 shows that Myricetin interaction has the highest positive value of -CDOCKER energy 19.5732 and minimum value of the difference 2.5703 between - C DOCKER interaction energy and - C DOCKER energy followed by Beta-Caryophyllene,Vanillin,Gallic acid,Kaempferol,Rhamnetin,Eugenol. Thus, the results indicated that Myricetin can effectively deactivate crystal structure of COVID-19 Main Protease in apo form enzyme thereby interrupting the metabolic pathway of the virus. Higher positive values for Myricetin indicated that it was the most active ingredient against SARS-CoV-2 virus. On the other hand, Beta-Carophyllene can deactivate the enzyme to a small extent (negative -CDocker energy but positive -CDocker interaction energy). Thus, the key phytochemicals preventing COVID-19 caused by SARS CoV-2 virus is Myricetin,Vanillin,Gallic acid,Rhamnetin,Kaempferol,Eugenol.

CONCLUSION

It was recently realized that *Syzygium aromaticum* plant has restorative activity against COVID-19. COVID-19 is brought about by SARS-CoV-2. This examination was completed to give the hypothetical premise of this perception. Utilizing Discovery studio module of Biovia programming, atomic docking activity was performed to recognize the phytochemical Myricetin,Vanillin, Gallic acid,Beta-Caryophyllene, Kaempferol, Rhamnetin,Eugenol which can have a huge collaboration with the indispensable Protease in apo structure Enzyme. It was discovered that Myricetin can shape solid bond with the catalyst followed by Beta-Carophyllene,Vanillin,Gallic corrosive, Kaemferol, Rhamnetin,Eugenol effectively restraining the lipid metabolic pattern of the organism. Stigmasterol,Olenoic corrosive were seen as very little compelling in deactivating the chemical of the organism. Accordingly, this examination could clarify that the nearness of myricetin gave the therapeutic qualities against COVID-19 brought about by SARS-CoV-2.

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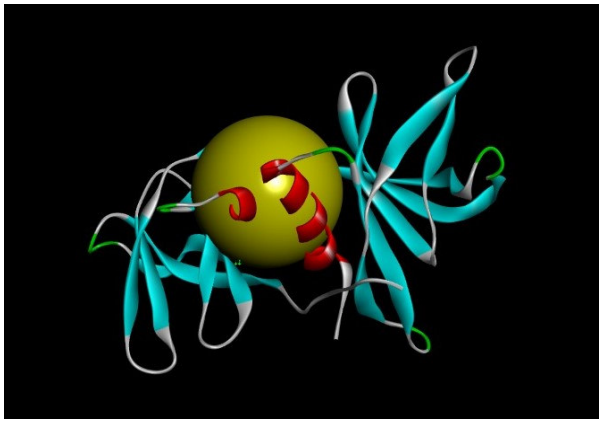

Figure 1. Active site of (Nsp9 RNA binding protein) enzyme

Table 1. Results of CDocking of Phytochemicals with Protease (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Myricetin	19.5732	22.1435	2.5703
2	Beta-Caryophyllene	22.7097	19.8602	2.8495
3	vanillin	14.5247	17.7653	3.2406
4	Gallic acid	19.8199	16.4905	3.3294
5	Kaempferol	19.227	23.6424	4.4154
6	Rhamnetin	16.5698	22.8884	6.3186
7	Eugenol	9.8973	19.8199	9.8973
8	Compesterol 3-beta-d-glucoside	Failed	Failed	Failed
9	Oleanoic acid	Failed	Failed	Failed
10	Stigmasterol	Failed	Failed	Failed

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RESEARCH ARTICLE

COVID-19 Prevention using *Syzygium aromaticum* Extract by Blocking Structural Protein Nucleocapsid Protein N-terminal RNA Binding Domain: An *In silico* Analysis

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory protein syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with protein nucleocapsid protein N - Terminal RNA was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Myricetin of *Syzygium aromaticum* can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has afraid the whole world.The researchers try to find the vaccine of this disease but they are unable to get till now.[1][2], However, till now there is no established treatment.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective.syzygium aromaticumbelongs to family myrtaceae. It contains Beta- caryophyllene,eugenol,Gallic acid,kaempferol, Myricetin quercetin,vanillin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Syzygium aromaticum* containbeta-caryophyllene, eugenol,Gallic acid,kaempferol, Myricetin, quercetin, vanillin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting nucleocapsid protein N- Terminal RNAand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the nucleocapsid protein N-Terminal RNA viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Myricetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Syzygium aromaticum* plantcan prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatMyricetin can significantly interact with the viralprotein nucleocapsid protein N- Terminal RNA

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Table 1. Results of CDocking of phytochemicals with nucleocapsid protein N-Terminal RNA (receptor)

SL NO	LIGAND	-C DOCKER ENERGY	-C DOCKER INTERACTION ENERGY	Differencebetween-CDOCKER interaction energy and-CDOCKER energy	Remark
1	Myricetin	27.0413	29.5263	2.485	Maximum inhibition of viral protein
2	Vanillin	13.4349	16.7968	3.3619	
3	GallicAcid	18.9185	15.1424	3.7761	
4	Rhamnetin	21.5095	27.4628	5.9533	
5	Kaempferol	19.8813	27.4993	7.618	
6	Eugenol	5.94869	16.382	10.43331	
7	β-Caryophyllene	-25.0454	17.1463	42.1917	Minimum inhibition of viral protein
8	Stigmasterol	Failed	Failed	Failed	
9	Oleanoidacid	Failed	Failed	Failed	

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RESEARCH ARTICLE

In Silico Analysis of COVID-19 Prevention using *Commiphora wightii* Extract By Blocking Papain-Like Protease of SARS CoV-2

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with papain like protease of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "CDocker energy and –Cdocker interaction energy" indicated that Quercetin of *Commiphora wightii* extract can effectively fight against"SARS-CoV-2 virus".

Key words: Biovia, Phytochemicals, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

In recent few times, an outbreak of 2019 Coronavirus diseases (COVID-19 has increase quickly worldwide [1-2]. However, to the best of our knowledge so far there is no such treatments have reported in the literatures [3]. Moreover, there are many academic and pharmaceutical industries to identify medicines of corona virus. The numbers of medicinal plants treating various diseases and their phytochemicals have low-priced but cost effective way [4]. More interestingly *Commiphora wightii* extract belongs to family Burceraaceae. Generally, the *Commiphora wightii* is a flowering plant in the family Burseraceae, which gives a fragrant resin called gugal, guggul or gugul, that is used in incense and vedic medicine (or ayurveda). Besides, these investigations have to extend the phytochemicals to cure the spread virus COVID-19 outbreak.

MATERIALS AND METHODS

Biovia Discovery studio (Dassault Systemes of France) was used for investigation of Insilco analysis of COVID-19. Moreover, the previous work showed that *Commiphora wightii* comprises bdellium-tree and it is a flowering plant in the family of Burseraceae. These families are more effective against viruses. This work is paying much attention on identification of the particular phytochemical responsible for inhibiting Papain-like Protease controlling of COVID-19. In addition, the molecular docking technique has been used to identify the phytochemical from the plant extract

that can deactivate the Papain-like Protease protein. The detailed method has been illustrated in the previous literatures [5].

RESULTS AND DISCUSSION

CDOCK technique was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand confirmations were obtained by "Molecular Dynamic methods". Further, the high positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. The following table-1 shows that Quercetin is the phytochemical that can really prevent the attack of COVID-19.

CONCLUSION

In the summary, the identification of *Commiphora wightii* plant can prevent the attack of COVID-19. This results using Discovery Studio module of Biovia software was identified that Quercetin can noteworthy interact with the viral of Papain-like Protease.

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Table 1: Results of C-Docking of phytochemicals with Papain-like Protease (receptor)

SL NO	LIGAND	C-DOCKER ENERGY	C-DOCKER INTERACTION ENERGY	Difference between -C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Alpha-pinene	-6.75824	18.1999	27.94	
2	Alpha-terpineol	-6.3509	22.0324	28.38	
3	D-limonene	-19.8703	18.3385	38.2	
4	Eugenol	11.5363	21.0124	9.48	
5	Linalool	-5.97972	24.137	30.1	

6	Quercetin	31.5442	34.8942	3.35	Maximum inhibition of viral protein
7	Progestrone	-17.0596	37.0458	54.09	
8	Z-guggulsterone	-33.263	32.4155	65.67	
9	Bornyl acetate	FAILED	FAILD	N/A	

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RESEARCH ARTICLE

In Silico Analysis of COVID-19 Prevention using *Cinnamomum verum* Extract by Blocking ADP Ribose Phosphates Protein of NSP3 Enzyme

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ABSTRACT

The spread of Coronavirus disease 2019 (COVID-19) is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with ADP ribose phosphates protein of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and –C Docker interaction energy" indicated that Quercetin of *Cinnamomum verum* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemicals, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

Recently, the spread of coronavirus disease 2019 (COVID-19) has paying much attention in more than 100 000 people in 100 countries [1-2]. So far there are no reports based on the treatment of COVID-19 [3]. There are a number of medicinal plants treating a variety of diseases and its phytochemicals will be low-cost but cost effective [4]. However, Cinnamomum verum belongs to the family of solanaceae. It is the most economically important genus and composed of nearly 30 species and its bell-shape and a wide range of colours, such as yellow, green, red and orange. This study identifies those phytochemicals which can cure the attack of COVID-19 outbreak.

MATERIALS AND METHODS

Biovia Discovery studio (Dassault Systems) was used for analysis. *Cinnamomum verum* containing approximately 50000 varieties of pepper and its plants belonging to this family are effective against viruses. This work is focused on identification of the particular photochemical responsible for inhibiting ADP ribose phosphates protein and controlling of COVID-19. Molecular docking method has been used to identify the phytochemicals from the plant extract, which can deactivate the ADP ribose phosphates protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 show that Quercetin is the phytochemicals that can really prevent COVID-19 attack.

CONCLUSIONS

In the summary, *Cinnamomum verum* plant can prevent the outbreak of COVID-19 outbreak. The Discovery Studio module of Biovia software and was identified that Quercetin can considerable interact with the viral ADP ribose phosphates protein.

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Table 1 Results of C-Docking of phytochemicals with ADP ribose phosphates (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	31.2634	34.2403	2.9769	Maximum inhibition of viral protein
2	Luteolin	29.25	33.8368	4.5868	
3	Apigenin	27.6776	33.1745	5.4969	
4	Beta-myrcene	-10.3142	19.8176	9.5034	
5	Capsaicin	22.7911	35.0795	12.2884	

6	Alpha-terpineol	-4.63606	23.9765	19.34044	
7	Linalool	-5.14219	25.463	20.32081	
8	Camphene	-48.169	16.3745	31.7945	
9	1, 8-cineole	Failed	Failed	Failed	
10	Beta-carotene	Failed	Failed	Failed	
11	Beta-pinene	Failed	Failed	Failed	
12	Rutin	Failed	Failed	Failed	

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RESEARCH ARTICLE

In silico Analysis of Effects of Phytochemicals of *Champa* against the ADP Ribose Phosphatase Causing SARS CoV- 2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Champa* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"has been identified as the most critical disease in human history. This disease has already been declared as pandemic.[1][2], The treatment of the disease is not clear till now[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4].Their phytochemicals will be low-cost but effective. *Champa* belongs to family Magnoliaceae. It contains Quercetin, Nerolidol structure, Gamma cadinene, Gallic acid , Camphorsulfonic acid, Beta caryaPhylleneetc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Champa* contains Quercetin , Nerolidol structure, Gamma cadinene, Gallic acid , Camphorsulfonic acid, Beta carya Phylleneetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting ADP ribose phosphataseand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the ADP ribose phosphataseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetinis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Champa* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetincan significantly interact with the viralADP ribose phosphatase.

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	34.5065	36.9318	2.4253	Maximum inhibition of viral protein
2	Alpha humelence	FAILED	FAILED	NA	
3	Docosanoic acid	FAILED	FAILED	NA	

4	Nerolidol structure	- 23.316	26.7339	50.0499	
5	Beta caryoPhyllene	-21.7273	20.7484	42.7457	
6	Camphorsulfonic acid	- 18.1182	23.2809	41.3982	
7	Gamma cadinine	-22.8013	22.3201	45.1214	
8	Gallic acid	28.9931	26.0082	2.9849	
9					
10	Alpha cardinol	FAILED	FAILED	NA	
11	Oleic acid	FAILED	FAILED	NA	
12	Stigmasterol	FAILED	FAILED	NA	

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RESEARCH ARTICLE

In silico Analysis of Effects of Phytochemicals of *Theobroma cacao* against the ADP Ribose Phosphatase Causing SARS CoV- 2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "ADP ribose phosphatase"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Theobroma cacao* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is one of the most drastic viral disease till date. All the criteria for the term pandemic, has been fulfilled by the disease.[1][2], The definite medicine for the disease is yet to be known[3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases [4].Their phytochemicals will be low-cost but effective. *Theobroma cacao* belongs to family Malvaceae. It contains Quercetin, phenylacetic acid, ferulic acid, chlorogenic acid, Luteolin, Vanillic acid etc.This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Theobroma cacao* contains Quercetin, phenylacetic acid, ferulic acid, chlorogenic acid, Luteolin, Vanillicacid etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting ADP ribose phosphatise and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the ADP ribose phosphatise viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods".

High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetinis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Theobroma cacao* can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetincan significantly interact with the viralADP ribose phosphatase.

REFERENCES

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Table 1. Results of CDocking of phytochemicals with ADP ribose phosphatase(receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Phloretic acid	25.7301	25.5668	0.1633	
2	Phenylacetic acid	19.7761	19.5892	0.1869	
3	Quercetin	34.5065	36.9318	2.4253	Maximum inhibition of viral protein

4	ferulic acid	20.7566	23.2606	2.504	
5	Chlorogenic acid	12.2332	28.3635	16.1303	
6	Luteolin	33.1894	36.1938	3.0044	
7	Vanillic acid	21.0855	22.2075	1.122	
8	Procyanidin B1	FAILED	FAILED	NA	
9	Syringic Acid	FAILED	FAILED	NA	
10	Theobromine	FAILED	FAILED	NA	
11	Vitexin	FAILED	FAILED	NA	
12	Orientic	FAILED	FAILED	NA	

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RESEARCH ARTICLE

In silico Analysis of Gas Permeability Properties of Polyacrylic Acid and Poly12a D Glucose Composite

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ABSTRACT

A blend is a mixture of more than one components. The desired property of a blend is its homogeneity. The composition of polyacrylic acid and poly12aD glucose to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in polyacrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of acrylic acid. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Key words: components, poly12aD, polyacrylic,

INTRODUCTION

Blends are composites materials which are made from more than one component. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials, mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer.

Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural

Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs. Among the various polymers, polyacrylic acid is a promising material due to its high dielectric strength, easy film formation, adhesiveness and whose properties can be controlled by dopant concentrations [8, 9]. The film forming ability of polyacrylic acid is widely used in packaging industry to form strong polymeric films. It is because of their high mechanical strength, environmental stability and easy processability [10]. On the other hand, polyacrylic acid is non-toxic, semicrystalline, hydrophilic, biocompatible and easily soluble in water [11].

However, the glucose is the key component of osmotic agent and used in peritoneal dialysis (PD), it is sometimes associated with a relatively short duration of effective ultra-filtration. Besides, the use of polyglucose as a PD fluid extends time on PD treatment [12]. This study is intended to identify the interaction of polyacrylic acid and poly12aD glucose to form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyacrylic acid and poly12aD glucose were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Molar volume: "It is the volume occupied by one mole of a substance". Figure 1 shows that the molar volume of the composite decreases linearly with increase in mass fraction of acrylic acid.

Density: "Increase in density indicates decrease in porosity". Figure 2 shows that the density of the composite decreases linearly with increase in mass fraction of acrylic acid.

Permeability of gas: "Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium". Figure 3 shows that the permeability of oxygenthrough the composite decreases with increase in mass fraction of acrylic acid.

Figure 4 shows that the permeability of nitrogenthrough the composite decreases with increase in mass fraction of acrylic acid. Figure 5 shows that the permeability of carbon dioxidethrough the composite decreases with increase in mass fraction of acrylic acid. Thus the results indicated that an increase in acrylic acid fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of polyacrylic acid and poly12aD glucose to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties.The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the

perme abilityfor all the gases decreased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally. This silico study will help us to determine components of a blend without performing laboratory experiments saving materials, money and time.

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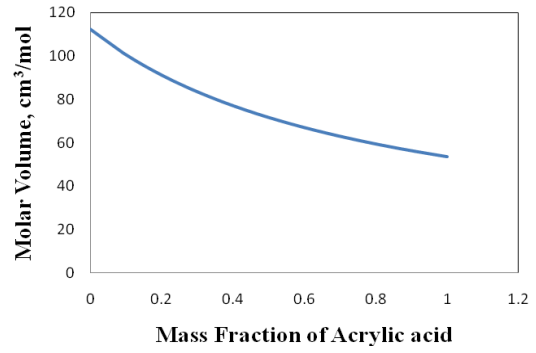

Figure1. Change in molar volume with mass fraction of acrylic acid

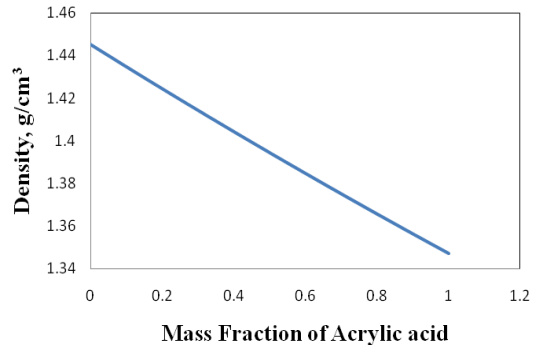

Figure 2. Change in density with mass fraction of acrylic acid

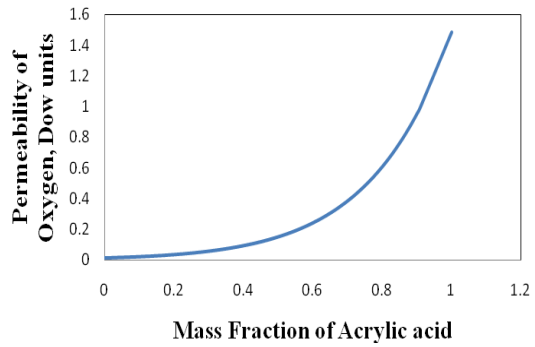

Figure 3. Change in permeability of oxygen with mass fraction of acrylic acid

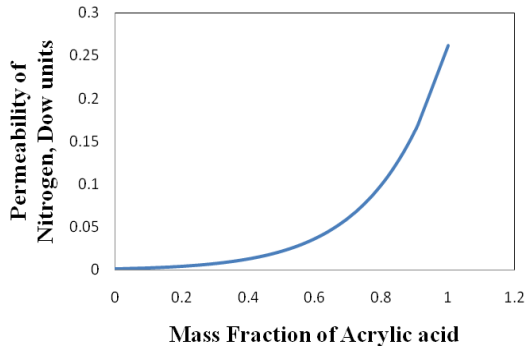

Figure 4. Change in permeability of nitrogen with mass fraction of acrylic acid

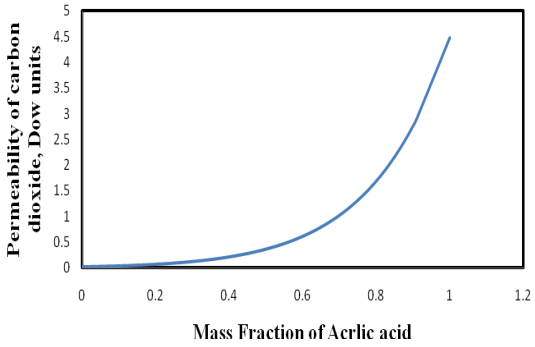

Figure 5. Change in permeability of carbon dioxide with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Phytochemicals of *Champa* Flower against the Protease (Apo form) of SARS CoV-2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Protease enzyme (protein database code 6M03) of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Gallic Acid of *Champa* flower extract can effectively fight against "SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has primarily spreads through droplets of saliva or discharge from the nose when an infected person coughs and sneezes.. It has been declared as a pandemic.[1][2], At this time ,there are no specific vaccines or treatments for COVID-19.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Michelia Champa ca* belongs to family Magnoliaceae It contains Beta selinene, Camforsulfonic acid, Farnesol, Gallic acid, Gamma cadinene nerolidol quercetin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Michelia Champaca* contains Beta selinene, Camforsulfonic acid, Farnesol, Gallic acid, Gamma cadinene nerolidol quercetin etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting "Protease enzyme (protein database code 6M03) and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the "Protease enzyme (protein database code 6M03) viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Gallic Acid is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Michelia Champa ca* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that **Gallic Acid** can significantly interact with the viral "Protease enzyme (protein database code 6M03)".

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Table 1. Results of CDocking of phytochemicals with "Protease enzyme (protein database code 6M03) (receptor)

Sl No	Ligand	-CDocker energy	-CDocker interaction	Difference between CDocker interaction and energy	Remarks
1	Gallic Acid	21.2467	18.9767	2.27	Maximum inhibition of viral protein

2	Quercetin	15.2421	17.7416	2.4995	
3	Campfhorsulfhonic acid	-22.4359	21.084	43.5199	
4	Beta Selinene	-22.454	17.4615	39.9155	
5	Nerolidol	-27.5019	22.9935	50.4954	
6	Gamma Cadinene	-31.7964	15.8334	47.6298	
7	Farnesol	-49.9047	24.0705	73.9752	

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RESEARCH ARTICLE

In silico Analysis of Phytochemicals of *Cinnamon* against the Protease (Apo form) of SARS CoV-2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "proteases of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Cinnamon* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"is a pandemic which has been affected almost all of the countries of the world. [1][2], No effective treatment is available yet to the scientists of the globe.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Cinnamon* plant belongs to family Lauraceae. It contains Cinnamic Acid, Quercetin, Vanillin, Eugenol, Nicotine, Beta- caryophyllene, Gossypetin etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that Cinnamoncontains Cinnamic Acid, Quercetin, Vanillin, Eugenol, Nicotine, Beta- caryophyllene, Gossypetinetc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting protease and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the protease viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cinnamon* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified thatQuercetin can significantly interact with the viral Protease.

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Table 1. Results of CDocking of phytochemicals with protease (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	26.7445	29.4942	2.7497	Maximum inhibition of viral protein
2	Gossypetin	20.7775	21.9174	1.1399	
3	Vanillin	14.5338	17.6824	3.1486	
4	Eugenol	9.8973	19.3507	9.4534	

5	Cinnamic acid	9.56395	12.6976	3.13365	
6	Nicotine	1.69068	22.811	21.12032	
7	Beta Caryophellene	-19.0675	17.5303	36.5978	

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RESEARCH ARTICLE

In silico Analysis of Phytochemicals of *Cocoa* against the Protease (Apo form) of SARS CoV-2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "Protease " was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Quercetin of *Cocoa* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)", is the pandemic viral disease which is has become the headache to human race.[1][2], Still we do not have any authenticated medication to cure the disease [3].There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Cocoa* belongs to family Malvaceae. It contains phytochemicals like Phloretic acid, Phenyl acetic acid, Quercetin, P-Coumaric acid, Ferulic Acid, Vanillic Acid, Theobromine, Caffine, Luteolin, Naringenin, Syringic acid, Coumaric acid etc.This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis.Published works showed that *Cocoa* contains Phloretic acid, Phenyl acetic acid, Quercetin, P-Coumaric acid, Ferulic Acid, Vanillic Acid, Theobromine, Caffine, Luteolin, Naringenin, Syringic acid, Coumaric acid etc.. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting Protease and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the Protease viralprotein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetinis the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that Cocoacan prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral Protease .

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Table 1. Results of CDocking of phytochemicals with Protease (receptor)

Sl No	Ligand	-CDOCKER ENERGY	-CDOCKER INTERACTION	Difference between -CDocker interaction and Energy	Remarks
1	Quercetin	26.7445	29.4942	2.7497	Maximum inhibition of viral protein
2	P Coumaric Acid	19.0117	19.2303	0.2186	
3	phloretic acid	17.2588	16.1006	1.1582	

4	Leuteolin	16.633	19.9238	3.2908	
5	Vanillic acid	16.525	18.1707	1.6457	
6	Naringenin	15.9748	23.6704	7.6956	
7	Ferulic acid	14.7293	18.494	3.7647	
8	Phenylacetic acid	13.8556	13.7947	0.0609	
9	Syringic acid	13.5837	18.491	4.9073	
10	Caffeine	12.6627	21.4364	8.7737	
11	Coumarinic acid	11.0201	17.4927	6.4726	
12	Theobromine	9.33425	14.7273	5.39305	

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties of Polyacrylic Acid and Polybutylenes Isophalate Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of acrylic acid. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Key words: blend, parameters, experiments, materials

INTRODUCTION

Blends or composites are materials containing more than one component. The components do not lose their uniqueness in the mixture. They combine and contribute to the property of the blend thereby improving its quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. So a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers; latex polymer cementations composites [6] were

developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments. Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs.

Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denture repair materials, maxilla facial appliances for skeletal defects etc. [8], bone repair [9], dispersing agent, super absorbent polymer, ion-exchange resin, etc.[10]. Polyacrylic acid is a polyelectrolyte soluble in aqueous media at neutral pH it is used for preparing hydrogels. It is not toxic and does not cause irritation [11]. Researchers have used Poly butylenes isophalate in combination with other materials to act as adsorbent [12]. The influence of the development of crystalline structure on the segmental dynamics of the amorphous phase in polybutylene isophthalate (PBI) has been studied by a combination of relaxation and scattering techniques [13].

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systems of France) was used for analysis.

Methodology: The design of polyacrylic acid and Poly butylenes isophalate were fed to the synthia menu of Materials Studio. It was then run in different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Heat capacity: "It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase".

Thermal conductivity: "It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat".

Dielectric constant: "It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant."

CONCLUSIONS

The possibility of use of polyacrylic acid and Poly butylenes isophalate to form a blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally.

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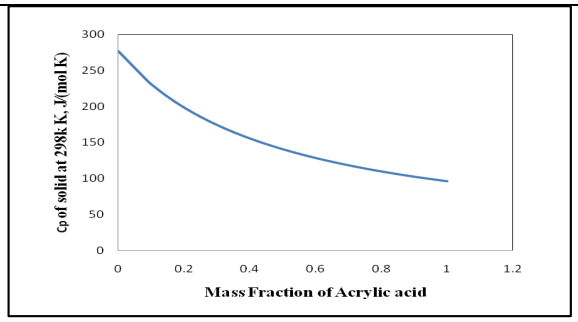

Figure 1. Change in heat capacity with mass fraction of acrylic acid

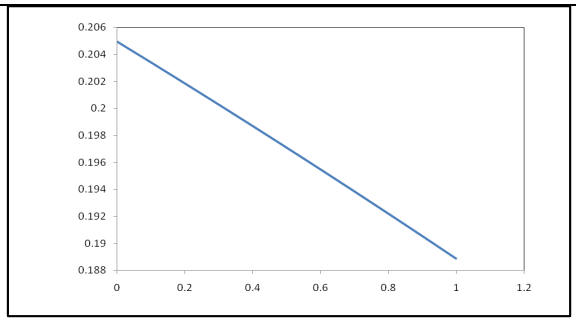

Figure 2. Change in thermal conductivity with mass fraction of acrylic acid

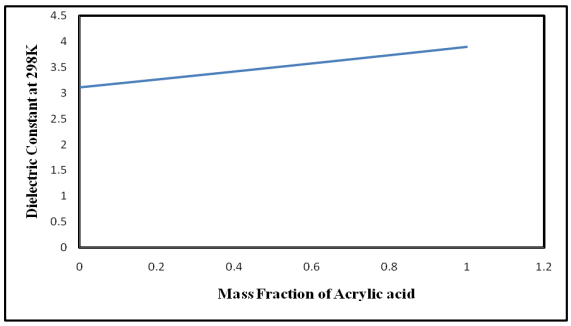

Figure 3. Change in dielectric constant with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties of Polyvinyl Alcohol and Polyoxymethylene Composite

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ABSTRACT

"A blend is a mixture of more than one component". This property of a blend is its homogeneity. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of Vinyl alcohol. The study will help to determine pairs without performing laboratory experiments saving materials, money and time.

Key words: component, homogeneity, parameters, money

INTRODUCTION

"Blends or composites are materials containing more than one component". The components will not going to lose their identity in the mixture. They combine and contribute to the property of the blend by improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the benefits of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers; latex polymer cementations composites [6] were

developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments. Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) has been used to identify compatible pairs.

Vinyl polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denture repair materials, maxillofacial appliances for skeletal defects etc. [8], bone repair [9], dispersing agent, superabsorbent polymer, ion-exchange resin, etc.[10]. Polyvinyl alcohol is a polyelectrolyte soluble in aqueous media at neutral pH It is used for preparing hydrogels. It is not toxic and does not cause irritation [11]. Researchers have used polyoxymethylene in combination with other materials to act as adsorbent [12]. The radiochemical degradation of a polyoxymethylene homopolymer (POM) was used to study the effects of molar mass changes in the crystalline structure. [13] .Polyvinyl alcohol (PVA) gel has been used as a carrier for immobilized cells and enzymes, its use as an immobilization matrix for inactivated cells for biosorption studies [14]

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systems of France) was used for analysis and computation.

Methodology: The structures of Poly vinyl alcohol and polyoxymethylene were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used by plotting graphs to identify the effects of weight fraction of polyvinyl alcohol on its mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of polyvinyl alcohol and polyoxymethylene as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their depending upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Heat capacity: "It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase".

Thermal conductivity: "It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat."

Dielectric constant: "It is defined as the ratio of the electric permeability of the material to the electric permeability of free space. As the dielectric constant increases, the electric flux density increases, while all other factors are maintained constant."

CONCLUSIONS

The possibility of use of polyvinyl alcohol and Polyoxymethylene to form a blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of vinyl alcohol. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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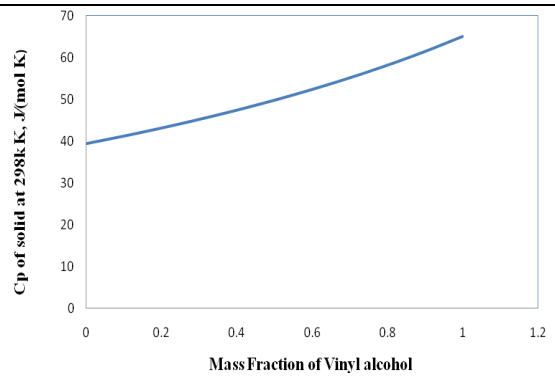
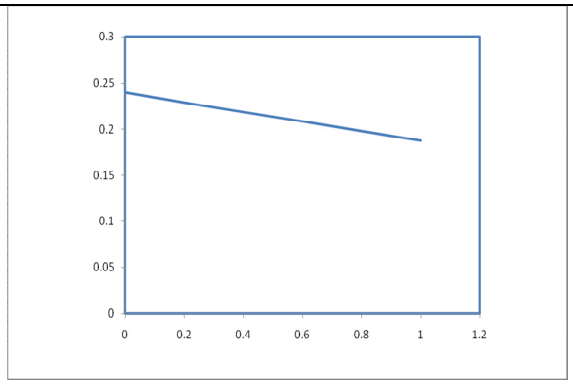
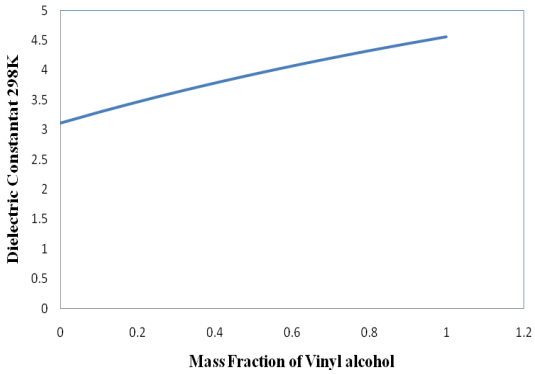


(Figure 1. Change in heat capacity with mass fraction of Vinyl alcohol)



(Figure 2. Change in thermal conductivity with mass fraction of Vinyl alcohol)



(Figure 3. Change in dielectric constant with mass fraction of Vinyl alcohol)

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RESEARCH ARTICLE

In-silico Analysis of Phytochemicals of *Cinnamomum verum* against RNA-Dependent RNA Polymerase (Complex with Cofactors) of SARS-CoV-2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)"is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "RNA dependent RNA polymerase of SARS-CoV-2"was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy"indicated that Proanthocyanidin *A2* of *Cinnamomum verum* extract can effectively fight against"SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Coronavirus disease 2019 (COVID-19)"become pandemic in this year and speeding exponentially worldwide. [1][2], Till now there is no effective treatment available.[3]There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4]Their phytochemicals will be low-cost but effective. *Cinnamomum verum* belongs to family Lauraceae. It contains proanthocyanidin A2, curcumin, gossypetin, quercetin, vanillin, cinnamic acid, eugenol, nicotine, sucrose, beta-caryophyllene etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Cinnamomum verum* contains proanthocyanidin A2, curcumin, gossypetin, quercetin, vanillin, cinnamic acid, eugenol, nicotine, sucrose, beta-caryophyllene etc. It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting RNA dependent RNA polymeraseand controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the RNA dependent RNA polymeraseviral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Proanthocyanidin *A2* is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Cinnamomum verum* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Proanthocyanidin *A2* can significantly interact with the viralRNA dependent RNA polymerase.

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Table 1. Results of CDocking of phytochemicals with RNA dependent RNA polymerase (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Proanthocyanidin A2	30.3623	46.3848	16.0225	Maximum inhibition of viral protein
2	Curcumin	30.2609	41.2526	10.9917	

3	Gossypetin	27.767	29.9841	2.2171	
4	Quercetin	27.3296	33.2892	5.9596	
5	Vanillin	13.7266	16.9866	3.26	
6	Cinnamic Acid	13.5471	15.2478	1.7007	
7	Eugenol	8.55719	17.7939	9.23671	
8	Nicotine	-2.54785	18.5789	21.12675	
9	Sucrose	-14.7201	32.4614	47.1815	
10	Beta-caryophyllene	-22.5913	19.8241	42.4154	

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RESEARCH ARTICLE

In-silico Analysis of Phytochemicals of *Magnolia champaca* against RNA-Dependent RNA Polymerase (Complex with Cofactors) of SARS-CoV-2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with "RNA-Dependent RNA polymerase in complex with cofactors (6M71)" of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Quercetin of *Magnolia Champaca* extract can effectively fight against "SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" has been spread on the whole world. It has been declared as a pandemic.It is a very dangerous disease.We will be able to cure this disease only to follow the rule of social distancing.[1][2], However, till now there is no established treatment or vaccine but we should take care of self and to follow the rules that explained on Ayurveda.[3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Magnolia Champaca* belongs to family Magnoliaceae. It contains vanillin, vanillic corrosive, syringic corrosive, gallic corrosive, quercetin, chlorogenic corrosive, beta selinene, beta-caryophyllene, nerolidol, farnesol. etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Magnolia Champaca* contains vanillin, vanillic corrosive, syringic corrosive, gallic corrosive, quercetin, chlorogenic corrosive, beta selinene, beta-caryophyllene, nerolidol, farnesol. etc It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical

responsible for inhibiting "RNA-Dependent RNA polymerase in complex with cofactors (6M71)" and controlling of COVID-19. Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the "RNA-Dependent RNA polymerase in complex with cofactors (6M71)" viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Quercetin is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Magnolia Champaca* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Quercetin can significantly interact with the viral "RNA-Dependent RNA polymerase in complex with cofactors (6M71)".

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Table 1. Results of CDocking of phytochemicals with "RNA-Dependent RNA polymerase in complex with cofactors (6M71)" (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Quercetin	27.3296	33.2892	5.9596	Maximum inhibition of viral protein
2	Gallic acid	24.4303	21.1087	3.3216	
3	Chlorogenic acid	21.221	37.0868	15.8847	
4	Syringic acid	18.341	25.2192	6.8782	
5	Vanillic acid	15.5569	17.5609	2.004	
6	Vanillin	13.7266	16.9866	3.26	
7	Beta selinene	-20.9129	19.2183	40.1312	
8	Beta caryophyllene	-22.5913	19.8241	42.4154	
9	Nerolidol	-28.0466	23.7946	51.8412	
10	Farnesol	-43.5686	21.2975	64.8661	

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RESEARCH ARTICLE

In-silico Analysis of Phytochemicals of *Theobroma cacao* against RNA-Dependent RNA Polymerase (Complex with Cofactors) of SARS-CoV-2

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ABSTRACT

"Coronavirus disease 2019 (COVID-19)" is caused by "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)". The molecular docking of the phytochemicals with RNA-Dependent RNA polymerase in complex with cofactors (6M71) of SARS-CoV-2" was studied using "Biovia Discovery Studio". High positive values of "-CDocker energy and -CDocker interaction energy" indicated that Procyanidin B4 3-O-gallate of *Theobroma cacao* extract can effectively fight against "SARS-CoV-2 virus".

Key words: phytochemical, Biovia, Discovery studio, COVID-19, SARS-CoV-2

INTRODUCTION

"Corona virus disease 2019 (COVID-19)" is an infectious disease caused by a newly discovered virus coronavirus .it is a very dangerous virus spread by air and will experience mild to moderate respiratory illness .[1][2], However, till now there is no established treatment,or vaccines so the best way to prevent and slow down its transmission is to protection of self from others. [3] There is a need to identify medicines against the virus. There are a number of medicinal plants treating various diseases.[4] Their phytochemicals will be low-cost but effective. *Theobroma cacao* belongs to family Malvaceae. It contains phloretic acid, phenyl acetic acid, quercetin, ferulic acid, vanillic acid, theobromine, luteolin, naringenin, syringic acid, quercetin 3-galactoside, iso-vitexin, chlorogenic acid, procyanidin B4-3-O-gallate, iso-orientin, procyanidin B3, procyanidin B4, procyanidin, iso-quercetin, procyanidin D, orientin.etc. This study identifies those phytochemicals which can cure COVID-19 attack.

MATERIALS AND METHODS

"Biovia Discovery studio" module (Dassault Systemes of France) was used for analysis. Published works showed that *Theobroma cacao* contains phloretic acid, phenyl acetic acid, quercetin, ferulic acid, vanillic acid, theobromine, luteolin, naringenin, syringic acid, quercetin 3-galactoside, iso-vitexin, chlorogenic acid, procyanidin B4-3-O-gallate,

iso-orientin, procyanidin B3, procyanidin B4, procyanidin, iso-quercetin, procyanidin D, orientin.etc . It is known that plants belonging to this family are effective against viruses. This work is focused on identification of the particular phytochemical responsible for inhibiting RNA-Dependent RNA polymerase in complex with cofactors (6M71) and controlling of COVID-19.

Brenda enzyme database was used to list different enzymes found in COVID-19. Molecular docking method has been used to identify the phytochemical from the plant extract, that can deactivate the RNA-Dependent RNA polymerase in complex with cofactors (6M71) viral protein. The detailed method has been described elsewhere [5].

RESULTS AND DISCUSSION

CDOCK method was used for molecular docking. "CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy". The ligand conformations were obtained by "Molecular Dynamic methods". High positive value of -CDOCKER energy and small difference between -CDOCKER energy and -CDOCKER interaction energy are the criteria to identify the drug. Table 1 shows that Procyanidin B4 3-O-gallate is the phytochemical that can really prevent COVID-19 attack.

CONCLUSIONS

It was identified that *Theobroma cacao* plant can prevent COVID-19 attack. Using "Discovery Studio module of Biovia software", it was identified that Procyanidin B4 3-O-gallate can significantly interact with the viral RNA-Dependent RNA polymerase in complex with cofactors (6M71).

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Table 1. Results of CDocking of phytochemicals with RNA-Dependent RNA polymerase in complex with cofactors (6M71) (receptor)

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy	Remarks
1	Procyanidin B4 3-O-gallate	52.7317	58.2845	5.5528	Maximum inhibition of viral protein
2	Procyanidin B4	40.0311	50.6751	10.644	
3	Procyanidin	37.6394	48.4961	10.8567	
4	Procyanidin B3	37.2228	50.133	12.9102	
5	Procyanidin D	32.7924	47.1987	14.4063	
6	Quercetin	27.3296	33.2892	5.9596	
7	Luteolin	26.0626	30.4012	4.3386	
8	Naringenin	22.8832	28.5632	5.68	
9	Phloretic acid	22.0273	21.4346	0.5927	
10	Chlorogenic acid	21.2021	37.0868	15.8847	
11	Quercetin-3-O-Galactoside	19.8913	48.4001	28.5088	
12	Isovitexin	18.8194	44.2116	25.3922	
13	Orientin	18.6765	41.5452	22.8687	
14	Ferulic acid	18.4259	22.5489	4.123	
15	Syringic Acid	18.341	25.2192	6.8782	
16	Iso-orientin	17.0022	39.0816	22.0794	
17	Phenylacetic acid	16.0189	16.1622	0.1433	
18	Vanillic acid	15.5569	17.5609	2.004	
19	Theobromine	13.8084	19.0162	5.2078	
20	Isoquercetin	7.2405	44.3427	37.1022	

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RESEARCH ARTICLE

In silico Analysis of Mechanical Properties of Polyacrylic Acid and Poly12aD Glucose Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of acrylic acid and 12aD glucose to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of acrylic acid. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Key words: Studio, mechanical, laboratory, modulus, glucose

INTRODUCTION

Blends or composites are materials that are containing more than one components. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made up of two or more polymers, or fibres and polymer, or particles and polymer. Nano material modified polymers saved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. [6] were developed for construction of

bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments. Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money. [7]). Acrylic acid have a wide variety of applications in dentistry as denture bases, artificial teeth, denturerepair materials, maxillofacial appliances for skeletal defects etc. [8], bone repair [9], dispersing agent, superabsorbent polymer, ion-exchange resin, etc.[10]. Polyacrylic acid is used as an electrolyte soluble in aqueous media at neutral pH, good adsorbent, hydrophobic [11]. However, the glucose is the key component of osmotic agent and used in peritoneal dialysis (PD), the use of polyglucose as a PD fluid extends time on PD treatment [12]. This study is intended to identify the interaction of polyacrylic acid and poly12aDglucose to form blends.

MATERIALS AND METHODS

Software Used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of acrylic acid and 12aD glucose were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of acrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of polyacrylic acid and poly12aD glucose as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Bulk modulus: "Bulk modulus is the measure of the decrease in volume with an increase in pressure". Figure 1 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Shear modulus: "It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation". Figure 2 shows that the shear modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Young's modulus: "It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite". Figure 3 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Poisson ratio: "It is the ratio of lateral strain to longitudinal strain". Figure 4 shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of acrylic acid.

Brittle fracture stress: "Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs". Figure 5 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of acrylic acid.

CONCLUSIONS

The possibility of use of acrylic acid and 12aD glucose to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to mechanical properties.The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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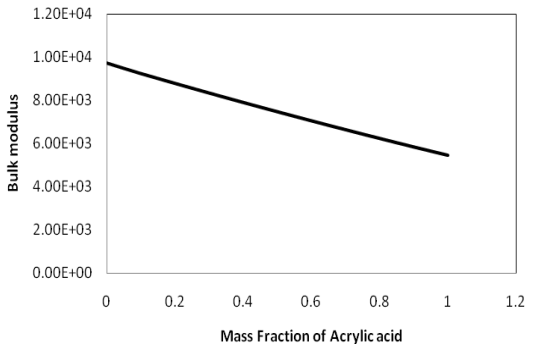

Figure 1. Change in bulk modulus with mass fraction of acrylic acid

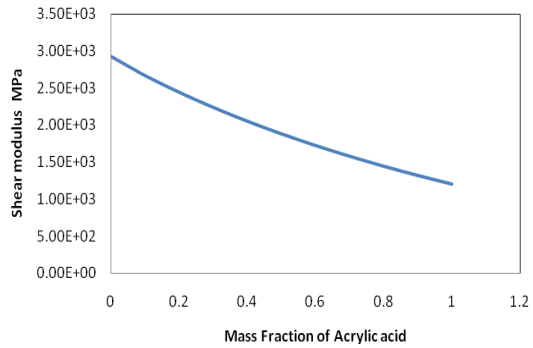

Figure 2. Change in shear modulus with mass fraction of acrylic acid

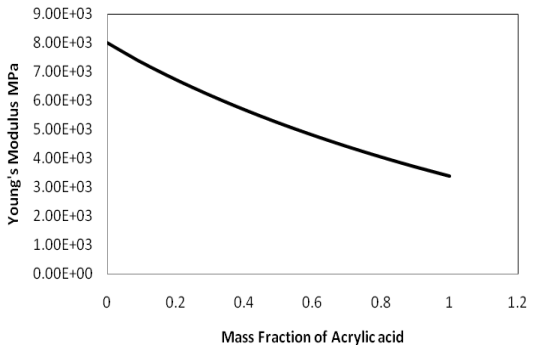

Figure 3. Change in Young's modulus with mass fraction of acrylic acid

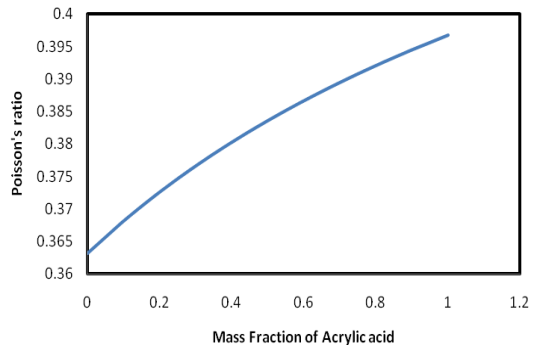

Figure 4. Change in Poisson modulus with mass fraction of acrylic acid

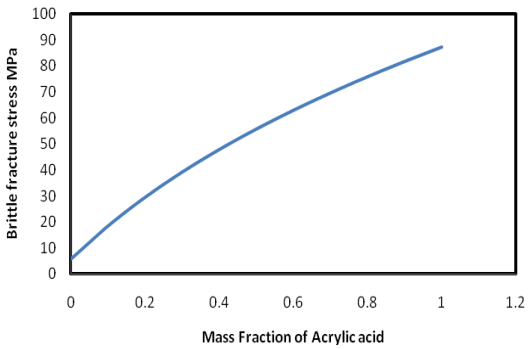

Figure 5. Change in brittle fracture stress with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Mechanical Properties of Polyacrylic Acid and Polymethyl Acrylate Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of polyacrylic acid and polymethyl acrylate to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of acrylic acid.This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Key words: component, performing, ratio, time, properties

INTRODUCTION

Blends are composites materials which are made from more than one component. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials, mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer.

Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. The, glass fiber reinforced polymers, latex polymer

cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs.Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denturerepair materials, maxillofacial appliances for skeletal defects etc. [8], bone repair [9], dispersing agent, superabsorbent polymer, ion-exchange resin, etc.[10]. Polyacrylic acid is a polyelectrolyte soluble in aqueous media at neutral pHIt is used for preparing hydrogels. It is not toxic and does not cause irritation [11]. Further, the investigation of polymethylacrylate (PMA) have study the photo degradation of films of poly (methy acrylate) (PMA) in air and in vacuum at room temperatures under irradiation by a low pressure mercury source. It is observed to crosslink during both radiolysis and thermolysis and used as as photolysis in the presence of specific sensitizers [12]. This study is intended to identify the interaction of polyacrylic acid and polymethyl acrylate to form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyacrylic acid and polymethyl acrylate were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Bulk modulus: "Bulk modulus is the measure of the decrease in volume with an increase in pressure". Figure 1 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Shear modulus: "It is defined as the ratio of shear stress and shear strain". Figure 2 shows that the shear modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Young's modulus: "It is defined as the ratio of stress and strain". Figure 3 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of acrylic acid.

Poisson ratio: "It is the ratio of lateral strain to longitudinal strain". Figure 4 shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of acrylic acid.

Brittle fracture stress: "Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs". Figure 5 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of acrylic acid.

CONCLUSIONS

The possibility of use of polyacrylic acid and polymethyl acrylate to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to mechanical properties.The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally. This silico study will help us to determine components of a blend without performing laboratory experiments it saves our materials, money and time.

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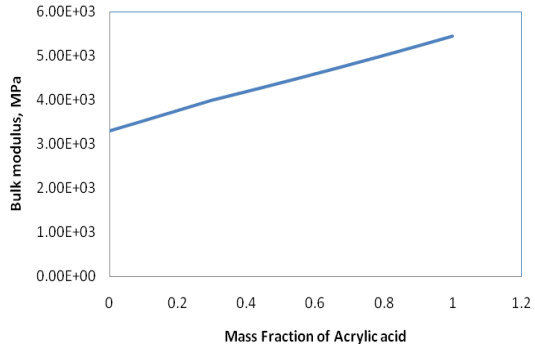

Figure 1. Change in bulk modulus with mass fraction of acrylic acid

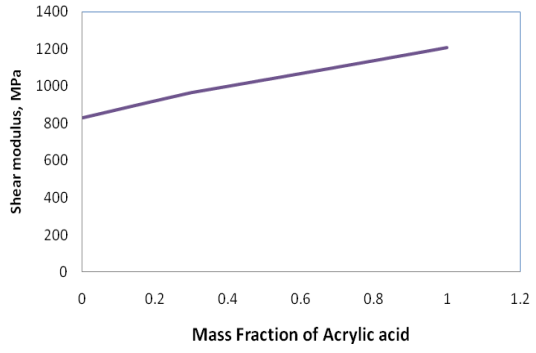

Figure 2. Change in shear modulus with mass fraction of acrylic acid

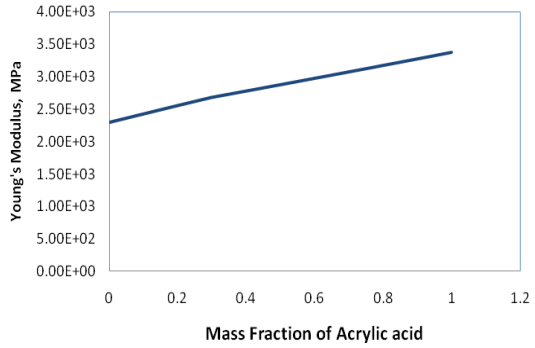

Figure 3. Change in Young's modulus with mass fraction of acrylic acid

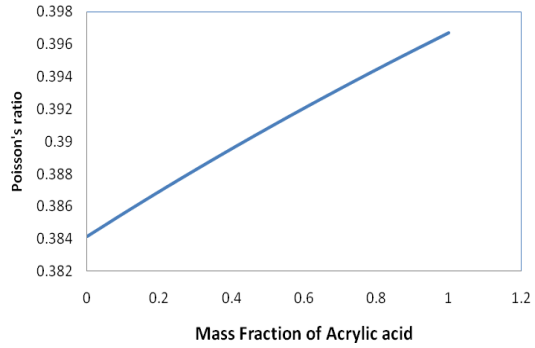

Figure 4. Change in Poisson modulus with mass fraction of acrylic acid

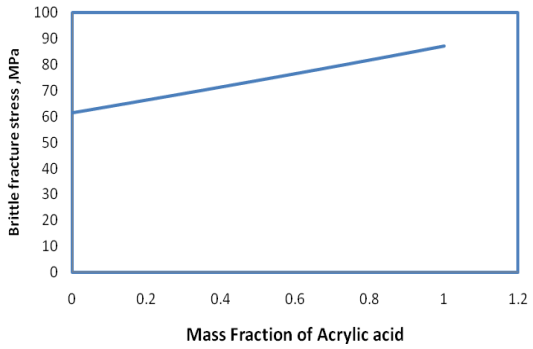

Figure 5. Change in brittle fracture stress with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Mechanical Properties of Polyvinylalcohol and Polydichloroethylene Composite

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ABSTRACT

The desired property of a blend, a mixture of more than one components,is its homogeneity. The composition of poly vinylalcoholand poly dichloroethylene to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of vinylalcohol.This work will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: Biovia, Poisson, pairs, components, materials

INTRODUCTION

In a blend the components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials, mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of

transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money.Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs. Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denturerepair materials, maxillofacial appliances for skeletal defects etc. [8], bone repair [9], dispersing agent, superabsorbent polymer, ion-exchange resin, etc.[10].

polyvinylalcoholis a polyelectrolyte soluble in aqueous media at neutral pHIt is used for preparing hydrogels. It is not toxic and does not cause irritation [11]. Researchers have used poly dichloroethylene in combination with other materials to act as adsorbent [12]. Poly dichloroethylene have been reported to be used in Curtius reaction. This study is intended to identify the interaction of poly vinylalcohol and poly dichloroethylene to form blends.

MATERIALS AND METHODS

Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes standard algorithms to predict the level of interaction. The structures of poly vinylalcohol and poly dichloroethylene were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of poly vinylalcoholon the mechanical properties of the composite.

RESULTS AND DISCUSSION

BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Bulk modulus: Bulk modulus is the measure of the decrease in volume with an increase in pressure. Figure 1 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of vinylalcohol

Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 2 shows that the shear modulus of the composite increases linearly with increase in mass fraction of vinylalcohol.

Young's modulus: It is defined as the ratio of stress and strain. It compares the relative stiffness of the composite. Figure 3 shows that the Young's modulus of the composite increases linearly with increase in mass fraction of vinylalcohol.

Poisson ratio: It is the ratio of lateral strain to longitudinal strain. Figure 4 shows that the Poisson ratio of the composite increases linearly with increase in mass fraction of vinylalcohol.

Brittle fracture stress: Brittle Fracture is the sudden, rapid cracking of a material under stress where the material exhibited practically no evidence of ductility or plastic degradation before the fracture occurs. Figure 5 shows that the brittle fracture stress of the composite increases linearly with increase in mass fraction of vinylalcohol.

CONCLUSIONS

The composition of the blend poly vinylalcohol and poly dichloroethylenewas analyzed with respect to mechanical propertiesusing Biovia Materials Studio.The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young' modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of vinylalcohol. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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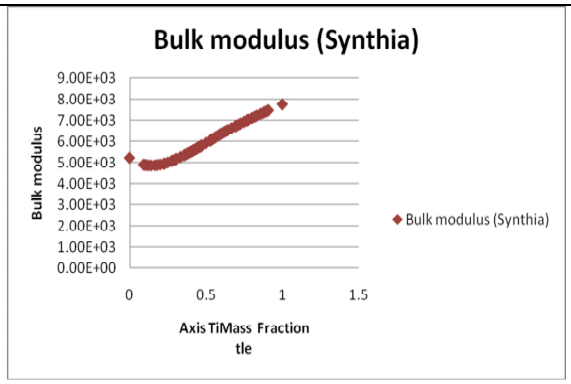
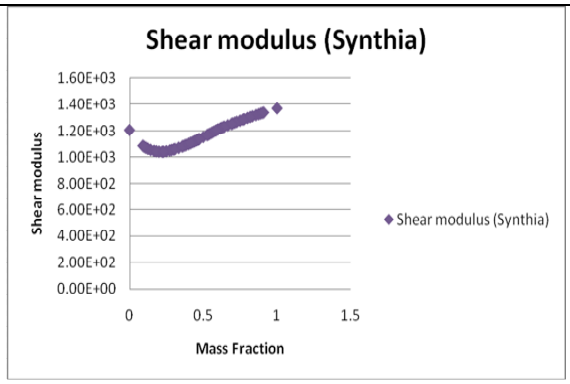


Figure 2. Change in shear modulus with mass fraction of vinylalcohol



3. Change in Young's modulus with mass fraction of vinylalcohol

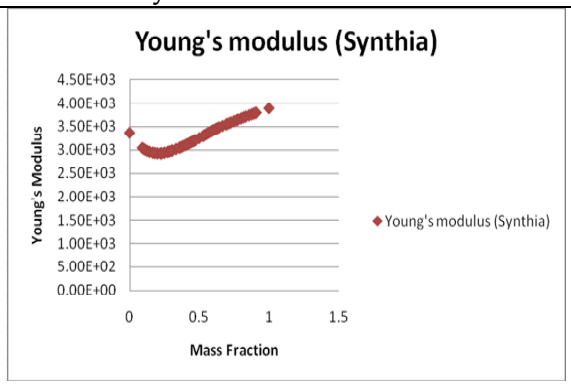


Figure 4. Change in Poisson modulus with mass fraction of vinylalcohol

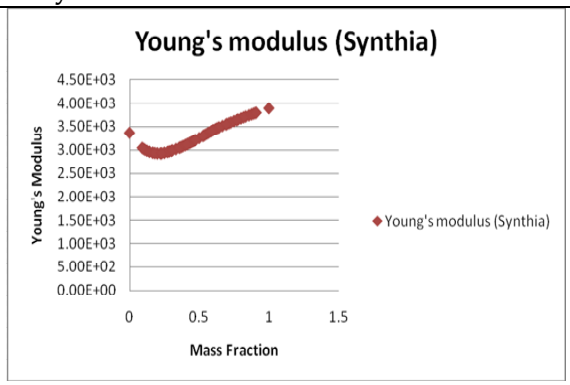
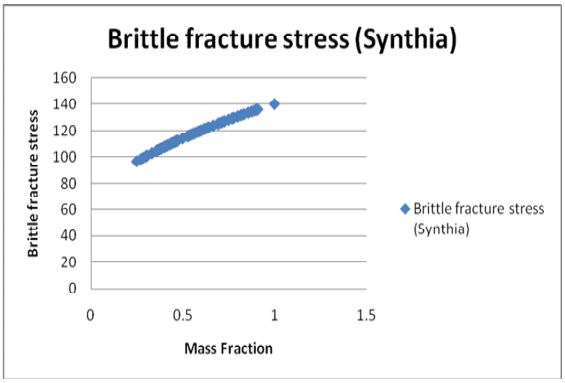


Figure 5. Change in brittle fracture stress with mass fraction of vinylalcohol



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RESEARCH ARTICLE

In silico Analysis of Mechanical Properties of Polyvinyl Alcohol and Polyurea Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of polyvinyl alcohol and polyurea to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The mechanical properties of the composite were studied based on bulk modulus, shear modulus, Young's modulus, Poisson ratio and brittle stress fracture. The results indicated that the values of all the properties increased with increase in mass fraction of vinyl alcohol. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: Blend, In Silico, 12cd-Glucose, Dichloro-Ethylene

INTRODUCTION

Blends or composites are materials containing more than one components. The components do not lose their identity in the mixture. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials, mix them to get the desired property. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers-natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4.There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers; latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

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Methodology: The structures of polyvinyl alcohol and polyurea were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyvinyl alcohol on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Bulk modulus: "Bulk modulus is the measure of the decrease in volume with an increase in pressure". Figure 1 shows that the bulk modulus of the composite increases linearly with increase in mass fraction of vinyl alcohol. Shear modulus: It is defined as the ratio of shear stress and shear strain. It shows the response of the composite to shear deformation. Figure 2 shows that the shear modulus of the composite increases linearly with increase in mass fraction of vinyl alcohol.

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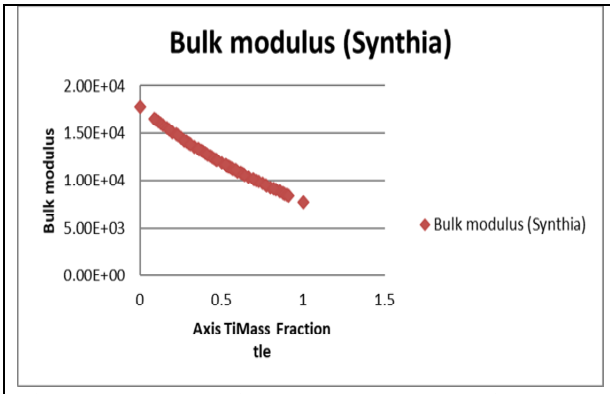

Figure1. Change in bulk modulus with mass fraction of vinyl alcohol

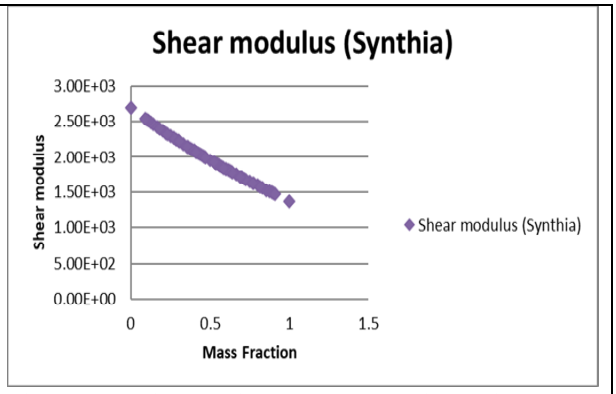

Figure 2. Change in shear modulus with mass fraction of vinyl alcohol

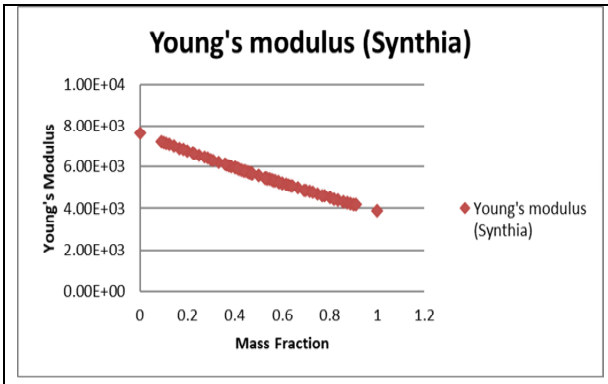

Figure 3. Change in Young's modulus with mass fraction of vinyl alcohol

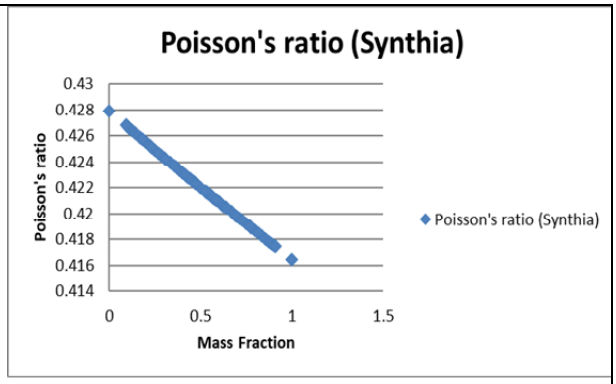

Figure 4. Change in Poisson modulus with mass fraction of vinyl alcohol

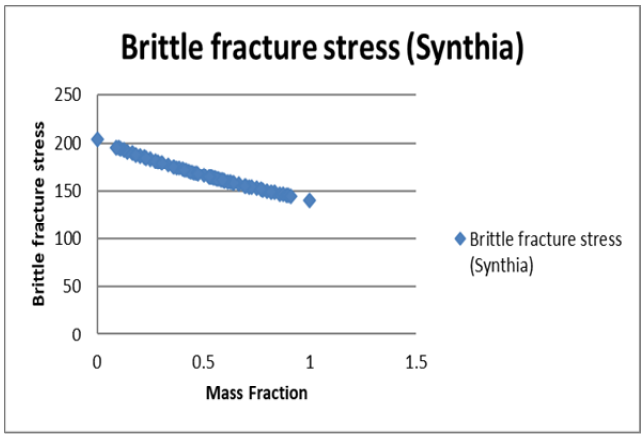

Figure 5. Change in brittle fracture stress with mass fraction of vinyl alcohol

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RESEARCH ARTICLE

In silico Analysis of Gas Permeability Properties of Polyacrylic Acid and Polybutylene isopthalate Composite

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ABSTRACT

A blend is a mixture of more than one components. The desired property of a blend is its homogeneity. The composition of polyacrylic acid and poly butylene isopthalate to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in polyvinyl alcohol fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of polyvinyl alcohol. This study will help determine pairs without performing laboratory experiments saving materials, money and time

Keywords: carbon, oxygen, laboratory, materials, fraction, acid, components

INTRODUCTION

Blends or composites are materials containing more than one components. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials, mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer. Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio

and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments. Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money.Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs.

Among the various polymers, poly butylene isopthalate (PBI) is a promising material due to its high dielectric strength, easy film formation, adhesiveness and whose properties can be controlled by dopant concentrations [8, 9]. The film forming ability of PBI is widely used in packaging industry to form strong polymeric films. It is because of their high mechanical strength, environmental stability and easy processability [10]. On the other hand, PBI is non-toxic, semicrystalline, hydrophilic, biocompatible and easily soluble in water. Researchers have used polyacrylochloride in combination with other materials to act as adsorbent [12]. Polyacrylochloride have been reported to be used in Curtius reaction. This study is intended to identify the interaction of polyacrylic acid and polyacrylochloride to form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyacrylic acid and poly butylene isopthalate were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of polyacrylic acid and poly butylene isopthalate as potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Molar volume: It is the volume occupied by one mole of a substance. Figure 1 shows that the molar volume of the composite decreases linearly with increase in mass fraction of acrylic acid.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 2 shows that the density of the composite decreases linearly with increase in mass fraction of acrylic acid. Permeability of gas: Permeability is the rate at which

the gas can pass through the polymer membrane after the gas has come to equilibrium.Lower permeability indicates longer time lag for the gas to pass through the mebrane. Figure 3 shows that the permeability of oxygenthrough the composite decreases with increase in mass fraction of acrylic acid.

Figure 4 shows that the permeability of nitrogenthrough the composite decreases with increase in mass fraction of acrylic acid Figure 5 shows that the permeability of carbon dioxidethrough the composite decreases with increase in mass fraction of acrylic acid. Thus the results indicated that an increase in acrylic acid fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases

CONCLUSIONS

The possibility of use of polyacrylic acid and poly butylene isopthalate to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties.The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeabilityfor all the gases decreased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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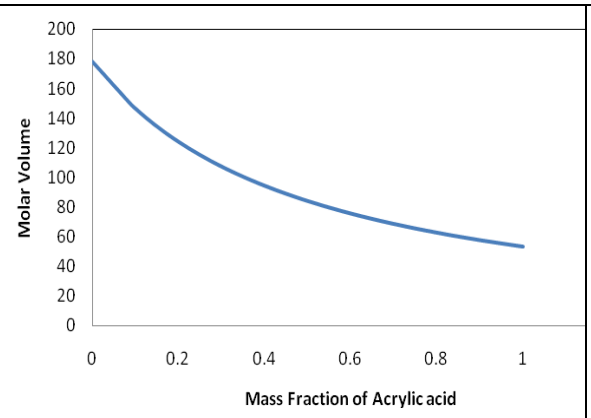

Figure 1. Change in molar volume with mass fraction of acrylic acid

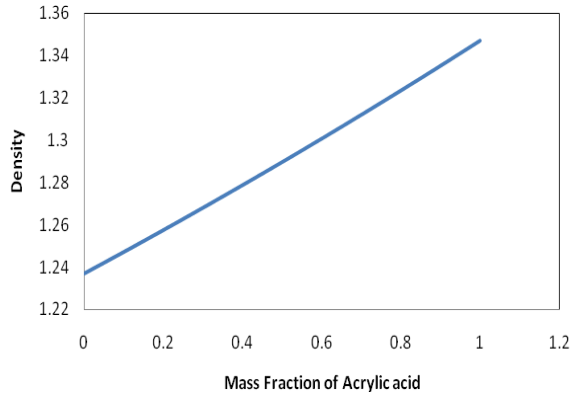

Figure 2. Change in density with mass fraction of acrylic acid

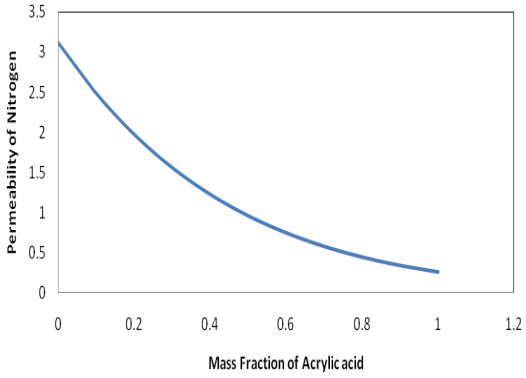

Figure 3. Change in permeability of oxygen with mass fraction of acrylic acid

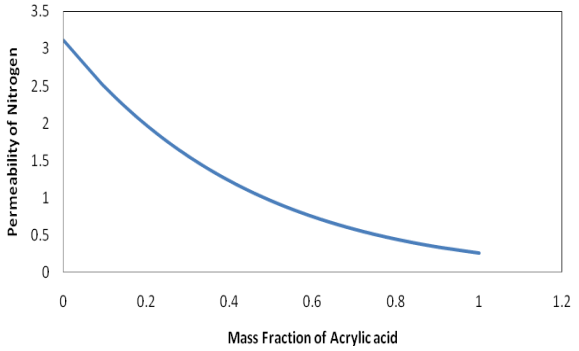

Figure 4. Change in permeability of nitrogen with mass fraction of acrylic acid

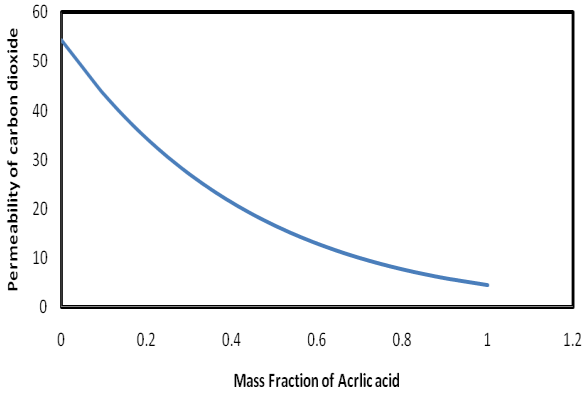

Figure 5. Change in permeability of carbon dioxide with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Gas Permeability Properties of Polyvinyl Alcohol and Polyoxyethelene Composite

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Received: 23 Mar 2020 Revised: 24 Apr 2020 Accepted: 26 May 2020

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of polyvinylalcohal acid and polyoxyethelene to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The composition of the blend was analyzed by its permeability properties. The molar volume and density decreased with increase in polyvinyl alcohol fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with a little bit increase in mass fraction of polyvinyl alcohol. This study will help to determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: properties, fraction, Studio, acid

INTRODUCTION

"Blends or composites are those materials which contains more than one component". The components are not going to lose their identity in the mixture. Both have combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research work and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymers.

Nano material modified polymers paved the way to multi functional materials. Polymers hve been coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers-natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that

can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers; latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money.Thus; researchers have focused on the use of in silico approach to develop the new blends. Software (Materials Studio [7]) has been used to identify compatible pairs. Among the various polymers, polyvinyl alcohol (PVA) is a promising material due to its high dielectric strength, easy film formation, adhesiveness and whose properties can be controlled by dopant concentrations [8, 9]. The film forming ability of PVA is widely used in packaging industry to form strong polymeric films. It is because of their high mechanical strength, environmental stability and easy processability [10]. On the other hand, PVA is non-toxic, semicrystalline, hydrophilic, biocompatible and easily soluble in water [11].

Researchers have used polyoxyethelene in combination with other materials to act as adsorbent [12]. The thermal behavior (from 20 to 500°C) of high-molecular polyoxyethylene-urea mixtures which formed a molecular complex was investigated by means of a derivatograph. This study is intended to identify the interaction of polyvinyl alcohol which is converted into a sponge-like material by foaming agents and hardened with formaldehyde and polyoxyethelene to form blends [13]

MATERIALS AND METHODS

Software used: Materials studio of Biovia software (Dassault Systems of France) was used for analysis.

Methodology used: The structures of polyavinylalcohol and polyoxyethelene were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form.

RESULTS AND DISCUSSION

Molar volume: "It is the volume occupied by one mole of a substance".

Density:" Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications."

"Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium.Lower permeability indicates longer time lag for the gas to pass through the membrane."

Figure 4 "shows that the permeability of nitrogenthrough the composite decreases with increase in mass fraction of Vinyl alcohol." Figure 5:"show that the permeability of carbon dioxidethrough the composite decreases with increase in mass fraction of Vinyl alcohol."

CONCLUSIONS

The possibility of use of polyvinyl alcohol and polyoxyethenol to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties.The molar volume and density decreased with increase in vinyl alcohol fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeabilityfor all the gases decreased with increase in mass fraction of acrylic acid. Usually components for a blend

are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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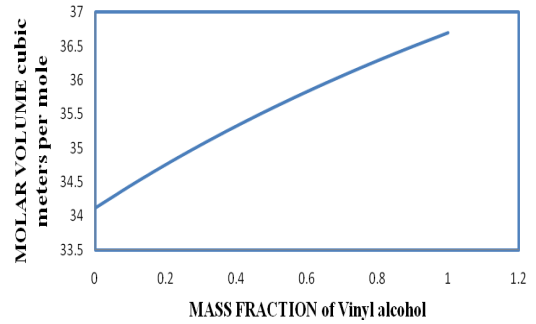
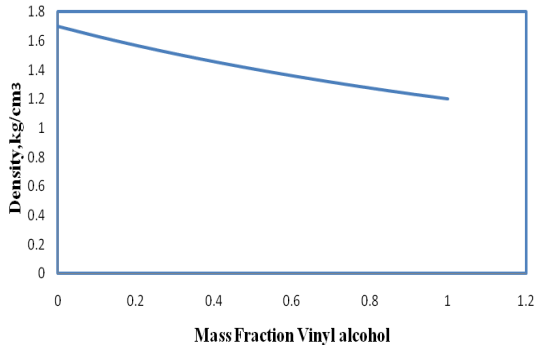
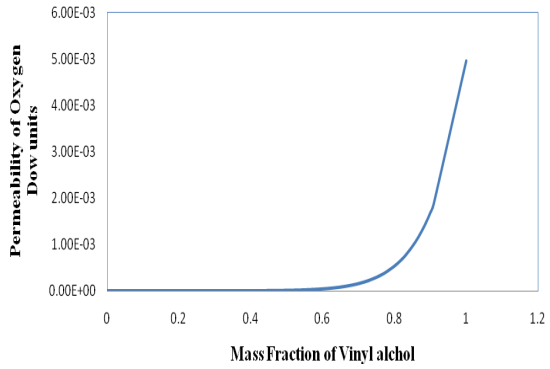


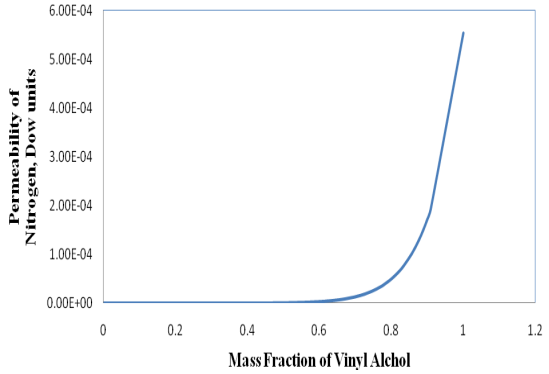
(Figure 1. Change in molar volume with mass fraction of Vinyl alcohol)



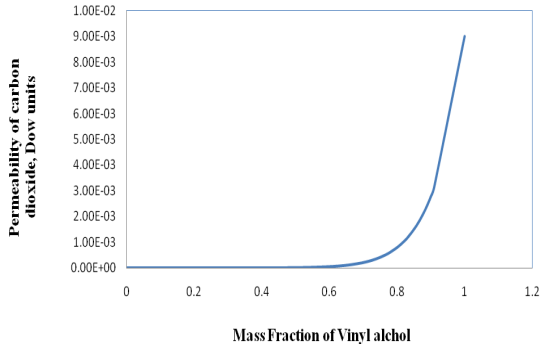
(Figure 2. Change in density with mass fraction Vinyl alcohol)



(Figure 3. Change in permeability of oxygen with mass fraction of Vinyl alcohol)



(Figure 4. Change in permeability of nitrogen with mass fraction of Vinyl alcohol)



(Figure 5. Change in permeability of carbon dioxide with mass fraction of Vinyl Alcohol)

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RESEARCH ARTICLE

In silico Analysis of Gas Permeability Properties of Polyacrylic Acid and Polymethyl Acrylate Composite

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ABSTRACT

A blend is a mixture of more than one components. The desired property of a blend is its homogeneity. The composition of polyacrylic acid andpolymethyl acrylate toprovide desired mechanical properties of the blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties. The molar volume decreases and density increases with increase in polyacrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreases exponentially with increase in mass fraction of polyacrylica cid.This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: gases, experiments, polyacrylic acid, *In silico*

INTRODUCTION

Blends are composites materials which are made from more than one component. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials, mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer.

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enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs. Among the various polymers, polyacrylic acid is a promising material due to its high dielectric strength, easy film formation, adhesiveness and whose properties can be controlled by dopant concentrations [8, 9]. The film forming ability of polyacrylicacid is widely used in packaging industry to form strong polymeric films. It is because of their high mechanical strength, environmental stability and easy processability [10]. On the other hand, polyacrylic acid is non-toxic, semicrystalline, hydrophilic, biocompatible and easily soluble in water [11].

Researchers have found that polyacrylicacid is a polyelectrolyte which is soluble in aqueous media at neutral PH, due to the ionization of the pendent carboxyl side chain. Further, the investigation of polymethylacrylate (PMA) have study the photo degradation of films of poly(methy acrylate) (PMA) in air and in vacuum at room temperatures under irradiation by a low pressure mercury source. It is observed to crosslink during both radiolysis and thermolysis and used as as photolysis in the presence of specific sensitizers [12]. This study is intended to identify the interaction of polyacrylic acid and polymethyl acrylate to form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyacrylic acid and polymethyl acrylate were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of acrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Molar volume: "It is the volume occupied by one mole of a substance". Figure 1 shows that the molar volume of the composite decreases linearly with increase in mass fraction of acrylic acid.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 2 shows that the density of the composite increases linearly with increase in mass fraction ofacrylic acid.

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium.Lower permeability indicates longer time lag for the gas to pass through the mebrane. Figure 3 shows that the permeability of oxygenthrough the composite decreases with increase in mass fraction of acrylic acid.

Figure 4 shows that the permeability of nitrogenthrough the composite decreases with increase in mass fraction of acrylic acid. Figure 5 shows that the permeability of carbon dioxidethrough the composite decreases with increase in mass fraction of acrylic acid. Thus the results indicated that an increase in acrylic acid fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The possibility of use of polyacrylic acid and polymethyl acrylate to form a homogeneous blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties.The molar volume decreases and density increases with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeabilityfor all the gases decreased with increase in mass fraction of acrylic acid usually components for a blend are identified experimentally. This silico study will help us to determine components of a blend without performing laboratory experiments it saves our materials, money and time.

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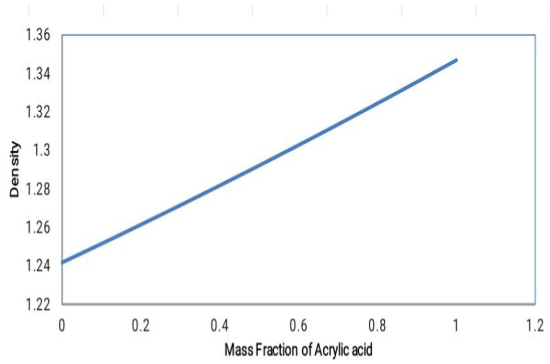

Figure 1. Change in molar volume with mass fraction of acrylic acid.

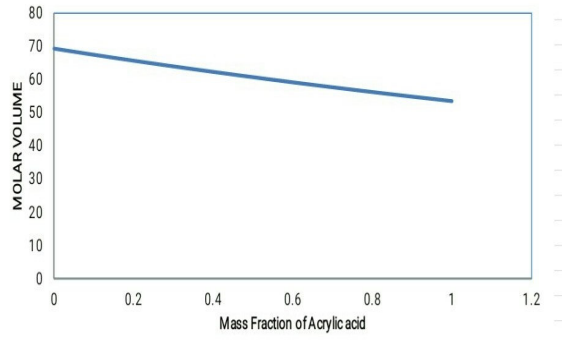

Figure 2. Change in density with mass fraction of acrylic acid.

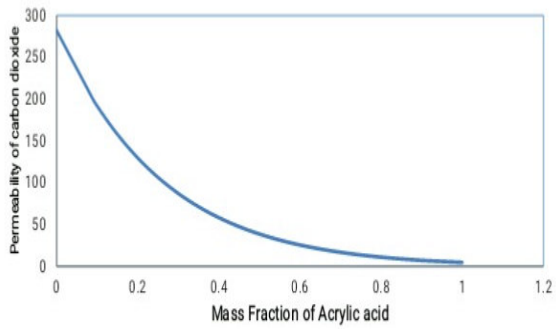

Figure 3. Change in permeability of oxygen with mass fraction of acrylic acid.

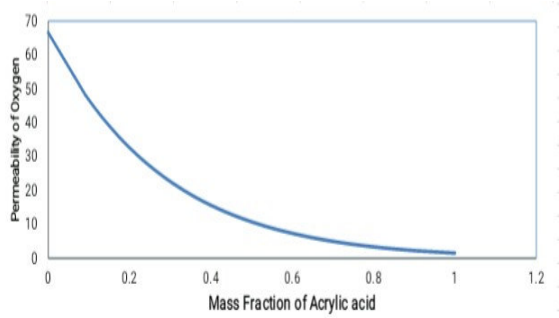

Figure 4. Change in permeability of nitrogen with mass fraction of acrylic acid.

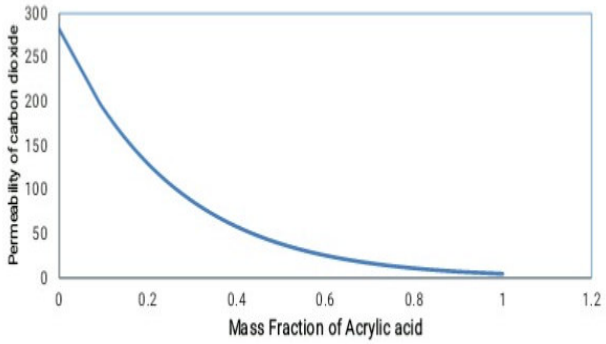

Figure 5. Change in permeability of carbon dioxide with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Gas Permeability Properties of Polyvinyl Alcohol and Polyacrylocholoride Composite

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ABSTRACT

The desired property of a blend consisting of more than one component is its homogeneity. The composition vinyl alcohol and polyacrylochloride to provide desired mechanical properties of the blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to permeability properties. The molar volume and density decreased with increase in vinyl alcohol fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results showed that the permeability for all the gases decreased with increase in mass fraction of vinyl alcohol. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: property, composite, Biodegradable, polymer, products

INTRODUCTION

The components in a blend do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials,mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of

lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money.Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs. Among the various polymers, vinyl alcohol is a promising material due to its high dielectric strength, easy film formation, adhesiveness and whose properties can be controlled by dopant concentrations [8, 9]. The film forming ability of vinyl alcohol is widely used in packaging industry to form strong polymeric films. It is because of their high mechanical strength, environmental stability and easy processability [10]. On the other hand, PVA is non-toxic, semicrystalline, hydrophilic, biocompatible and easily soluble in water [11]. Researchers have used polyacrylochloride in combination with other materials to act as adsorbent [12]. Polyacrylochloride have been reported to be used in Curtius reaction. This study is intended to identify the interaction of vinyl alcohol and polyacrylochloride to form blends.

MATERIALS AND METHODS

Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction. The structures of vinyl alcohol and polyacrylochloride were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of vinyl alcohol on the mechanical properties of the composite.

RESULTS AND DISCUSSION

In this work the use of vinyl alcohol and polyacrylochlorideas potential components of a composite was analyzed using Biovia Materials Studio. BIOVIA Materials Studio Synthia uses pre-defined correlations (advanced quantitative structure-property relationships) to evaluate a wide range of polymer properties. Group additive methods were used for many years to predict the properties of polymers as well as small molecules. These methods are extremely fast and easy to use. Consequently, they are of greatest utility when a rapid estimate of a property is required without a detailed understanding of the atomistic interactions that give rise to it. However, the principal shortcoming of these methods is their dependence upon a database of group contributions. Thus, if a polymer contains a group for which the group contribution cannot be estimated, then the property of that polymer cannot be calculated.

To overcome this limitation, the method implemented in Synthia uses topological information about polymers in the predictive correlations. The connectivity indices derived from graph theory are employed. Thus, no database of group contributions is required and properties may be predicted for any polymer composed of any combination of the following nine elements: carbon, hydrogen, nitrogen, oxygen, silicon, sulfur, fluorine, chlorine, bromine.

Molar volume

It is the volume occupied by one mole of a substance. Figure 1 shows that the molar volume of the composite decreases linearly with increase in mass fraction of vinyl alcohol.

Density: Increase in density indicates decrease in porosity. A higher porosity will enhance the surface area making in suitable for absorption/adsorption applications. Figure 2 shows that the density of the composite decreases linearly with increase in mass fraction of vinyl alcohol

Permeability of gas: Permeability is the rate at which the gas can pass through the polymer membrane after the gas has come to equilibrium.Lower permeability indicates longer time lag for the gas to pass through the mebrane. Figure 3 shows that the permeability of oxygenthrough the composite decreases with increase in mass fraction of acrylic acid

Figure 4 shows that the permeability of nitrogenthrough the composite decreases with increase in mass fraction of vinyl alcohol. Figure 5 shows that the permeability of carbon dioxidethrough the composite decreases with increase in mass fraction of vinyl alcohol. Thus the results indicated that an increase in acrylic acid fraction reduces the permeability of different gases. The rate of permeability might be influence by the molecular weight of the gases.

CONCLUSIONS

The composition of the blend vinyl alcohol and polyacrylochloridewas analyzed with respect to permeability properties using Biovia Materials Studio.The molar volume and density decreased with increase in acrylic acid fraction. The permeability properties of the composite were studied based on permeability of oxygen, nitrogen and carbon dioxide. The results indicated that the permeabilityfor all the gases decreased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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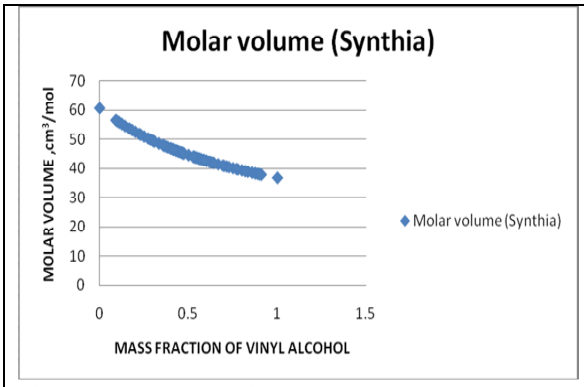

Figure 1. Change in molar volume with mass fraction of vinyl alcohol

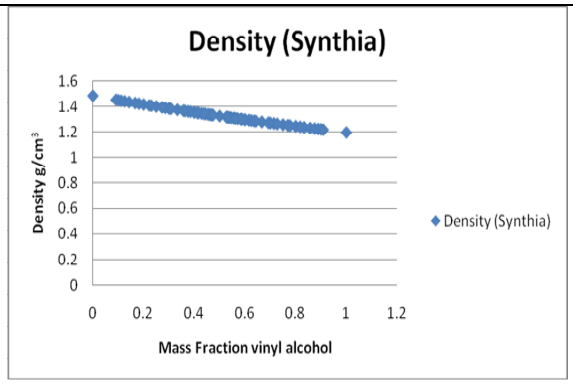

Figure 2. Change in density with mass fraction of vinyl alcohol

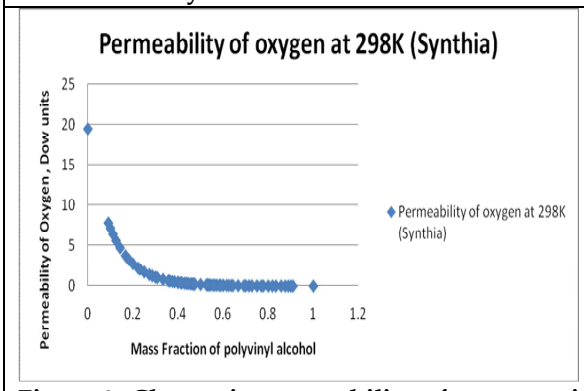

Figure 3. Change in permeability of oxygen with mass fraction of vinyl alcohol

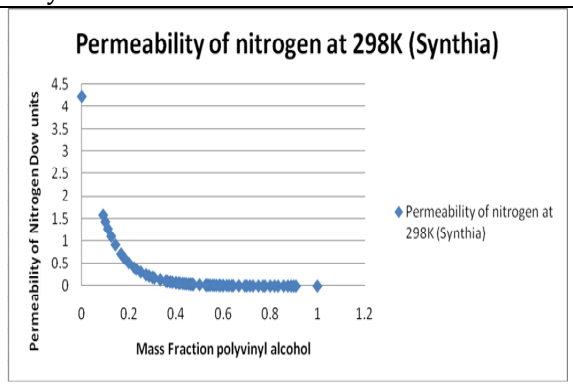

Figure 4. Change in permeability of nitrogen with mass fraction of vinyl alcohol

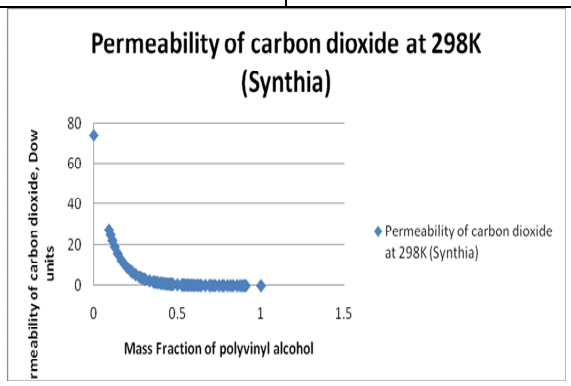

Figure 5. Change in permeability of carbon dioxide with mass fraction of vinyl alcohol

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties of Polyacrylic Acid and Poly12a D Glucose Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of polyacrylic acid. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: laboratory, Polymers, flame, development, properties

INTRODUCTION

Blends are made from multiple components. The components remain constant their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Researchers are working on fire retardant/fire proof materials [2]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [3]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [4]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers; latex polymer cementitious composites [5] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [6]) have been used to identify compatible pairs.

Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denture repair materials, maxillofacial appliances for skeletal defects etc. [7], bone repair [8], dispersing agent, super absorbent polymer, ion-exchange resin, etc.[9]. Polyacrylic acid is used as an electrolyte soluble in aqueous media at neutral pH, good adsorbent, hydrophobic, biocompatible and used as electrolyte [10]. However, the glucose is the key component of osmotic agent and used in peritoneal dialysis (PD), it is sometimes associated with a relatively short duration of effective ultra-filtration. Besides, the use of polyglucose as a PD fluid extends time on PD treatment [11]. This study is intended to identify the interaction of polyacrylic acid and poly12aDglucose to form blends. This study is intended to identify the interaction of polyacrylic acid and poly12aDglucose to form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyacrylic acid and poly12aDglucose were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Heat capacity: It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase.'' Figure 1 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of acrylic acid.

Thermal conductivity: It indicates the correlation between heat flux per unit area and temperature gradient. It refers to the intrinsic ability of a material to transfer heat.'' Figure 2 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of acrylic acid.

Dielectric constant: It is defined as the ratio of the electric permeability of the material to the electric permeability of free space.'' Figure 3 shows that the dielectric constant of the composite increases with increase in mass fraction of acrylic acid Figure 3. Change in dielectric constant with mass fraction of Acrylic acid

CONCLUSIONS

The possibility of use of polyacrylic acid and poly12a D glucose to form a blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of polyacrylic acid. Usually components for a blend are identified experimentally. This in silico study will help determine components of a blend without performing laboratory experiments saving materials, money and time.

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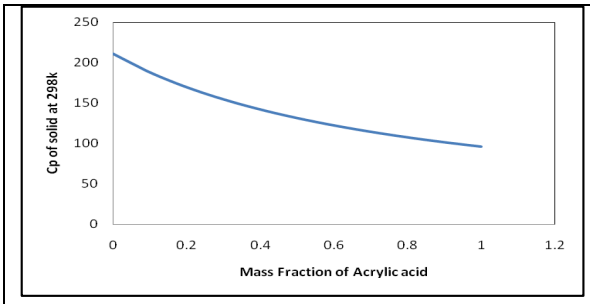

Figure 1. Change in heat capacity with mass fraction of Acrylic acid

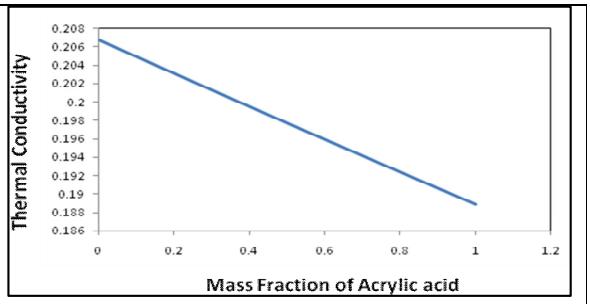

Figure2. Change in thermal conductivity with mass fraction of Acrylic acid

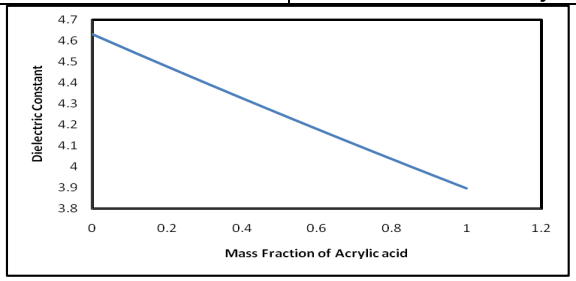

Figure 3. Change in dielectric constant with mass fraction of Acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties of Polyvinyl Alcohol and Dichloroethylene Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of vinyl alcohol. This study will help determine pairs without performing laboratory experiments by saving materials, money and time

Keywords: parameters, significant, polymer, mechanical, strength

INTRODUCTION

Blends or composites are the materials which containing more than one components. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory

experiments. Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money.Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs.

Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denture repair materials, maxilla facial appliances for skeletal defects etc. [8], bone repair [9], dispersing agent, super absorbent polymer, ion-exchange resin, etc.[10]. Polyvinyl alcohol is a polyelectrolyte soluble in aqueous media at neutral pH It is used for preparing hydrogels. It is not toxic and does not cause irritation [11].

Researchers have used 1,2-dicholoethane is one of the most abundant synthetic chemicals and is mainly used as an intermediate in the production of vinyl chloride. [12]. However, the thermal degradation of polyvinyl alcohol (PVA) has been initially investigated with thermal analysis. Generally, polyvinyl alcohol thermally degrades in two processes. The first degradation step mainly involves the elimination reactions, while the second one is dominated by chain-scission and cyclization reactions [13]. This study is intended to identify the interaction of polyvinylalcohol and dichloroethyleneto form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyvinyl alcohol and dichloroethylene were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyvinyl alcohol on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Heat capacity: "It is the amount of heatrequired to raise the temperature of one unit weight of a substance by 1°C without change of phase".Figure 1 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of vinyl alcohol.

Thermal conductivity : "It indicates the correlation between heat flux per unit area and temperature gradient".Figure 2 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of vinyl alcohol.

Dielectric constant: "It is defined as the ratio of the electric permeability of the material to the electric permeability of free space". Figure 3 shows that the dielectric constant of the composite increases with increase in mass fraction of vinyl alcohol.

CONCLUSIONS

The possibility of use of polyvinyl alcohol and dichloroethylene to form a blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parametersincreased with increase in mass fraction of vinyl alcohol. Usually components for a blend are identified experimentally. Thus the silico study will help to determine components of a blend without performing laboratory experiments, which will help in saving materials, money and time.

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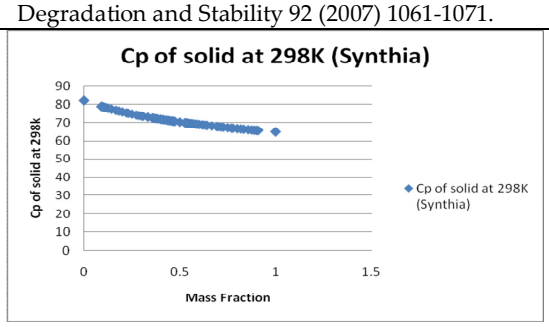

Figure 1. Change in heat capacity with mass fraction of vinyl alcohol

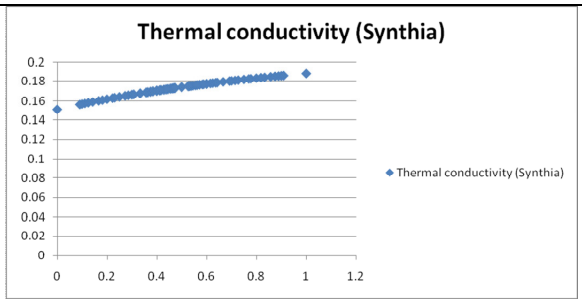

Figure 2. Change in thermal conductivity with mass fraction of vinyl alcohol

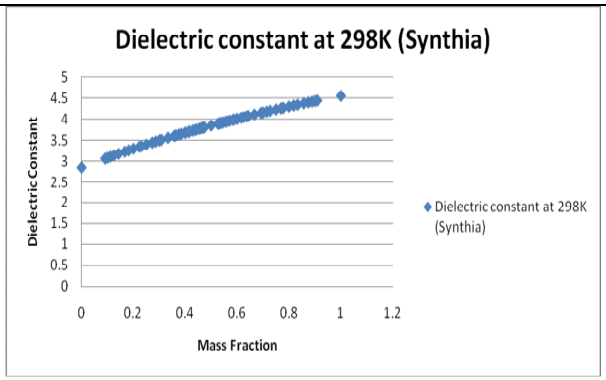

Figure 3. Change in dielectric constant with mass fraction of vinyl alcohol

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties of Polyacrylic Acid and Poly bisphendimeth Carbonate Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of acrylic acid.This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: capacity, heat, acrylic acid, carbon, properties

INTRODUCTION

Blends are made from more than one component. The components remain unchanged their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [4]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [5] were developed for construction of bridges, light rail transit, mining and tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [6]) have been used to identify compatible pairs.

Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denture repair materials, maxilla facial appliances for skeletal defects etc. [7], bone repair [8], dispersing agent, super absorbent polymer, ion-exchange resin, etc.[9]. Polyacrylic acid is a polyelectrolyte soluble in aqueous media at neutral pH It is used for preparing hydrogels. It is not toxic and does not cause irritation [10]. Researchers have used poly (bisphenol A carbonate) (polycarbonate or PC), a leading engineering plastic materials with high strength and transparent properties in the end used applicability in the field of electronics, containers, automobiles, safety, and optics [11]. This study is intended to identify the interaction of polyacrylic acid and polybisphendimeth carbonate to form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systems of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyacrylic acid and poly12aDglucose were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Heat capacity: "It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase." Figure 1 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of acrylic acid.

Thermal conductivity: "It indicates the correlation between heat flux per unit area and temperature gradient." Figure 2 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of acrylic acid.

Dielectric constant: "It is defined as the ratio of the electric permeability of the material to the electric permeability of free space." Figure 3 shows that the dielectric constant of the composite increases with increase in mass fraction of acrylic acid.

CONCLUSIONS

The possibility of use of polyacrylic acid and polybisphendimeth carbonate to form a blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally. This will help to determine components of a blend without performing laboratory experiments saving materials, money and time.

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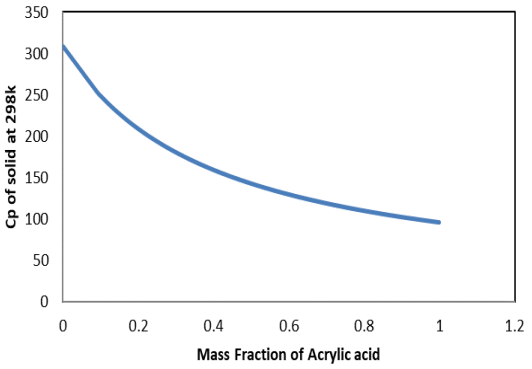

Figure 1. Change in heat capacity with mass fraction of acrylic acid

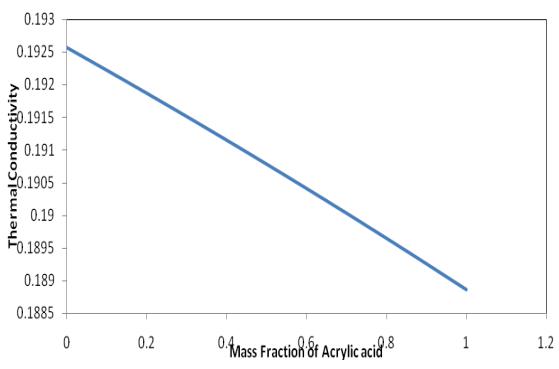

Figure 2. Change in thermal conductivity with mass fraction of acrylic acid

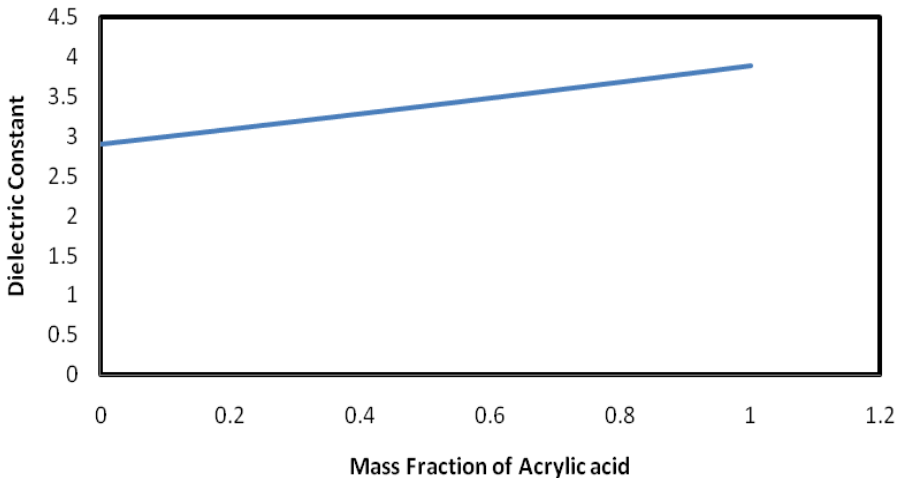

Figure 3. Change in dielectric constant with mass fraction of acrylic acid

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties of Polyacrylic acId and polybutylene isophalate Composite

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ABSTRACT

A blend is a mixture of more than one component. The desired property of a blend is its homogeneity. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all those parameters increased with increase in mass fraction of acrylic acid. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: mixture, parameters, quality, Biodegradable, working

INTRODUCTION

Blends are made from multiple components. The components remain unchanged their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend uses the advantages of different materials; mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties. Polymer blends can be made of two or more polymers, or fibers and polymer, or particles and polymer.

Nano material modified polymers paved the way to multi functional materials. Polymers coupled with carbon based (graphene, carbon nano-tube) nano-materials [1] have drawn attention. Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5].All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money. Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [6]) have been used to identify compatible pairs.

Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denture repair materials, maxilla facial appliances for skeletal defects etc. [7], bone repair [8], dispersing agent, super absorbent polymer, ion-exchange resin, etc.[9]. Polyacrylic acid is a poly electrolyte soluble in aqueous media at neutral pH it is used for preparing hydrogels. It is not toxic and does not cause irritation [10]. However, the poly (butylene isophthalate) (PBI) which is a polyester belonging to the class of the poly(alkylene phthalate)s. The chemical structure of PBI is similar to that of the well-known poly (butylene terephthalate) (PBT), but with the two ester groups located in the 'meta' position of the phenyl group [11]. The influence of the development of crystalline structure on the segmental dynamics of the amorphous phase in polybutylene isophthalate (PBI) has been studied by a combination of relaxation and scattering techniques [12].

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyacrylic acid and Poly butylenes isophalate were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of polyacrylic acid on the mechanical properties of the composite.

RESULTS AND DISCUSSION

Heat capacity: "It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase." Figure 1 shows that the heat capacity (Cp) of the composite increases linearly with increase in mass fraction of acrylic acid.

Thermal conductivity: "It indicates the correlation between heat flux per unit area and temperature gradient." Figure 2 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of acrylic acid.

Dielectric constant: " It is defined as the ratio of the electric permeability of the material to the electric permeability of free space." Figure 3 shows that the dielectric constant of the composite increases with increase in mass fraction of acrylic acid.

CONCLUSIONS

The possibility of use of polyacrylic acid and Poly butylenes isophalate to form a blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that all the three parameters increased with increase in mass fraction of acrylic acid. Usually components for a blend are identified experimentally. This will help to determine components of a blend without performing laboratory experiments saving materials, money and time.

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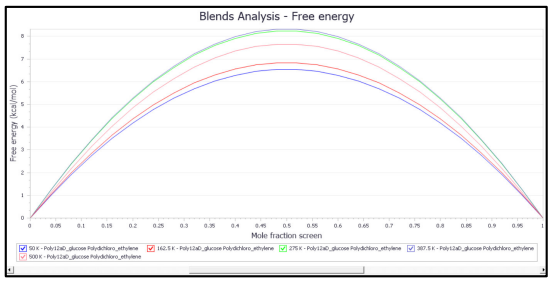
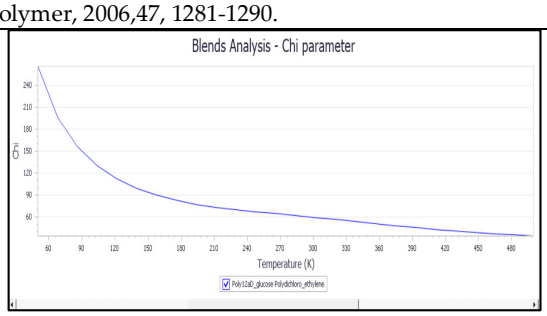
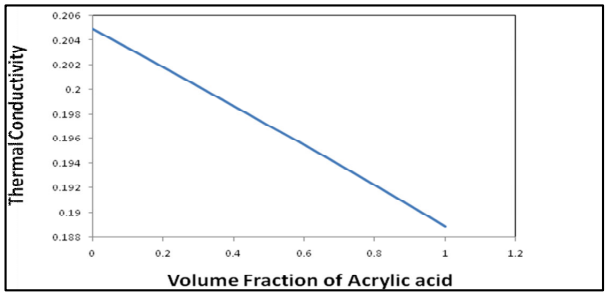


(Figure 1. Change in heat capacity with mass fraction of acrylic acid)



(Figure 2. Change in thermal conductivity with mass fraction of acrylic acid)



(Figure 3. Change in dielectric constant with mass fraction of acrylic acid)

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RESEARCH ARTICLE

In silico Analysis of Thermal and Dielectric Properties of Poly Vinylalcohol and Polyacrylochloride Composite

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Received: 23 Mar 2020 Revised: 24 Apr 2020 Accepted: 26 May 2020

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ABSTRACT

A blend is a mixture of more than one components. The desired property of a blend is its homogeneity. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that the parameters thermal conductivity and dielectric constant increased with increase in mass fraction of acrylochloride. This study will help determine pairs without performing laboratory experiments saving materials, money and time.

Keywords: materials, money, research, transportation, particles

INTRODUCTION

Blends or composites are formed with mixing of more than one substance where substances do retain their identity Blends or composites are the materials that containing more than one components. The components do not lose their identity in the mixture. They combine and contribute to the property of the blend thereby improving the quality of the material. Development of a single material with the desired property involves significant research and time. A blend utilizes the advantages of different materials, mix them to get the desired property. Thus a blend saves time to develop a new material thereby reducing the cost of development of products with desired properties.Polymer blends can be made of two or more polymers, or fibres and polymer, or particles and polymer.

Biodegradable polymers- natural fiber composites [2] have been reported to enhance mechanical properties and water resistance. Researchers are working on fire retardant/fire proof materials [3]. There are reports of inorganic additives in polypropylene; that can enhance flame retardancy without increasing the weight [4]. Researchers have emphasized on synthesis and production of lightweight composite materials having high strength important for enhancing fuel efficiency in the field of transportation [5]. There are applications of composites in structural Engineering due to high strength to weight ratio and resistance to corrosion. Thus, glass fiber reinforced polymers, latex polymer cementitious composites [6] were developed for construction of bridges, light rail transit, mining and

tunneling, retaining walls and other waterside buildings. All the above mentioned examples relied on laboratory experiments.

Usually blends are prepared by trial and error method. Thus it involves wastage of materials, time and money.Thus, researchers have focused on the use of in silico approach to develop new blends. Software (Materials Studio [7]) have been used to identify compatible pairs. Acrylic polymers have a wide variety of applications in dentistry as denture bases, artificial teeth, denture repair materials, maxillofacial appliances for skeletal defects etc. [8], bone repair [9], dispersing agent, superabsorbent polymer, ion-exchange resin, etc.[10]. Polyacrylic acid is a polyelectrolyte soluble in aqueous media at neutral pH It is used for preparing hydrogels. It is not toxic and does not cause irritation [11]. Researchers have used polyacrylochloride in combination with other materials to act as adsorbent [12]. This study is intended to identify the interaction of acrylochloride and polyvinlyl alcohol to form blends.

MATERIALS AND METHODS

Software used: Materials studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques and standard algorithms to predict the level of interaction.

Methodology: The structures of polyvinyl alcohol and acrylochloride were fed to the synthia menu of Materials Studio. It was then run for different weight fractions of the components. Different properties of the composite were displayed in a tabular form. The values were used to plot graphs to identify the effect of weight fraction of acrylochloride on the thermal and dielectric properties of the composite.

RESULTS AND DISCUSSION

Heat capacity:"It is the amount of heat required to raise the temperature of one unit weight of a substance by 1°C without change of phase". Figure 1 shows that the heat capacity (Cp) of the composite decreases linearly with increase in mass fraction of acrylochloride..

Thermal conductivity:"It indicates the correlation between heat flux per unit area and temperature gradient".Figure 2 shows that the thermal conductivity of the composite increases linearly with increase in mass fraction of acrylochloride

Dielectric constant: "It is defined as the ratio of the electric permeability of the material to the electric permeability of free space".Figure 3 shows that the dielectric constant of the composite increases with increase in mass fraction of acrylochloride

CONCLUSIONS

The possibility of use of polyvinyl alcohol and acrylochlorideto form a blend was explored using Biovia Materials Studio. The composition of the blend was analyzed with respect to heat capacity, thermal conductivity and dielectric constant. The results indicated that the two parametersthermal conductivity and dielectric constant increased with increase in mass fraction of acrylochloride. Usually components for a blend are identified experimentally. The silico study will help to determine the components of a blend without performing laboratory experiments. Which effects for saving materials, money and time.

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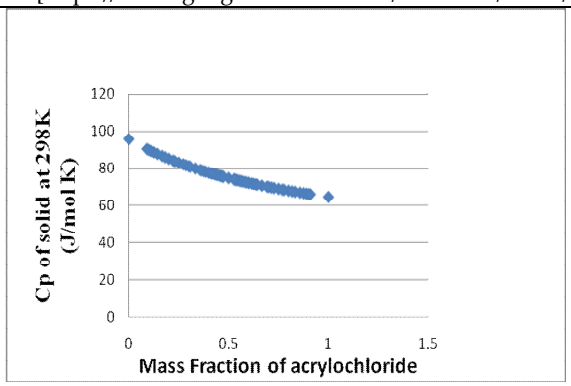

Figure 1. Variation in heat capacity with mass fraction of acrylochloride

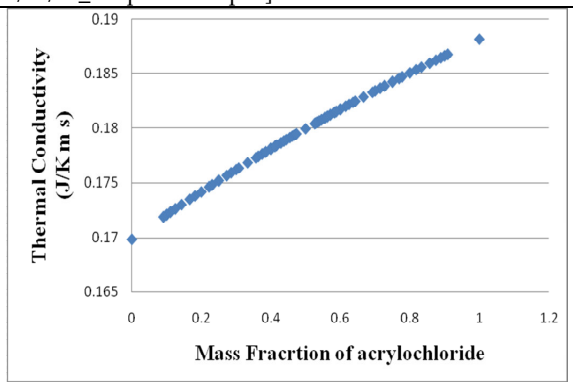

Figure 2. Variation in thermal conductivity with mass fraction of acrylochloride

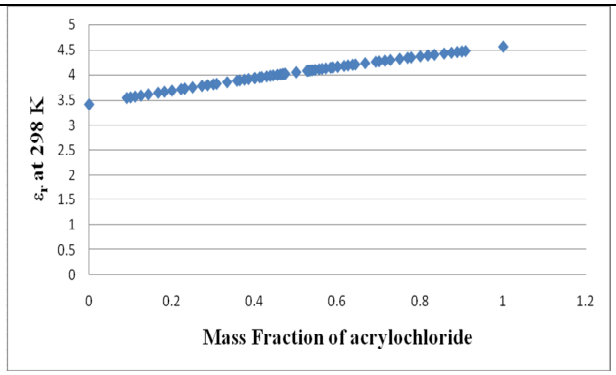

Figure 3. Change in dielectric constant with mass fraction of acrylochloride