RESEARCH ARTICLE

Eradication of Safety Threat and Improvement of Safety Standard of Highway through RSA

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ABSTRACT

India is a developing country with 1.35 billion populations and growing rapidly to cope with developed nation. In the processes of getting developed nation is aggressively developing its road infrastructure but still this large connectivity is not enough for the mounting pressure of vehicle which is creating safety threats for the road user. In the report of Accident in india-2018" which is Published by Ministry of road highways and transportation it is mentioned that the total Number of deaths in 2018 stood at 1, 51,417and most sad thing is approximately 85% accident-related deaths happens in most productive age 18 to 60.Death related to road safety is not only tragedy for the victim's family also a great loss to the nation. Hence road safety shall look as a public health concern and in order to safety measures attention must require to this. In India road accident are not uncommon. The main cause for accident are extraordinary heavy traffic, Disobey of traffic rule and loop holes in road safety features. The modern transport system is able to reduce the distances but it has increases the chances of road accident. As per report of Ministry of road highways and transportation unfortunately India contributes 11% of total fatality throughout the world. The person controlling the vehicle is plays important role in most of the accident cases.

Keywords: Population, road safety, accident

INTRODUCTION

India has 60 lakh km of road network and is the second largest in the world. Out of 60 lakh km road approximately 142,126 km is coming under National highway which is 2.45% of total length but NH carries 40% road traffic. It has been two decades, the lifestyle of middle-class family is changing .but Development of Highway Infrastructure has not able to cope-up with the increasing of traffic volume. So this Imbalance is leading to road traffic accident and posing a great challenge to deal with. People may surprise to know that in 2018 approximately1, 51,417people get killed due to road accident which is far more then malaria, tuberculosis and any other disease. Now a days driving a vehicle in India is becoming a dangerous experience and Indian roads are becoming death traps.

To make the world accident free the United Nations has declared the decade of 2011- 2020 as the road safety decade thus increasing the importance of Road Safety Audit. This is a means to identify potential safety threat. Now-a-days, road accidents are become huge problem to the user and emerging as a serious issue to public and property. It is found out that from last decade that number of accidents is more creating loss to life and property. Due to this unnatural death road safety has become a crucial task. The study is an assessment of safety risk and to take preventive measures to reduce the accidents with the road safety audit. If we go through the economic point of view R.S.A is not expenditure, it's an investment. It is also defined as a systematic process for evaluation of existing or new roads by an audit team at the stages of planning, design, construction, operation & maintenance to achieve roads free of accident and to enhance holistic safety performance.

Accident Statistics in India

In the year 2018, there were almost 4, 67,000 road accidents in India, Out of which killed 1, 51,417people and injured 4, 69,418people. In the year 2015India become signatory to the Brasilia declaration on road safety, pledged to reduce road accidents and traffic fatalities by 50% by 2022. The New Motor Vehicles act, 2019 have been enacted to reduce road accident. It seeks to address issues related to road accidents and road safety measures. In this context, we present some data on road accidents, causes of accidents. From last two decades it was observed that road network in the country has been grown by 39% and New registered vehicle has been grown by 158%. While growth in road network was limited (due to various problem), a constant increase in the number of vehicles on roads is leading to more vehicle density on the road which leads to congestion and road fatalities.

In terms of accident fatalities index, Tamil Nadu state had the highest share in 2018 (23 fatalities/ lakhs persons) followed by Haryana (18 fatalities/ lakh persons), and Karnataka (18 fatalities/ lakhs persons). In 2018, almost 17. % of all road accidents occurred between 15:00 hours and 18:00 hours, followed by 17.3% between 18:00 hours to 21:00 hours. This mentioning that more vehicles present on roads during these hours (peak traffic hours). In 2018, the maximum number of Road accident death were seen in the age group of 18 to 34 (50%), followed by the age group of 35-64 years (36%). World Health Organization has cited that road accidents are a major public health problem as road accidents kill more than 1.25 million people and injure about 50 million people a year around the world and developing country like India contributing 90% in it.

LITERATURE REVIEW

India has just started realizing the importance of RSA. At present no formal qualification is required to become a road safety expert/auditor, only a few training programs are designed to gain knowledge about Road Safety Audit. In India the 1st RSA was carried out by CRRI in the year 2000 on Indore Bypass, in year 2002, The Ministry of Road Transport and Highways (MoRT&H) decided to form a methodology for safety audit of existing road section .As fatal road accidents are increasing in India, the International Road Federation (IRF) is advising toemphasize the need for regular RSAs, By the result now the Ministry of Road Transport and Highways realize it and make it mandatory for various project. Although RSA is much talked about in seminars and workshops and not so well implemented

in India, to reduce future road accident an appropriate RSA policy is required at the National and State levels. The first RSA guidelines were produced in 2003 and revised in 2009 by CRRI and now IRC:SP:88-Manual for road safety audit. However, still there is a need to make highway professionals aware and knowledgeable in making roads safer and the highway authorities would need to commit themselves much more seriously on road safety aspects. As per the recently approved road safety manual the experts must carry out safety audits, not just during the design and implementation phases of the projects, but also in the post operation period to identify and rectify deficiencies.

This section of literature review different methodologies taken in research work done by different researchers. Most of the studies are based on methods of assessment of road accident causes. Road safety Audit methods improve the understanding of the safety performance of roads. After studying various review paper. I have found that the main aim of road safety audit is to assure that all new road schemes operate as safely as practicable. This means that safety should be considered whole cycle of design, construction & pre-opening of any project facility and also during operation & maintenance of the highway.

METHODOLOGY

RSA is a recognized technique for safety assessment of a road to eradicate future accident at prone locations. In India RSAs can be conducted at five stages to ensure that the needs of all road users are considered during each phase of project development –

a. Feasibility Stage
b. Detailed Design stage
c. Construction Stage
d. Pre-opening Stage
e. Existing/Maintenance Stage

In this research, the RSA was performed on an existing road at the operation and maintenance stage. The following steps are followed in this project.

Road Safety Audit Process

The audit process included inspection of operating condition of the highways during both day and night. To do that the Audit team traveled through the entire project corridor (both at day and night time) and identified several potential safety hazard. Notes were taken on the way with respect to horizontal and vertical alignments, High Embankment, available sight distance, layouts of curves and intersections/interchanges, road cross-section, bridges and culverts, side drains, provision for parked vehicles, slow moving vehicles (tractors, bullock carts, bicycles) and pedestrians, bus bays, truck parking etc. In addition to these, the audit team examined appropriate markings and signs, presence of clear zone, road side friction, traffic control devices, lighting requirement and other interim measures. During the audit the team gave importance in observing the type of geometry and traffic behavior at a site, which would lead to a certain type of conflict and crash types with probable severity level. All recommendations related to safety audit were compiled in the form of audit report with measures.

Identification of Risk Factors at Hazardous Location

In this study, potential safety threats were identified at the hazardous locations based on the RSA conducted. It is observed and assessed all the risk elements along the project highway and any unsafe road geometry, traffic operation, sub-standard design elements, and lack of appropriate infrastructure were noted. Based on the findings of RSA, suitable countermeasures were proposed.

Case Study of NH-59

The objective of the assessment was to study the safety features and identifying the potential threat in the stretch from CH-181/000 TO CH-195/000. This road is 2 lane paved shoulder with 1.5mtr earthen shoulder on both side of the road.

RSA Findings

The potential safety hazardous elements identified in this RSA were categorized. Each hazardous element is associated with numerous risk factors. The risk elements are discussed in detail in the following section. A comprehensive list of the risk factors associated with a hazardous element and the corresponding proposed countermeasuresalso cited below.

Horizontal curves were found to be the most accident-prone locations along both the highways. Frequent head-on conflicts were observed on the horizontal curves. In some curves, the lateral shift of vehicles was quite high. In the RSA it was noticed that most of the curves lacked sufficient sight distance, informatory/ warning sign board, Solid Centre line marking for sharp curve, Transverse Bar Marking and Raised Pavement Marker.

Intersections

In this project most of the intersections along the highways were not signalized and uncontrolled. Lack of proper signage making it a potential safety hazard. Several intersections were located on the curve. The approach speed of vehicles from the arterial road was high and drivers seldom stopped or reduced their speed before merging with the major road traffic. Moreover, as the opposing traffic were not separated vehicles were found to take wrong turns. During the audit visit, it was found that at major road TBM(Transverse bar making), Intersection sign board, Speed limit is not available. Further, the approach of such intersections was often not visible due to encroachments and bushes; therefore, the drivers were unable to judge the situation ahead. In addition to that, the Lacking of major road ahead, stop sign and rambler sign board increasing the chances of accident. Such intersections can result in lateral swipes, head-on or rear-end collisions. Identified Risk Factors and Proposed Countermeasures for Hazardous location Related Safety Issues

Narrow bridges

Another safety concern identify in this report was the lacking of safety features on narrow bridges and culverts. In most of the cases the approach road to narrow bridge/Culvert had no warning signs or speed limits and Object Hazard marker Provided and the guardrails/Crash barrier were broken and covered with vegetation. In a few cases, the abutments posed as road side hazards.Due to the sudden decrease in the lane width, maneuvering at such narrow bridges was found to be dangerous especially at night.

Road Side Hazard

Objects adjacent carriageway is high safety threat for all type of user at all the time. Formation width of the road needs to be free of obstruction.

Major Junction

Lacking of safety Measures at major Junction is tends to high probability of road collision. A large proportion of road accidents on Indian roads take place at junctions, most often due to motorists pulling out from side roads and colliding with oncoming vehicles. Other factors like congestion, weather conditions, the presence of cyclists and pedestrians, the layout of the junction and lake of traffic sign board including the positioning of traffic lights and filter lanes may contributing to accident.

Illumination

Most of the unsignalized intersections and built-up areas were not adequately illuminated. As a result, spotting a pedestrian or non-motorized vehicle at night was a challenging job for the driver. Sudden exposure of pedestrians

can lead to severe accidents at such locations. High mast street lamps should be provided at such intersections and stretches with a high number of access points.

Unauthorized Parking

Unauthorized Truck Parking was noticed at various location of the highway. Such parking leads to edge drop and poor visibility. Moreover, the effective width of the carriageway decreased. Since a large proportion of heavy vehicles plied through these highways, provision should be made to construct truck lay bays with necessary facilities. In industrial areas where truck parking is utmost necessary, paved shoulders should be provided. In addition to that, information signs to notify the drivers of the truck parking and edge rumble to alert drivers if they are driving off should be provided.

CONCLUSIONS

In this study, the priority scope of the RSA was to identify the potential safety deficiencies at the prone zones on the two-lane highways and provide appropriate recommendations & measures. During the audit, several risk factors were identified, and it clearly emerged that the elements of risk in the case of a two-lane highway were different when compared with a four-lane highway. Although signs and markings were missing in some of the critical locations but in the Indian context absence of such passive safety devices (signs are marking) are probably less detrimental but when it combine with the poor design then it making the stretch accident prone location or black spot. The salient findings emerged from the RSA based safety assessments are as follows -

- Sight distance is one of the major requirements on high-speed corridors such as NHs to provide smooth flow of traffic, but lack of adequate sight distance was consistently observed at the horizontal curves, and at the intersection approaches throughout the study highways.
- Vulnerable location like school and health care need special attention all these locations should have speed limit, school/ hospital sign board and pedestrian crossing and TBM for smooth flow of traffic.
- Managing the inter relationship between travel speed, road infrastructure design, and road users are the fundamental concept of safety on highways. However, speed limits or speed zones were seldom noticed at the highway stretches. As with the change in the road environment, the nature of the highway changes .it is crucial to specify speed limits especially at built-up areas, near health care center, schools, markets etc. Even in a curve and straight segments with inadequate sight distance, the speed limits should be provided.
- it was observed that the road users lack the basic concept of road safety. This is due to the fact that road users are not accustomed to high-speed facilities through dense built-up areas. Education and awareness among the road users can influence and change their present attitudes and behaviors**.** Introducing school-based road safety education can instill safe attitudes of young people early, which can reduce the number of road accidents in the future. Spreading consciousness about traffic rules and safe road driving can help in producing better drivers.

Nevertheless, it is a fact that road safety is a complex issue and is characterized by different sectors such as road engineering, human psychology, vehicle design etc. A systematic incorporation of engineering measures with planning and enforcement can improve better and safer road use.

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Tale 1. Intersections

Sl. No	Risk Element	Risk Factors	Measures
1	**Horizontal Curve**	Limited sight distance, Absence of Chevron, Curve type, and speed limit sign board, TBM and solid centre line marking	Chevron, Curve type, speed limit sign board required to govern the traffic flow, raised pavement marker, TBM and solid centre line marking, required to warn the user.
2	**Intersection**	Lack of type of intersection sign board and Transverse Bar Marking. Safety features on arterial road are absence	Type of intersection, Rumbler sign board and TBM require for either side of the traffic on major road. Rumbler, stop, Major road ahead sign board is required to warn all type of traffic.

Table 2. Narrow bridges

Sl. No	Risk Element	Risk Factors	Measures
1	**Narrow Bridge**	Sudden reduce of carriageway, Absence of Narrow bridge and speed limit sign board, Settlement of bridge approach	Narrow bridge ahead, speed limit sign board required to govern the traffic flow, raised pavement marker along the edge line, TBM and solid centre line marking, required to undisturbed traffic flow. Crash barrier painting require. The approach of the narrow bridge should be clear from vegetation to provide a clear view of the bridge
2	**Culvert**	Lacking of and vandalized object hazard markers at bridge are potential safety hazard not only during night hours but also in day time. .	Object hazard marker need to be installed at every parapet of CD/bridge on faces of traffic direction.

Table 3. Road Side hazard

Sl. No	Risk Element	Risk Factors	Measures
1	**Object Near carriageway (Tree, Vandalized house, Temple, Series of Electric Pole)**	All the Object under formation width are potential safety threat for all type of user.	Object Hazard marker shall install before large object and retro reflective tape shall paste on series of object like electric pole and tree.

Table 4. Major Junction

Sl. No	Risk Element	Risk Factors	Measures
1	**Major Junction**	Lack of Junction Sign board, Speed limit , Built-up area and rambler sign board are absence, Transverse Bar Marking also not available	Junction sign board shall installed for both side of traffic , Speed limit, Built-up area and rambler sign board shall installed and Transverse Bar Marking is required or smooth flow of traffic.

Table 5. Illumination

Sl. No	Risk Element	Risk Factors	Risk Factors
1	**Illumination**	Poor visibility at junctions and built-up areas specially at night	High mast illumination should be provided at uncontrolled intersections and built-up areas to provide better visibility at night

Table 6. Truck parking

Sl. No	Risk Element	Risk Factors	Risk Factors
1	**Truck parking**	Edge drop of earthen shoulder, Restricted vision specially at night	Need to Provide truck lay bays, paved shoulders for truck parking.

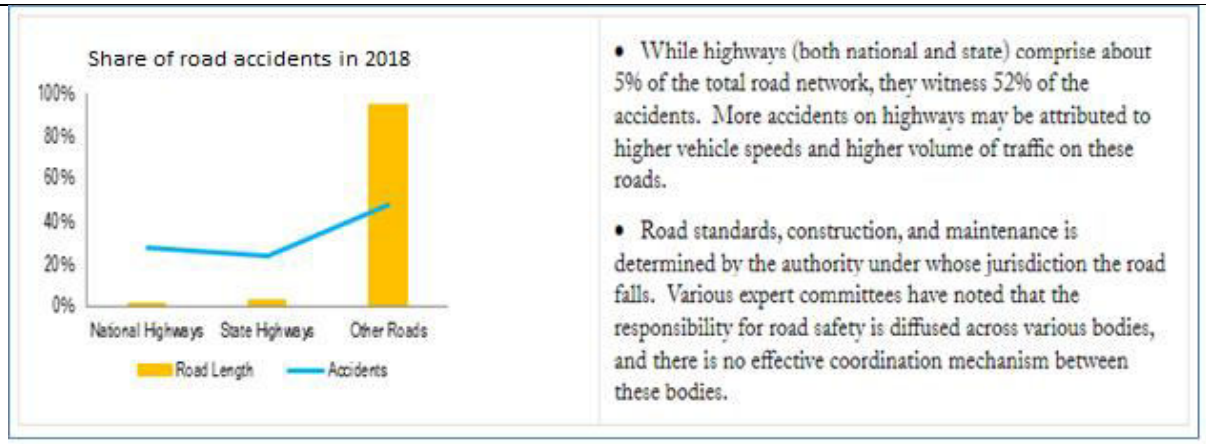

Fig.1. Statistics of road accidents in year 2018 in different roads of India "National Highways comprise 2.4 % of the total road network, but witness 28% of the road accidents"

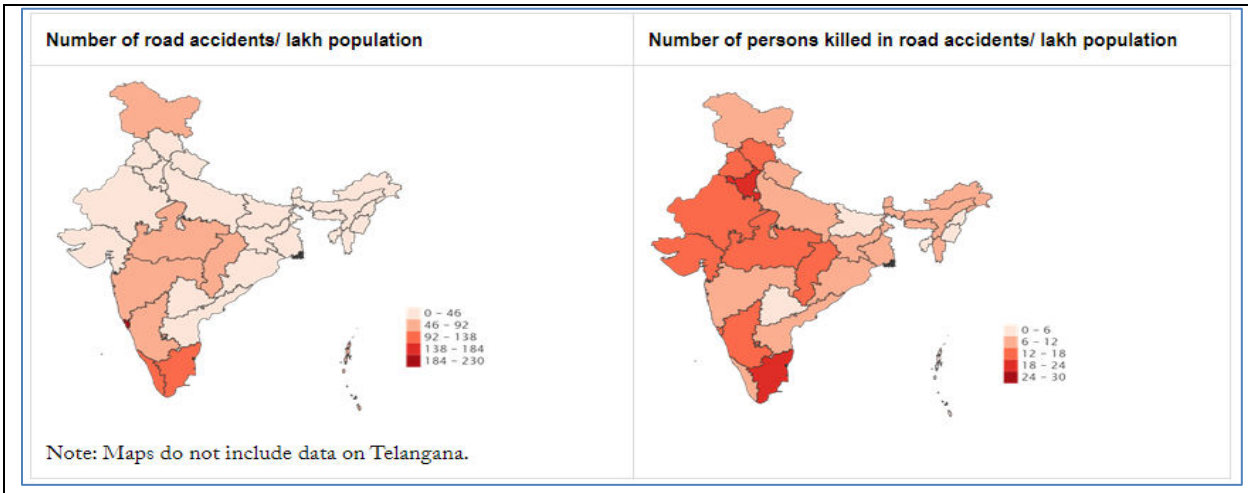

Fig.2. Share of number of road accidents per lakh of population in states of India "67% road accidents take place between 9AM and 9PM; 18-34 years old are most affected"

Fig.3.Horizontal Curve

Fig.4. Intersection

Fig.5. Narrow bridges

Fig.6. Road Side hazard

Fig.7. Major Junction

Fig.8.Illumination

Fig.9. Unauthorized Parking

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RESEARCH ARTICLE

Synthesis of Nano hydrogel based Cellulose-g-Hema /Nano Cao using Snail Shell for Removal of Cr (VI) from Waste Water

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ABSTRACT

The most challenging aspects of water technology now-a-days is to remove toxic and heavy metals ions like Cr(IV) from water coming out from industrial and agricultural sectors that contaminates with ground as well as other sources of drinking water and creates severe health issues in terrestrial animals , aquatic creatures and human civilization. In this study the grafting of 2-hydroxyethyl methacrylate (HEMA) and acrylic acid (AA) onto Cellulose (CE) via redox initiator system of ammonium persulfate (APS) and complex catalyst $CuSO_4$/glycine(1:1) in the presence of foaming agent sorbitol was designed. The CE-g-P(HEMA-co-AA)/snail shell a novel thin film was prepared from the combination of CE-g-P (HEMA-co-AA) polymers with the modified snail shell,(nano-CaO) as a nano filler,then the so prepared CE-g-P(HEMA-co-AA)/nano-CaO nano gel thin film is used for biosorption of heavy metal ions at varying pH in waste water. Characterization of TNGs was done by FT-IR,XRD, TGA, and FESEM. TNGs are potentially suitable for use as pressure-sensitive adhesives (PSAs) and super absorbents exhibiting good biodegradability for cost effective removal of toxic elements from waste water.

Keywords: Nano Hydrogel, PSAs, Biosorption, Heavy Metal ions, Nano filler.

INTRODUCTION

Recently, one of the forefront environmental issue that facing the humanity is the widespread contamination of freshwater system[1-2].Various heavy metal ions such as Cd^{2+},Pb^{2+},Cu^{2+}, Hg^{2+}, As^{3+}, Cr^{6+}, etc... can cause severe health problems there by causing detrimental effects on the intellectual development of the human central nervous system function and resulting semi-permanent brain [1-5].These heavy mental ions can cause severe health problems in

animals and human beings as these metal ions can be stored, accumulated and transferred by the organisms. Among all the toxic heavy metal ions arising from tanning, electroplating, dyeing and from textiles, industries are of particular environmental safety concern in aquatic systems, which normally exists in two main stable states such as Cr (III) and Cr (VI) . Among these Cr (III) is less toxic, harmful and hence has low solubility in aquifers where as Cr (VI) is a well-known highly toxic, carcinogenic, mutagenic and teratogenic mobile ion in the environment [4,6]. Considering these properties of Cr (VI), it must be removed from the contaminated water physically as well as chemically before being discharged into the environment as well as aquatic system.

Cellulose (CE) is a natural polysaccharide with extreme biological properties, being biocompatible, biodegradable, non-toxic, non-antigenic, excellent film-forming ability, bio adsorptive as well as superabsorbent and macro porosity [4,5,7-10,15,16,18]. It is an ecologically interesting and promising adsorbent for removal of heavy metal ions from the aqueous system [10]. All these important properties make cellulose a very interesting component of hydrogels in the environmental and biological fields as well. Nano hydrogels are a three-dimensional swollen cross-linked network of polymer chains with particle sizes in the nanometer range [11,12]. However, nanogels with particle size between 10 and 200 nm are very efficient in removal of heavy metal ions from contaminated aqueous systems [4, 5]. Chemically cross-linked nano hydrogels are produced by internal or external covalent cross linking of the polymer chains through micro- or mini-emulsion or by grafting of monomers with the biopolymer or from self-assembled nano aggregates [13-15].

Now-a-days, bio adsorbents are getting increasing attention excellent film-forming ability, bio adsorptive, bio adhesive as well superabsorbent and macroporous properties [4-5,10,15-16, 18]. The thin film is used as adsorbent surface for metal adsorption. Upto now many more conventional methods are being employed for the removal of heavy metal ions from the waste water systems including precipitation, solvent extraction, ion-exchange, reverse osmosis, filtration, coagulation, But, adsorption is considered to be the most promising method owing to its cost-effective, versatile and operational simplicity for removal of traces of Cr(VI) ions from water system [4-6,10-12]. Now-a-days, bio adsorbents are getting increasing attention as nontoxic, biodegradable and biocompatible. Due to the abundancy as a natural biopolymer cellulose is greatly used as a biosorbent for the treatment of various wastewater systems including industrial wastewaters because of its low toxicity, biocompatibility, biodegradability and presence of a large number of hydroxyl groups and primary amine groups [4, 6, 19-20].

Here, in this piece of research work polymer-porous nano-CaO represents a new class of novel materials with high performance and is of great environmental as well as industrial interest. Many more works have been carried out on biopolymer based material synthesis and its application as biosorbents such as nanocrystals@carbon nanosphere LDHs, Mg-Al LDHs, and graphene oxide nanocomposites for As(VI) removal, magnetic chitosan-Iron(III) hydrogel as Cr (VI) adsorbent, ecofriendly cellulose composite for Th(IV) removal, radiation crosslinked polyvinyl alcohol/acrylic for heavy metal ions removal, etc..have been reported [1, 3, 4, 21-22] . However, no work till date has been reported on modified chitosan with copolymer {Chitosan-g-P(HEMA-co-AA} as well as nano filler (nanoCaO), our vision is to design a hydrophilic bioadsorbent keeping the superporous nature of the hydrogel for the successive removal of Cr(VI) leading to water remediation. Hence, hydrogel form of chitosan could better improve the adsorption capacity than any other form [5, 12, 23].

MATERIALS AND METHODS

Materials

Cellulose powder was purchased from sigma Aldrich Ltd. Sodiumhydroxide was purchased from Ranbaxylaboratories Ltd. Ammonium persulfate (APS), HEMA and AA ware purchased from Himedia Mumbai, India. Orthophosphoric acid, ethanol, and sorbitol were purchased from Qualigen India Ltd. Snail shells were collected from the rice field and washed with deionized water for 3 times and then oven dried at 140 °C for 3 h.

Methods

Preparation of copolymer, P(HEMA-co-AA)

In a reaction vessel, desired quantity of monomers HEMA and AA, surfactant sorbitol, complex catalystCuSO$_4$/glycine(1:1) and distilled water were taken and the temperature was maintained at 55^{o}C in the N_2 atmosphere. Then initiator APS was added with continuous stirring. The reaction was ceased after 4 h by quenching the reaction vessel in ice water. The sample was coagulated with the non-solvent and then washed with hot water for three times and then oven dried at 65^{o}C for 3 h. Then the copolymer {P(HEMA-co-AA)} was kept in the desiccator for 1 h and weighed.

Preparation of nano-CaO

The clean and dry rice field snail shell was cleaned from dirt and sticking flesh, then sun dried. The sample was dried in oven once again over 24 h at 120 ^{o}C. Then the dried snail shells were crushed and grinded in a mechanical attritor. In the next step, the snail shell powder was reduced by adding 10% o-phosphoric acid and then the sample was heated in a furnace at a temperature of 1000^{o}C for 2 h to produce nano-CaO compound. Upon cooling, the sample was stored in desiccator [27-28].

Preparation of cellulose-g-P(HEMA-co-AA) copolymer thin filmgel(TG) and cellulose-g-P(HEMA-co-AA)/nano-CaO Bionanocomposite thin film nanogel (TNG)

In a reaction vessel, desired quantity of cellulose (1.5 g), monomers HEMA and AA, surfactant sorbitol, and distilled water were taken and the temperature was maintained at 55^{o}C in the N_2 atmosphere. Then the initiator APS and complex catalyst CuSO$_4$/glycine (1:1) in the presence of foaming agent sorbitol was added with continuous stirring. The reaction was ceased after 3 h by quenching the reaction vessel in ice water. The sample was coagulated with the non-solvent and then washed with hot water for three times and then oven dried at 65^{o}C for 3 h. Then the graft copolymer {cellulose-g-P(HEMA-co-AA)}was kept in the desiccators for 1 h and weighed. To prepare the grafted nanogel (TNG13 to TNG21), cellulose (1.5g), monomers HEMA, AA, initiator (APS) and desired quantity of CaO nanoclay, surfactant, sorbitol (0.05g), complex catalyst were added sequentially to the reaction vessels. The reaction was carried out as per the method of the homo polymer and the copolymer mentioned earlier.

Calculation of Grafting Parameters

Calculation of grafting parameters for cellulose copolymers was obtained by using the following expression:
Yield of grafting (%) = [(wt. of graft copolymer – wt. of cellulose)/wt. of cellulose] x100------[1].

Batch adsorption studies

Adsorption of Cr (VI) metal ion on the cellulose as well as on the grafted cellulose thin nanohydrogel (TNG) from the aqueous solution was investigated in a batch adsorption experiment. For the batch wise adsorption studies, a stock solution of 1000 mg/L was prepared by dissolving an appropriate amount of analytical grade metal salt in distilled water. The adsorption was carried out at room temperature and at a pH of 5.0+0.05 to study the effects of various parameters on Cr(VI) adsorption by CE, CE-copolymer TG and finally by the nano TNG. A 0.05 g amount of CE/CE-copolymer/TNG powder was dispersed into 100 ml of mili-Q-water bottle and thus a 0.5g L^{-1} stock adsorbent concentration was achieved. Stopper conical flask of 100ml were used for the batch adsorption experiments each of which contained 50 ml solutions containing 20, 30, 50,75, 100 mg/L of Cr (VI) ion having 0.02g of beats agitated for 2h at a rpm speed of 180-200 in a thermostatic shaker. The solution was periodically monitored to detect the concentration of the metal ion remaining in the stock solution. The desired pH of the solution in each conical flask was adjusted by adding negligible volumes of 0.1M HCl and 0.1 M NaOH by using HANNA HI2215 digital pH meter. All the results of this batch adsorption were recorded in duplicate and the final data was taken as the mean. The effect of solution pH on adsorption was observed by varying the solution pH from pH-2 to pH-8 for a fixed concentration and volume of the solution. The results of kinetic batch adsorption process suggested that Cr(VI) adsorption by CE/CE-copolymer/TNG achieved equilibrium in several hours. Henceforth, the mixture was oscillated

for 24hrs and thus the solid liquid phases were separated by stirring the solution vigorously at 298 K. Then the suspensions were centrifuged at 10,000 rpm for 30 minutes to separate out the solid liquid phase. After the filtration through filter paper (Whatmann-42), the concentration of Cr(VI) in the filtrate was determined through the colorimetric process using 0.05% Arsenazo III, 0.1% L(+)-Ascorbic acid and sodium formate buffer [30-31].The Cr(VI) concentration in the supernatant was measured by the UV-visible spectrophotometer (JASCO, V2-650 model) at a maximum wavelength of 655 nm. For the optimization of adsorption condition the metal concentration (10-500ppm), adsorbent dose (0.02-0.5gm) and the pH of the metal solution (2-9) were varied till the equilibrium is achieved. The adsorption percentage Q (mg/g) and the removal efficiency (%E) of Cr(VI) on the CE/CE-copolymer/TNG were calculated from the difference between the initial concentration (C_0) and the equilibrium one (C_e) as given in equation [2] and [3] respectively.

$$\% E = \frac{(C_0 - C_e)}{C_0} \times 100 \quad \text{---------- [2]}$$

$$Q = \frac{(C_0 - C_e)}{m} V \quad \text{----------[3]}$$

The adsorbed amount *Q* (mg/g) and the removal efficiency *%E* were calculated according to the Eq. [2] and [3] where C_0 and C_e are the initial and equilibrium concentrations (mg/L) of Cr (VI) in the aqueous phase respectively. Here *m* (g) represents the mass of the adsorbent and *V* (L) is the volume of the aqueous phase.

Regeneration study of bio adsorbent

During the regeneration study, the CE/CE copolymer/TNG were tested for the removal and recovery of Cr (VI) ion. The adsorption experiment was carried out for 3h with the concentration of 50mg/L and 0.05g of bio-sorbent. The sample was centrifuged and the supernatant was taken for metal analysis. The Cr (VI) loaded adsorbent was rinsed thrice in deionized water and subjected to 0.1mol/L HCl. Then the regenerated biosorbent was taken to next adsorption cycle for Cr (VI) removal. The process was continued till the adsorption capacity of adsorbent shows its least capacity of adsorption.

Kinetics, Thermodynamics and Isotherm studies

The solutions were shaken at the optimized conditions and at predetermined time intervals, samples were separated by centrifugation followed by decantation for the investigation of the adsorption kinetics. The data obtained from the experiments were analyzed by the pseudo first order and pseudo second order models and the thermodynamic parameters were obtained at different temperatures and hence, the activation energy was calculated. The equilibrium data obtained from the batch experiments were better investigated by the Langmuir and Freundlich isotherms.

Characterization

The copolymer and nano-CaO of snail shell-based composite samples were characterized by FTIR, XRD, FESEM and TGA, etc. The grafting of P(HEMA-co-AA) onto the cellulose and incorporation of nanofiller was confirmed by using an FTIR analysis in the form of KBr pellets. The dispersion of grafted copolymer into nano snail shell based thin film and Cr(VI) adsorption studies in thin film was studied using XRD with diffraction angle 2θ from10º to 90º on a Bruker D8 Discover (Germany) instrument at 25°C. X-ray crystallographic unit equipped with a Guinier focusing camera with CuKα radiation (λ= 0.15059 nm) with a 0.02 2θ step size and a 2-s count time. Nanoscale structure of grafted samples was investigated by a field emission scanning electron microscope GEMINI®FE-SEM to examine the surface morphology of the coatings. For FESEM observation, all coating samples were coated in gold and low beam energy of 1 kV was operated to reduce the possibility of any thermal damage to the coatings. The ultrathin section (the edge of the sample sheet perpendicular to the compression mold) with a thickness of 100 nm was microtomed at -80°C.Thermal properties were measured by thermo gravimetric analysis (TGA) to observe changes in thermal events in the polymer films using a Shimadzu DTA-500 system. It was carried out in air from room temperature to 600°C at a heating rate of 10°C/min.

RESULTS AND DISCUSSION

FTIR spectra of TNG

The grafting of P(HEMA-co-AA) onto cellulose was confirmed by the FTIR spectral study as shown in Fig. 1. From Fig. 1(C) of Cellulose-g- P(HEMA-co-AA) /nano- CaO TNG segments, the ester function group(-CO-O-CH_2-) gives peak at 1745 cm^{-1} ,C-O at 1185 cm^{-1} and Ca-O-Ca peak at 895.5 cm^{-1} which confirmed the insertion of nano-CaO layer into the copolymer layer . The slight shifting of the peak to lower frequency might be due to the hydrogen bonding between the hydroxyl group of cellulose and the carbonyl group of the pendant graft. Fig.1(B) Spectrum of P(HEMA-co-AA) indicates the peak at 3150 cm^{-1} due to C-H stretching frequency and1745 cm^{-1}due to ester frequency. In Fig.1 (A) of nano-CaO, the Ca-O bond resembles the stretching frequency at 910 cm^{-1} and the bending frequency region of two frequency ranges 780cm^{-1}, 460 cm^{-1}.

XRD spectra of TNG

The crystallinity of samples like nano-CaO, cellulose-g-P(HEMA-co-AA) and cellulose-g-P(HEMA-co-AA)/nano-CaO,cellulose-g-P(HEMA-co-AA)/nano-CaO TNG after Cr(VI) adsorption were investigated by XRD study. The crystalline phases of the synthesized powders were analyzed by powder XRD. Micro structural observation was confirmed. In the X-ray pattern in Fig. 2, the (A) is the X-ray pattern of snail shell showing sharp peaks for its crystalline nature. The crystalline pattern at around $2\theta=10^0$ and 20^0, indicates lower degree of crystallinity [31-32]. In Fig. 2(B), the cellulose-g-P(HEMA-co-AA)/nano-CaO TNG confirms the insertion of polymer in the sheet structure of snail shell. This clearly reveals the grafted copolymer is introduced inside the sheet CaO matrix of the snail shell. In Fig. (C) cellulose-g-P(HEMA-co-AA)/nano-CaO TNG after the Cr (VI) adsorption from the aqueous system, clearly indicated that the spherical porous material nano-CaO based TNG and as such treated as a super bio-adsorbent.

FESEM of TNG

The FESEM micrographs of the nano-CaO(I),the copolymer without nano-CaO(II) and the copolymer with nano-CaO TNG(III) and after biodegradation of Cellulose-g-P(HEMA-co-AA)/nano-CaO TNG(IV)(G) are shown in Fig.3 at different magnifications 200KX,1µm 100KX. The micrographs confirmed the homogeneous insertion of the implant copolymer into the matrix of the snail shells as comparatively shown in Fig.3. (E and F).The cellulose based TNG is used in bioadsorption application due to their micro porosity. The surface morphology after biodegradation by activated sludge has been confirmed as shown in Fig. 3(G). This might be due to the decomposition or colony growth by the micro-organisms on the cellulose-g-P(HEMA-co-AA)/nano-CaO TNG resulting in the rough surface as compared to that of before biodegradation (Fig.3) E and F. Hence, the prepared novel TNG is eco-friendly in nature.

TGA of TNG

The thermal decay of (A)nano-CaO, (B)cellulose-g-P(HEMA-co-AA), (C)cellulose-g-P(HEMA-co-AA)/nano-CaO TNG and (D)cellulose-g-P(HEMA-co-AA)/nano-CaO TNG after Cr(VI) removal were considered by the TGA analysis as shown in Fig. 4. The initial decay of both the samples is due to the existence of little bit of moisture and amorphous nature of TNG material. The decay of the cellulose-g-(PHEMA-co-AA) copolymer at temperature 120 ^{0}C and that of cellulose-g-P(HEMA-co-AA)/nano-CaO TNG at 160 ^{0}C is explained on the fact that on the higher thermal decay of the cellulose-g-P(HEMA-co-AA)/nano-CaO TNG might be ascribed to the insertion of the copolymer into the sheet structures of the nano-CaO. This is an added advantage for this TNG as it can resist the higher temperature because the CaO is thermally stable and highly resistant.

Measurement of equilibrium water content (EWC)

The equilibrium water contents (EWC) of both the samples, cross linked copolymer hydrogel and cross linked TNG were immersed in different pH buffer solutions at (pH 3.5 to11) with different nano-CaO load (0.10,0.25, 0.5, 1.0, 1.25, 1.5 g) for 24h until equilibrium swelling was reached. The swollen samples were removed from the buffer till

excess buffer on the polymer matrix wiped off by filter paper, then samples were weighed. Equilibrium water content (EWC) was calculated by using the following equation [33]

EWC (%) = [Ws – Wd/ Ws]× 100----------[4]

Where, Ws and W_d are the weights of the polymer sample at the equilibrium swelling state and dry state respectively. The EWC at different pH were determined to know the working capability of the TNG, i.e., to know the most selected adsorption sites of the toxic Cr (VI) into the graft copolymer matrix as shown in Fig.5. A significant observation is that the swelling of samples in buffer solution is increased from pH 7.0 to 8.7 and then decreased. Further, the measurement of EWC of TNG also indicates the swelling of the grafted samples pH sensitive. At lower pH, the grafted TNG is less porous in nature and is optimum at pH 8.7. But, the TNG has shown better EWC than that of copolymer of CS. Thus the result is well explained by the fact that the porosity of the sample is optimum at the nano-CaO load of 1gm (Fig. 5) and at higher pH =8.7. The water swellability of the microsphere at pH 8.7 was better than those at pH 7 and pH 3.5. Thus, this enhancement is attributed to the change from COOH in acidic condition (pH 3.5) to COO^- in alkaline condition (pH =8.7) of TNG [32- 33] and also the ionic nature leads to increase in swelling of gel and Cr(VI) removal at higher pH 8.7 [34]. In addition, the protonated amino group changed to unionized amino group which led to decrease in swelling of gel and thus adsorption of Cr(VI) decreases gradually. The crosslink density of the polymer is higher, so it may get less space to adsorb Cr(VI) in its template and at lower pH≤ 7.0 the porosity of TNG decreases, the strength of the internal gel structure may be very less to retain the toxic Cr(VI). So as the Cr(VI) aqueous solution is highly acidic in nature adsorption is better preferred at lower pH 4/5 [4-6].

Biodegradation by activated sludge

Biodegradation of cross linked copolymer of hydrogel and cross linked TNG were studied under sludge water in order to compare the extent of biodegradation at different conditions. This contains many dissimilar types of microorganisms (bacteria, fungi and yeast, etc.) which are responsible for the biodegradation of waste materials. The sludge was collected in a polypropylene container, which was filled completely and then fully closed [36-37]. The samples (0.5 g) were deeped in the sludge water and incubated together in a sterilized vessel at room temperature (26 ± 2◦C) for 15, 45, 90 days. It was observed that the nano-CaO based TNGs exhibited good biodegradability than that of copolymer sample TGs. It might be ascribed to the development of hydrophilicity and porosity in the snail shell based TNG that could facilitate the insertion of water along with different types of micro-organisms into the polymer matrix. This observation was further confirmed from the FESEM micrographs (Fig.3D). Particularly, the TNG in Fig.3.D has shown comparatively better biodegradation than the others because of more hydrophilicity and more growth of the microorganisms. From Fig.6, the TNG16 sample showed maximum degradation among the samples.

Effect of solution pH with time on Cr(VI) adsorption

Effect of solution pH on Cr (VI) removal from the waste water system was conducted to test the effectiveness of the virgin cellulose, cellulose copolymer and finally the TNG. In this present study, there was a steady decline in the removal percentage of adsorption when pH was increased initially from 2 to 8 in a fixed condition of metal ion concentration and adsorbent dose as discussed in our previous paper [38]. The increase in pH value further leads to metal precipitation and metal accumulation thereby reaching the equilibrium**.** The result showed that the Cr (VI) adsorption was better by the TNG as compared to those of the virgin cellulose and the cellulose copolymer. Here, the adsorption by the TNG accounts for the 96% of the Cr (VI) removal from the aqueous system at optimum pH of 5.3 thereby decreases to 40% as the pH increases from 5-8 respectively [1,4,6]. Thus, the adsorption percentage is high at low pH and decreases with increase of pH value. It may be attributed to the fact that the metal reacts with OH^- and forms insoluble metal hydroxide which decreases the degree of adsorption**.** The periodical increase and decrease of adsorption with pH is as shown in Fig 8.

Effect of Time on Cr (VI) adsorption

Fig-9. Illustrates the removal efficiency of Cr(VI) using cellulose and grafted cellulose with the above optimized condition of pH within 24h. Appx. 95.8% and 94.5% of Cr(VI) were removed by the cellulose-g-P(HEMA-co-AA) and cellulose-g-P(HEMA-co-AA) nanoCaO TNG respectively while the efficiency of removal by the virgin cellulose was approx. below 20%. Except for the first hour, the removal efficiency of Cr(VI) gradually increased over the time upto 24h. The above adsorption of Cr (VI) by the grafted co-polymer cellulose and the TNG might have been resulted by the hydrophilicity as well as high porosity in the intercalated structure of cellulose biopolymer encapsulated by the nanoCaO fillers as identified by given SEM study [1,4-6]. The detailed description is well understood as shown in the fig-8 below.

Adsorption Isotherms:

Both the isotherms i.e Langmuir and Freundlich isotherms are interpreted here to describe the adsorption kinetics of Cr (VI) by cellulose, cellulose copolymer as well as cellulose TNG. Mostly Langmuir isotherm is applicable to homogeneous adsorption surface of the monolayer and hence adsorption tales place without any interaction between the adsorbed molecules. The Langmuir model assumes uniform energies of adsorption onto the monolayer surface and there is no transmigration of adsorbate occurs on the plane of the surface. Based upon these assumptions, the linear form of Langmuir is represented as follows.

$$\frac{C_e}{Q_e} = \frac{1}{b * Q_{max}} + \frac{C_e}{Q_{max}} \qquad \text{----------[5]}$$

Where *Ce* is initial concentration (mg/L), Qe is adsorption capacity (mg/g), *b* is related to the free energy of adsorption (L/mg), *Qmax* is the Langmuir maximum monolayer adsorption capacity (mg/g). The values of *b* and *Qmax* have calculated the slope and intercept of the Langmuir plot of *Ce* versus *Ce*/*Qe* (Fig-9). The Freundlich isotherm model assumes heterogeneity of adsorption surfaces due to the diversity of the adsorption sites or the diverse nature of the metal ions adsorbed. Free or hydrolysed species are characterized by the heterogeneity factor (1/n). The linear Freundlich equation is expressed as in equation-7 such as

$$q_e = Kce^{1/n} \qquad \text{---------- [6]}$$

Where, qe and ce are the amount of Cr(VI) adsorbed (mg/g) and Cr(VI) at equilibrium respectively. K an n are the Freundlich isotherm constants, here K indicates the adsorption capacity whereas n is related to the energetic heterogeneity. The parameters calculated from these two models are listed in the following Table-2. As can be seen, from the table the Langmuir model can be better to the experimental data with all R^2 value of 0.9984, indicating that the adsorption of Cr(VI) on the surface of the TNG which is the monolayer adsorption following pseudo second order as shown in the graphs shown below. (fig-10.1 &10.2)

Kinetic Studies

The kinetics of Cr(VI) removal on the adsorbate TNG {cellulose-g-P(HEMA-co-AA) nano-CaO} was further investigated by the two kinetic models namely, pseudo-first-order and pseudo-second order [1-3]. The pseudo-first-order model was presented as the following equation:

$\ln(qe-qt) = \ln qe - kt$----------[7]

The pseudo-second-order model equation can also be expressed as

$t/qt = 1/k_2qe^2 + t/qe$----------[8]

where qe(mg g^{-1}) was the amount of Cr(VI) adsorbed at equilibrium time, qt (mg g^{-1}) was the amount of Cr(VI) adsorbed on the TNG at time t (min), k_1 and k_2 (mg g^{-1} min^{-1}) were the pseudo-first-order model rate constant and the pseudo-second-order rate constants respectively. From the linear plots of ln(qe − qt) versus t , the adsorption of

the target Cr(VI) occurs within the first contact time of 60 minutes and then equilibrium achieved at 90 minutes.After certain time time at equilibrium the adsorption process ceased or slowed down, this is due to the less availability of the active sites and functional groups on the TNG sites for Cr(VI) removal [3,4,6]. The calculated q_e calculated from the slope and the intercept of the pltos t/qt versus t according to the above equation-9 and this The theoretical q_e values is the equilibrium value of Cr(VI) assuming 100% of Cr(VI) adsorbed. The calculated values of qe are in well agreement with the theoretical ones showing good linearity with R^2 value above 0.999 for the pseudo second order which is much higher than the pseudo first order model. Hence, the adsorption process follows the pseudo second order kinetics with the value of correlation coefficient indicated as R^2 = 0.9998 as shown below in the table-3, suggesting chemisorption is the predominant rate-limiting step.

CONCLUSION

The cellulose-g-P(HEMA-co-AA)/nano-CaO of snail shell based TNGs were synthesized via emulsion technique using APS as an initiator under N_2 atmosphere and were characterized by XRD, FTIR, , FESEM and TGA. Finally, the TNG being intelligently sensitive to pH may be considered as a high performance nanomaterial in removal of toxic Cr(VI) ion from waste water leading to water remediation. The high porosity and hydrophilicity increases the metal ion uptake in the polymeric nano matrix in thin film. In fact, the pH of the cellulose-based nanogels thin film are expected to become a promising tool, for use in the waste water treatment with the Langmuir adsorption following pseudo second order kinetics. Preliminary results of the synthesized TNGs are studied with a view to their novel application as a promising technology for environmental remediation

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Table 1: Variation of [HEMA], [AA] in cellulose-g-P(HEMA-co-AA)copolymer thin film gel (TG) and cellulose-g-P(HEMA-co-AA)/nano-CaO thin film nanogel (TNG) , their % grafting and % EWC at pH=8.7

Sample code	Wt. of Cellulose in gm	[HEMA] mol/L	[AA] mol/L	[APS] mol/L	Sorbitol, g	Snail Shell Nano-CaO, g	% Grafting	% ,EWC at pH= 8.7
TG1	1.2	0.071	0.034	0.01	0.05	-	83±1.33	314
TG2	1.2	0.071	0.068	0.01	0.05	-	86±1.33	321
TG3	1.2	0.142	0.087	0.01	0.05	-	92±1.33	341
TG4	1.2	0.178	0.104	0.01	0.05	-	98±1.33	365
TG5	1.2	0.178	0.122	0.01	0.05	-	94±1.33	343
TG6	1.2	0.214	0.034	0.01	0.05	-	91±1.33	335
TG7	1.2	0.142	0.034	0.01	0.05	-	93±1.33	342
TG8	1.2	0.071	0.104	0.01	0.05	-	89±1.33	331
TG9	1.2	0.178	0.087	0.01	0.05	-	91±1.33	335
TG10	1.2	0.142	0.122	0.01	0.05	-	93±1.33	342
TG11	1.2	0.214	0.104	0.01	0.05	-	96±1.33	359
TG12	1.2	0.071	0.139	0.01	0.05	-	91±1.33	335
TNG13	1.2	0.178	0.104	0.01	0.05	0.10	-	409
TNG14	1.2	0.178	0.104	0.01	0.05	0.25	-	415
TNG15	1.2	0.178	0.104	0.01	0.05	0.50	-	426
TNG16	1.2	0.178	0.104	0.01	0.05	1.00	-	434
TNG17	1.2	0.178	0.104	0.01	0.05	1.25	-	421
TNG18	1.2	0.178	0.104	0.01	0.05	1.50	-	417
TNG19	1.2	0.071	0.068	0.01	0.05	1.00	-	393
TNG20	1.2	0.142	0.087	0.01	0.05	1.00	-	412
TNG21	1.2	0.071	0.104	0.01	0.05	1.00		376

Table 2: Freundlich and Langmuir adsorption isotherms

	Freundlich				Langumuir		
T(^{0}C	T(^{0}C)	n	k	R^2	q_{max}(mg/g)	b	R^2
40	40	3.60	50.00	0.956	166.7	0.15	0.9953
30	30	4.32	53.25	0.8762	153.6	0.23	0.9984
25	20	4.42	55.25	0.9065	149.7	0.35	0.9976

Table 3: Pseudo first and second order kinetic models

Pseudo-first order kinetic model			Pseudo-second order kinetic model		
K_1 (g mg^{-1} min^{-1})	q_e (mg g^{-1})	R^2	K_2 (g mg^{-1} min^{-1})	q_e (mg g^{-1})	R^2
0.008225	125.2	0.9650	0.0042	128.4	0.9998

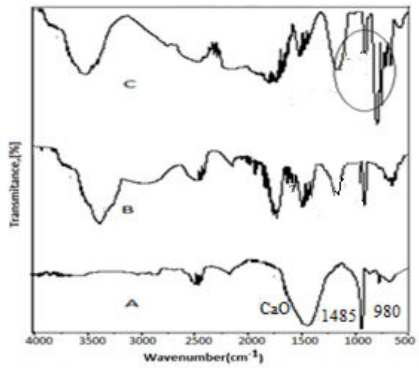

Fig-1: (A)Nano-CaO (B) Cellulose-g-(HEMA-co-AA)/Nano-CaO (C) Bio adsorption of Cr(VI) in Cellulose-g-P(HEMA-co-AA)/nano-CaO Hydrogel

Fig.1.FTIR spectra of TNG

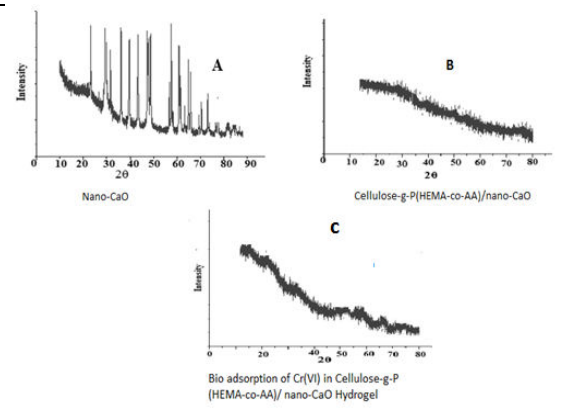

Fig.2. XRD of (A) nano-CaO (B) cellulose-g-P(HEMA-co-AA)/nano-CaO TNG and (C) cellulose-g-P(HEMA-co-AA)/nano-CaO TNG after Cr(VI) adsorption

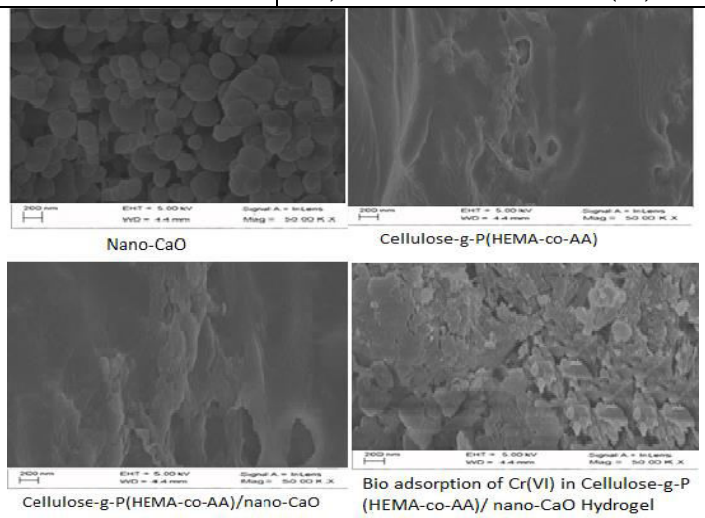

Fig.3. FESEM of (A)nano-CaO (B) Cellulose-g-P(HEMA-co-AA) (C) Cellulose-g-P(HEMA-co-AA) /nano-CaO TNG and (D) after biodegradation of Chitosan-g-P(HEMA-co-AA)/nano-CaO TNG

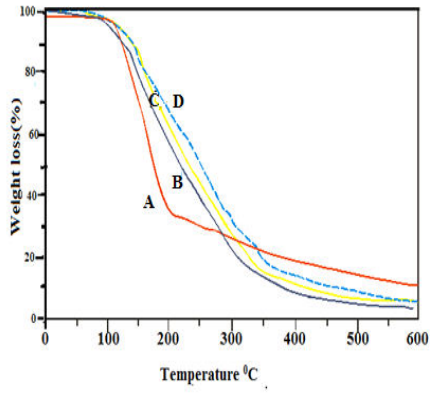

Fig.4. TGA thermograms of (A) nano-CaO (B) cellulose-g-P(HEMA-co-AA) (C) cellulose-g-P(HEMA-co-AA)/nano-CaO TNG and (D) cellulose-g-P(HEMA-co-AA)/nano-CaO TNG after Cr(VI) adsorption from aqueous systems.

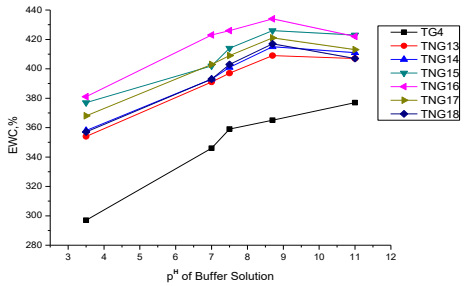

Fig.5. EWC study of Cellulose-g-P(HEMA-co-AA)(TG) and cellulose-g-P(HEMA-co-AA)/nano-CaO TNG (TNG13 to TNG18)

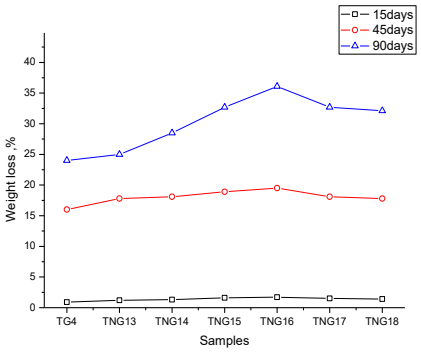

Fig.6. Biodegradation of Cellulose-g-P(HEMA-co-AA)(TG4) and Cellulose-g-P(HEMA-co-AA)/nano-CaO TNG (TNG13 to TNG18)

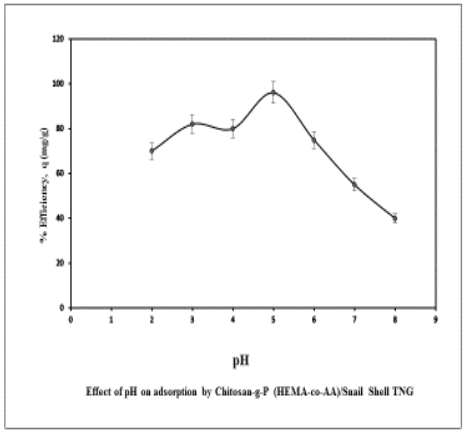

Fig.7: Effect of solution pH on Cr(VI) adsorption by the TNG

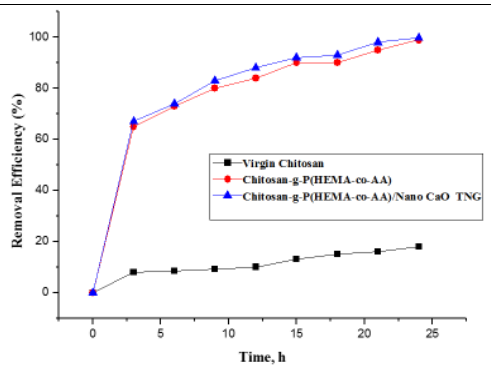

Fig.8: Effect of time on Cr(VI) adsorption by the TNG

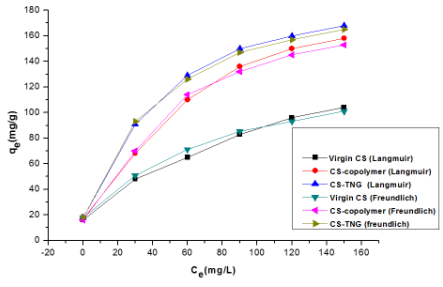

Fig.9: Adsorption isotherms (Langmuir and Freundlich models)

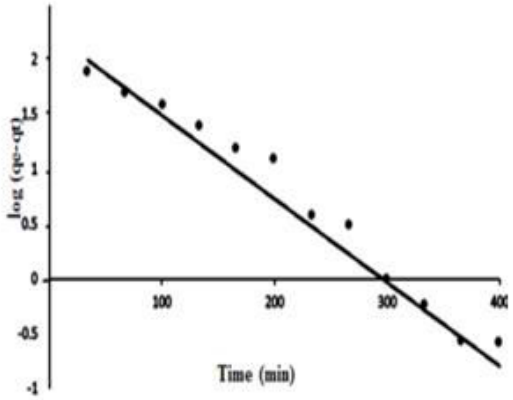

Fig-10.1: Pseudo first order kinetics for Chromium

Fig.10.1. Pseudo-first order kinetics for Choromium

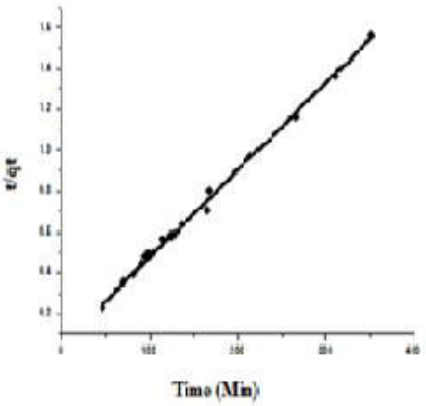

Fig-10.2: Pseudo second order kinetics for Chromium

Fig.10.1. Pseudo-Second order kinetics for Choromium

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RESEARCH ARTICLE

Perception of the Farmers towards the Quality of Service Provided By Co-Operative Banks

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ABSTRACT

The co-operative banks began in the west yet they have accepted significance in India in light of their immense system which is seldom resembled anywhere else in the world. This study is focused towards the perception of farmers towards the service quality offered by co-operative banks in this digital era. The main purpose of this study is to determine the service quality perceived by farmer's towards the Co-operative Banks and identify those dimensions that bring satisfaction to consumers. The research is descriptive in nature. The structured questionnaire was designed to collect data from the target respondents (Farmers). The population of the study includes the farmers who approach the Co-operative bank in Tamil Nadu for the business and transaction purpose. The researcher has distributed around 400 structured questionnaires and received back around 394 questionnaires. The sampling method adopted for the study was two stage randomized sampling. The pilot study was conducted with a sample of 40 respondents; Cronbach Alpha value has been identified more than 0.8.To meet this expectation of the customers' (farmers'), the Co - operative Bank officials has to focus on fulfilling the rural customers' needs in regard to the services offered by the co-operative banks. The bank has to give proper guidelines to its customers' (farmer) towards the procedures followed in availing the loans.

Keywords: Service Quality, Perception, Farmers and Co-operative Banks.

INTRODUCTION

The entire banking system in India is constrained by the Reserve Bank of India. In the banking system, there are 20 nationalized commercial banks, among them an enormous network of co-operative banks at state, district and block levels are available. The co-operative banks began in the west yet they have accepted significance in India in light of their immense system which is seldom resembled anywhere else in the world. Their function in rural financing keeps on being significant even today and their business in urban territories have likewise expanded in recent years, essentially because of the sharp increment in the quantity of primary co-operative banks.

Co-operative banks are a portion of the tremendous and amazing super structure of co-operative institutions which are occupied with the errands of rural and urban banking, agribusiness and agro processing including sugar products, dairy products, and production of fertilisers, promoting of farming supplies, and supply of buyer articles through retail outlets, etc. Co-operative banks stimulate employment opportunities and further earnings generation. The co-operative banks in Indian banking were begun with the objectives of prevention of convergence of monetary influence, accomplishing wide dispersal of responsibility for bountiful resources, dynamic contribution of individuals being developed projects, growth of the bountiful resources, insolvency of job loss and poverty, and dismissing the individuals from obligation to cash moneylenders. (Nagabhushanam, 2011) Information technology as e-banking assumes a critical job in offering enhanced services at lesser cost. A few inventive IT based services, for example, Automated Teller Machine (ATM), Internet banking, Smart Cards, Credit Cards, Mobile banking, Phone banking, Anywhere-Anytime banking have given number of helpful services to the client. So as the services quality progresses the likelihood of consumer loyalty raises.

This study is focused towards the perception of farmers towards the service quality offered by co-operative banks in this digital era. With the expanded rivalry among the private segment banks, this study would help in characterizing a system to accomplish the competitive edge and furthermore fulfilled clients (Farmers). What's more, thus service quality has been utilized to spot the banks in the intense market. Farmers' perceptions about the service quality elements like Tangibility, Security, Price and Product Variety, Responsiveness, Assurance, Empathy, Reliability and Accessibility and in the banking industry and the satisfaction level (the ultimate aim and result of every bank in general needs to satisfy their clients' (Farmers) service) towards the banks were also taken into account.

Aim of the Study

The main purpose of this study is to determine the service quality perceived by farmer's towards the Co-operative Banks and identify those dimensions that bring satisfaction to consumers. This will enable Co-operative Bankers to identify the most effective ways of closing service quality gaps and choose which gaps to focus on to bridge the gap. This will be achieved by measuring the farmer's expectations and perception on the various service quality dimensions. Hence evaluating the gap scores obtained between the farmer's expectations and perception of service experience will enable the researcher to identify strengths and weaknesses in service quality of Co-operative Banks and to identify gaps in delivering quality of service in order to ensure customer satisfaction.

Objective of the Study

- To find out the perception of farmers with regards to the quality of service provided by the Co - operative Banks.
- To examine the relation among the attributes of the service quality with reference to the farmer's expectation and perception.
- To provide suitable suggestion to co-operative banks in benefit of farmers.

Statement of the Problem

Parasuraman (1988) defined the service quality as the degree between customer's normative expectations for the service and their expectation from the service and their perceptions of the service performance. Recognition of service quality as a competitive weapon is relatively a recent phenomenon in the Indian Banking sector. The need of the hour in the Indian banking sector is to build up competitiveness through enhanced service quality, thus making the banks more market oriented and provide more loans to the customers as they want to improve their standard of living. Therefore the current problem for the Co-operative Banks in India is to determine the dimensionality of customer - perceived service quality.

Despite many fundamental banking reformations, still Co-operative banks are lagging behind on many fronts compared with commercial banks with wide range of capitalization, overseas network, modern management expertise, experience, technological advancement, etc. The Co-operative banks are relatively facing weakness in providing quality of service as well as quality product to their domestic customers (farmers).

Customers (farmers) can and do change their bank if their expectations are not met by their existing service provider. The customers (farmers) rarely communicate to the bank manager in advance what they have decided to do, especially when they decide to leave their existing bank for a competitor. To help the bank management to overcome the problem of customer defection, it becomes imperative for researchers to identify what is in the minds of customers (farmers) of bank services when they compare what should be offered and provided, and what is actually offered and provided.

Research Gap

After carefully analysing various research studies conducted so far, the researcher realise that many research works have been carried out in other banks (public and private sector banks) with main focus on the normal customers. The proposed study is an attempt to study about the various service quality dimensions of Co-operative banking services, with special interest shown on the Farmers. The credit facility is the ultimate determinant of Quality of Service and decides the motivated loyal customers (farmers) of a Co-operative bank.

REVIEW OF LITERATURE

Co-operative banks are profoundly established in local areas and communities. They are associated with local development and add to the sustainable development of their communities. The co-operative banks like numerous other financial service is confronting a quickly evolving market, new advances, financial vulnerabilities, furious rivalry and challenging clients and the changing atmosphere has introduced an extraordinary set of trials. Substantial and Intangible components would be an advantages, which make the employees of the bank to deliver the superb service for the bank's prosperity.

John & Thoomkuzhy (2018) has conducted an investigation on the service quality dimensions of Co-operative banks with special reference to Pathanamthitta Co-operative bank to examine the satisfaction level of the customers who are availing services from the bank. Their study was found to be vital because the sustainable development of individuals settled in the rural regions is the primary focus of governments' economic policy. There are numerous variables impacting their satisfaction level which is considered for the study. Based on the investigation of the study they inferred that the customers come under the low-salary class. Despite the fact that they are comfortable with the service rates, they are disappointed with the factor that the bank fails to update with information regarding new services.

Hennayake (2017) has concentrated on the effect of Service Quality on Customer Satisfaction of Public Sector Commercial Banks. Data was gathered with a sample size of 210 respondents. The hypotheses were tested utilizing

Co-relations and Regression analysis. Findings uncovered that the Human Related Factors of perceived service quality have a greater impact on consumer satisfaction while Reliability and Responsiveness are the most influential variables on consumer satisfaction.

The author Sreeja (2016) has conducted a research on service quality of co-operative banks with special reference to Thrissur District. SERVQUAL tool is used for this purpose. Reliability, Responsiveness, Assurance, Empathy and Tangibility were five dimensions considered for the study. Based on the analysis of service quality it is found that the expectation and the actual perception of customers are different, even more an enormous gap between perception and expectation. A huge quality gap existed in the variable assurance and least gap existed in tangibility and then concluded that the Co-operative banks must take care for improving service quality.

Yogeswaran (2015) conducted a study to customer perception towards services provided by public sector and private sector banks in Sivakasi Taluk only. He had selected 200 sample customers, 100 customers from each bank by adopting judgement sampling method for the study in order to ascertain the attitude of customers towards services. From the analysis it was found that the perceived quality of services provided by private sector bank (ICICI) is better than public sector bank (State Bank of India) in Sivakasi Taluk. It is evident that public sector banks have a strong presence in the market, but in recent times they are facing stiff competition from private sector banks in the range and quality of services offered.

Prasad & Prasad (2015) their study aims at assessing the service quality, that delivered by the banks in rural areas, using SERVQUAL model. The SERVQUAL model was used to assess and compare the service quality delivered by three major banks (SBH, DGB and HDFC) operating in rural areas of Kaimnagar district. Analysis of gap score reveals that the highest gap score in the dimension 'Responsiveness' in the case of HDFC (0.98) and State Bank of Hyderabad (0.96) indicates poor service quality and concluded that the overall service quality obtained shows that, although the customers are satisfied with the three banks, still proper attention is require to improve the service quality to retain the existing customers and to attract new customers.

Parasuraman *et al.* (1985) in their article focused on that the fulfilment of products quality and a service has become a significant concern of the 1980s. While marketers depict and estimate the quality of intangible products, quality in service is to a great extent unclear and un-investigated. The authors attempt to find remedy to this situation by reporting the experiences got in a broad exploratory examination of quality in four service organizations and by building up a model of service quality. Suggestions and proposals to animate future examination about service quality are presented.

MATERIAL AND METHOD

Research Methodology

The research is descriptive in nature. The primary as well as the secondary data was collected by the researcher. The structured questionnaire was designed to collect data from the target respondents (Farmers). The variables has been discussed furthermore that, the service quality of co-operative banks was determined by using the previous literature review of Parasuraman *et al.,* (1985). The researcher from the previous studies was able to consolidate the variables under three major dimensions like organization, employee & customer oriented dimensionalities. The variable like Tangibility, Security, Price and Product Variety comes under the Organizational oriented dimension. Likewise, Responsiveness, Assurance, Empathy, comes under the employee oriented dimension. The customer oriented dimension includes the variables like Reliability and Accessibility. The reason behind segregating the variables underneath the dimensions has helped the researcher to identify the drawbacks, which are reflected in analysis and also to provide very absolute suggestions related to the dimensionalities of service quality.

The geographic location identified for the research is Tamil Nadu. The population of the study includes the farmers who approach the Co-operative bank for the business and transaction purpose. The record related to the population of the farmers is not exactly available. The researcher hence considered the population to be infinite. With the help of De Morgan's sample size estimated table the researcher has confined the sampling for the research. From the De Morgan's table, the researcher has identified 381 samples with the confidence level of 95% and confidence interval of 5%. The researcher has distributed around 400 structured questionnaires and received back around 394 questionnaires. The remaining 6 questionnaire were found to be biased and unanswered. For convenience the questionnaire was designed in English as well regional language (Tamil). In certain cases the researcher has explained the questionnaire to the respondent in colloquial language to, where the respondents felt hard to understand the question.

The sampling method adopted for the study was two stage randomized sampling. In the first stage the number of districts was disintegrated. In the second stage randomized sampling was adopted to collect the data from respondents (farmers). There are 33 districts in Tamil Nadu, on an average 12 questionnaire were distributed to each district. On a whole the researcher was able to get back around 94 % of the filled in Questionnaires from the target samples. The pilot study was conducted with a sample of 40 respondents; Cronbach Alpha value has been identified more than 0.8. This clearly shows that questionnaire is valid and the researcher has proceeded with the research. The collected data was fed in the SPSS 20 software and the statistical tools like measures of central tendency (Mean), measures of dispersion (Standard Deviation), and correlation have been used to extract the research.

RESULTS AND DISCUSSION

Analysis & Interpretation

The measure of central tendency and dispersion has been used to identify the centre point as well as the variation which are prevailing in the service quality dimension, as opined by the respondents. Furthermore the gap has also been identified, to provide an in-depth understanding related to the variations in expectation & perception. Finally the inter-relationship between the expected and perceived service quality has been judged using Bi-variate correlation. The table and consolidation has been displayed below.

The respondents agree with the variable tangibility, security and price and product variety with the mean value of 3.31, 3.26, 3.06 and standard deviation of 0.637, 0.625 & 0.638 respectively whereas the perceived mean value for these variables are 1.77, 1.71 1.72 with a standard deviation of 0.76, 0.908 and 0.904 respectively. The gap difference value of (1.50), (1.54) & (1.32) for these variables clearly reveal that there is difference between expected and perceived value. The organisation oriented dimension depicts high for expected service quality with a mean value of 3.21 and with a standard deviation of 0.633 whereas their perceived quality has lower with a mean value of 1.73 and with a standard deviation of 0.869. It is evident from the gap difference that the expected value does not meet the perceived value is with a value of 1.48.

The respondents agree with the variable responsiveness, assurance and empathy with the mean value of 3.22, 3.25, 3.02 and standard deviation of 0.650, 0.620 & 0.710 respectively whereas the perceived mean value for these variables are 1.72, 1.70 1.70 with a standard deviation of 0.870, 0.910 and 0.960 respectively. The gap value (1.54), (1.55) & (1.34) of these variables clearly portrays the difference between expected and perceived value. The employee oriented dimension depicts high for expected service quality with a mean value of 3.19 and with a standard deviation of 0.645 whereas their perceived quality has lower with a mean value of 1.72 and with a standard deviation of 0.8889. Even the gap between the expected and perceived value is also high with a gap difference value of 1.47.

The respondents agree with the variable reliability and accessibility with the mean value of 3.26, 3.19 and standard deviation of 0.640 & 0.690 respectively whereas the perceived mean value for these variables is 1.80 & 1.74 with a

standard deviation of 0.900 and 0.940 respectively. The gap difference value of (1.46) & (1.46) for these variables clearly reveal that there is difference between expected and perceived value. The customer oriented dimension depicts high for expected service quality with a mean value of 3.20 and with a standard deviation of 0.649 whereas their perceived quality has lower with a mean value of 1.73 and with a standard deviation of 0.895. It is evident from the gap difference that the expected value does not meet the perceived value is with a value of 1.47.

Positive Correlation

- The independent variable expected Responsiveness has positive correlation with all the perceived dependent variables.
- The independent variable expected Assurance has positive correlation with the perceived dependent variables tangibility (0.109), responsiveness (0.146), and Price and Product Variety (0.77).
- The independent variable expected Empathy has positive correlation with the perceived dependent variables Responsiveness (0.153), accessibility (.079), and Price and Product Variety (0.107).
- The independent variable expected Accessibility, Security and Price and Product Variety has positive correlation with all the perceived dependent variables.

Negative correlation

- The independent variable expected reliability has negative correlation with the perceived dependent variables.

No Correlation

- The independent variable expected tangibility has no correlation with the perceived dependent variables.
- The independent variable expected Assurance has no correlation with the perceived dependent variables reliability, assurance, empathy, accessibility and security.
- The independent variable expected Empathy has no correlation with the perceived dependent variables tangibility, reliability, assurance, empathy and security.

Suggestion

The quality of the service provided by the Co - operative Bank is the main attribute for the current research. The researcher has given the hierarchy of service quality dimensionalities, which the co-operative bank has to implement in their regular service performance and delivery. The first and the foremost importance has to be given to tangibility (ie., the bank has to keep a keen interest in properly maintaining and managing the various materials associated with the service like the pamphlets, brochures and adequate ATM facilities) and accessibility (the bank has to reduce the complication in availing loans and maintaining a proper redressal grievance system). The next priority is given for the Price and Product Variety, Responsiveness, Security, Assurance and Empathy (the bank representatives should have to be compassionate and responsible (Sreeja, 2016) in addressing the various queries (similar to John & Thoomkuzhy, 2018 research) of the farmers as well as have keen knowledge on the subsidy banking procedures). Several awareness programs can also be conducted to the farmers regarding the updated banking service offered by co-operative banks. If all these above problems are addressed, then the bank is said to have sustainable development in the mere future

CONCLUSION

After LPG in 1991, the expectation of customers' related to all the sector has sustainably increased, this has made all the organizations to give more importance to provide quality service. This pre-dominantly has invaded the service sector also. The current research summarizes the quality of service provided by the co-operative banks located in Tamil Nadu. The requirement and expectation of the customers towards banking services are increasing day by day. To meet this expectation of the customers' (farmers'), the Co - operative Bank officials has to focus on fulfilling the rural customers' needs in regard to the services offered by the co-operative banks. The bank has to give more concern

towards the procedures followed in availing the loans and giving a proper guidance, information and explanation (in person) with regards to loan to its customers' (farmer). The above mentioned suggestions has to be given vital importance, so that it would enhance the sustainability and development of Co-operative banks, this in turn would pave the way for economic development of the entire geographic location.

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Table 1 Mean, Standard Deviation and Gap Analysis of on Service Quality

Dimensions	Expectation		Perception		GAP Difference
	Mean	Sd	Mean	Sd	
Tangibles (TAN)	3.31	0.637	1.77	0.796	1.54
Security (SEC)	3.26	0.625	1.71	0.908	1.55
Price and Product Variety (PPV)	3.06	0.638	1.72	0.904	1.34
Organisation Oriented Dimensions (A)	**3.21**	**0.633**	**1.73**	**0.869**	**1.48**
Responsiveness (RES)	3.22	0.650	1.72	0.870	1.50
Assurance (ASS)	3.25	0.620	1.70	0.910	1.54
Empathy (EMP)	3.02	0.710	1.70	0.960	1.32
Employee Oriented Dimensions (B)	**3.19**	**0.645**	**1.72**	**0.888**	**1.47**
Reliability (REL)	3.26	0.640	1.80	0.900	1.46
Accessibility (ACC)	3.19	0.690	1.74	0.940	1.46
Customer Oriented Dimensions (C)	**3.20**	**0.649**	**1.73**	**0.895**	**1.47**
Service Quality (A + B + C / 3)	**3.20**	**0.642**	**1.73**	**0.884**	**1.47**
** Primary Data*					

Table 2 Correlation between Expectations and Perception of Service Quality

Ho: There is no significant *correlation between the dimensions of expectations and perception of service quality*

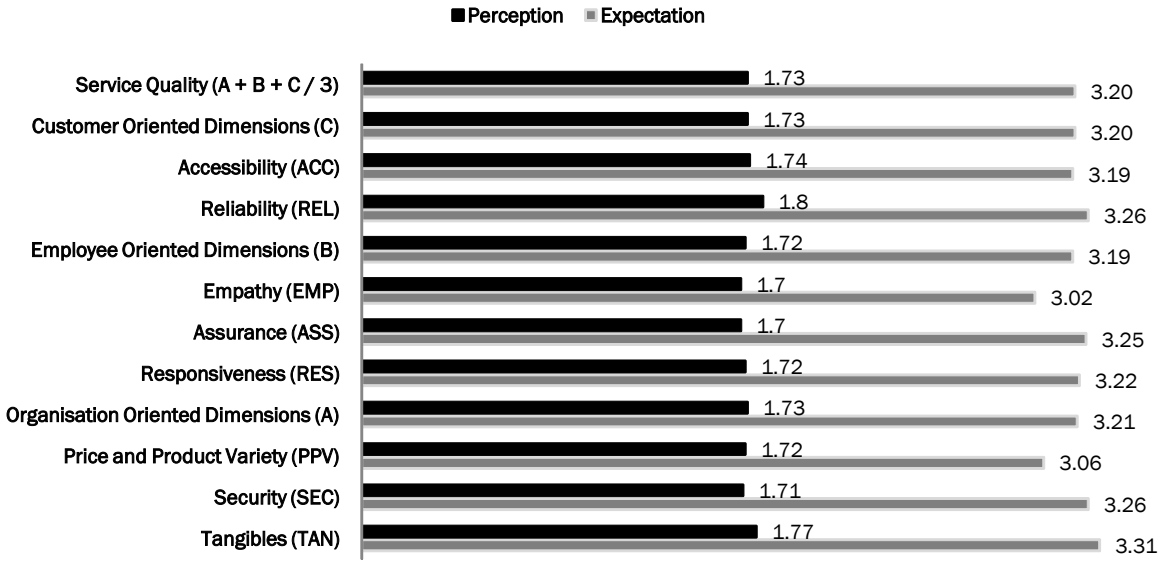
	Variables	Perception							
		TAN	**REL**	**RES**	**ASS**	**EMP**	**ACC**	**SEC**	**PPV**
Expectations	**TAN**	-.034	.006	.021	-.004	.026	.005	.003	.030
	REL	-.155**	-.187**	-.143**	-.154**	-.138**	-.172**	-.111**	-.152**
	RES	.168**	.188**	.214**	.170**	.166**	.184**	.199**	.173**
	ASS	.109**	.062	.146**	.065	.016	.050	.024	.077*
	EMP	.050	.024	.153**	.050	.021	.079*	.048	.107**
	ACC	762**	.893**	.830**	.911**	.772**	.885**	.794**	.871**
	SEC	.893**	.831**	.899**	.980**	.868**	.936**	.860**	.925**
	PPV	.830**	.899**	.823**	.881**	.853**	.898**	.863**	.930**

. Correlation is significant at the 0.01 level (2-tailed).

**. Correlation is significant at the 0.05 level (2-tailed).*

Pearson Correlation

Figure 1. Mean Comparison between Expected and Perceived Service Quality Dimensionalities



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RESEARCH ARTICLE

A Method for WSN Clustering Protocols using Game Theory Approach

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ABSTRACT

In wireless sensor network clustering plays an important role. The nodes get divided into clusters and then cluster head is elected. The elected CH (cluster head) is onus for the data assimilation. The cluster head plays a vital role in this topology so the selection of cluster heads has to be done with utmost care. Based on the concepts of game theory a model has been derived. Nash equilibrium is employed for that. If a cluster head and the sink node get disconnected then data replication model is adopted. Overall throughput of the network is still guarantee even if a cluster head fails. Wireless sensor network (WSN) consists of low size, power constrained nodes that sense the environment and communicate this information through wireless links. There are a number of research issues in WSN with energy efficiency being one of the prime issues for WSN applications. In clustering-based routing protocols, cluster head selection has significant effect on performance of the protocol, along with routing technique. Game theory as a mathematical notion, being able to analyze interactive decision situations, is applicable to a wide spectrum within WSN. It can assist in designing more efficient protocols.

Keywords: WSN, Clustering, Game Theory, Nash Equilibrium, Protocols.

INTRODUCTION

In a deployed wireless sensor network, there may be more than two thousand sensors. Those sensor nodes are used to monitor the environmental condition such as air quality, noise pollution, humidity, temperature, etc. The sensed data is then transferred to the base station. In general, there was an assumption that the sensor nodes are cooperative and share data with each other. But it's not true. The wireless sensor network is not like a traditional network. The wsn is limited to transmitting and receiving power. Some nodes pay attention to saving their energy those nodes will not participate in active communication. Such nodes are called selfish nodes. Even a single selfish node can bring down the throughput of the entire network to 30%.

The clustering of the wsn nodes is done worldwide. The following first process splits the network into clusters and elect a cluster head [CH]. The cluster head is responsible for data aggregation. There are many advantages in using cluster heads they are low energy, routing and scalability of the network. In general, the energy level of the cluster head will be higher than the nodes. This is because of faster communication between the member. By this method, a node with selfishness will get eradicated and it cannot be as a "head". Game theory is a concept in mathematics which deals with players in a strategy game. Here selfishness of a node is applied with game theory approach. Based on this method the cluster head will get elected.

Wireless Sensor Networks (WSNs) is a kind of networks consisting of numerous tiny sensor nodes which are capable of sensing, processing and communicating Owing to their low deployment cost, WSNs have gained extensive applications in recent years such as environmental monitoring, military monitoring, medical caring, endangered species tracking, disaster relieving, and so on .In general, most of the sensor nodes are powered by the battery, which means their energy supply is limited. Besides, the majority of the WSNs are deployed in the rugged environment and some of them are even out of human's reach. Therefore it is impossible or unpractical for them to be replenished When one or some of the sensor nodes lying in the crucial location exhaust their energy, the network partition occurs. It means the termination of the network lifespan. Since the purpose of WSNs is to acquire valid data as many as possible on a limited energy budget, it is vital to improve the energy efficiency.

LITERATURE REVIEW

In a tree based topology of wireless sensor network, the sensor node might fail due to lack of address configuration [1]. To overcome this limitation the author has proposed an algorithm know as address based routing. This scheme can be implemented over low-power IPv6 sensor network like vehicular network and so on. A super node is implemented which monitors the addressing issues and configure it automatically for multihop network. And also the super node will communicate with the next super node to find the optimal path. By this method the latency of the routing will get reduced. The analysis of the result shows the effective shortening of the routing latency. In a wireless sensor network, energy-saving optimization has become one of the hottest research areas in routing protocol design. This is because most wireless sensor nodes are equipped with non-rechargeable battery [2]. The author proposed a method for minimizing energy consumption and maximizing the network lifetime in a one-dimensional routing method. By using the optimistic routing theory a multihop decision method is employed to optimize the energy efficiency of a wireless network. the proposed method has significantly increased the performance of the network and also has saved a lot of energy in wsn routing.

A multi-hop routing scheme is needed for routing the data, this is because the intended sing node cannot be reached in a single hop routing[3]. By optimizing the routing path will significantly increase their performance. Usually, the sensors contain a small power source within it. The energy consumption routing has gained high attraction in the field of wireless sensor networks. The author has proposed add flooding based hierarchical protocol for this complex routing function. This method has been tested in various protocol family. By investigating the study the proposed algorithm has performed very well in large scale scenarios. A routing protocol is implemented in association with virtual coordinates. It is fabricated in a model composed of end nodes without routing [4]. The concept of the routing protocol is to transform a random structure of sink nodes. Visual form virtual circle and virtual nodes. The virtual circle registry of the greedy nodes which is the proposed strategy by using this method it can overhead the problems found in this routing scheme. The experimental results show that the proposed protocol has a higher delivery ratio and also less shortest path length and low energy consumption.

An opportunistic routing method is proposed here to increase the performance of duty-cycled wireless sensor networks eradicating the default broadcast nature [5]. The proposed method is totally contrasted with the existing routing techniques where the packets are transmitted in a predefined path. This routing protocol selects a set of

candidates as a potential forwarder to transmit the data. This will reduce the waiting time of sender nodes. But at the same time due to many candidates duplicate packet will get generated. This may affect the packet delivery ratio. To overcome these issues a priority-based metric system was implemented. By evaluating the performance in various small and large scale networks the proposed algorithm performed well by increasing the network lifetime and reducing the energy consumption along with time.

Proposed Game Theory Approach

Network model

Let us assume that there are n sensor nodes in a network. There are uniformly distributed within a range on the field it was also continuously monitored surrounding their environment. If your sink node is located far away from the base station then the data is delivered by the cluster heads. Suppose if a sink node is mobile which changes its position often. Then a set of rules should be followed.

- The nodes must be homogeneous and stationary after deployment
- The multiple nodes are pre located within the range.
- The nodes can adjust their transmitting and receiving power.
- Links will be in symmetric nature.

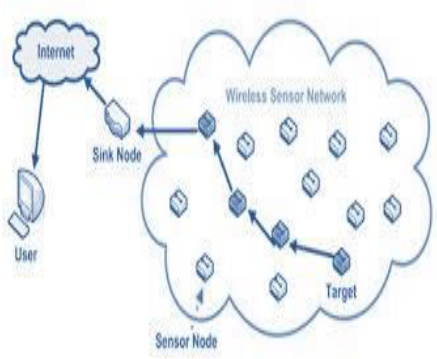

Fig 1. WSN Model

Energy model

Use node with similar energy. All the nodes will have the same energy model and also the same transmitting and receiving power along with free space. each sensor node will consume an amount of energy to transmit or to receive data. the energy consumed is directly proportional to the transmitting and receiving the power of the sensor node.

Game Theory Approach for CH

The cluster head takes much responsibility and uses high amount of energy for this. If the cluster head is selfish then the entire network throughput will go down to 50 percent. To overcome this issue Nash equilibrium what is a concept in game theory is applied to detect the exact cluster head for the cluster.

If Nash equilibrium has to be found for a game then the initial estimated value will be , say x_10, and $Z(x_1)$ unity-valued.

$x_1q+2 = (2 - \gamma q)x_1q + \gamma q Z\, x_1q$, q = 0, 1, 2,3,4 …,

where $0 < \gamma q <= 2$. The iterate at step q + 2 is taken as a weighted average of the updated point $Z(x_1q)$ and the present point x_1q. This merging of the algorithm under certain terms, explains formula. Algorithm will perform a static optimization of opponents in convergence to equilibrium.

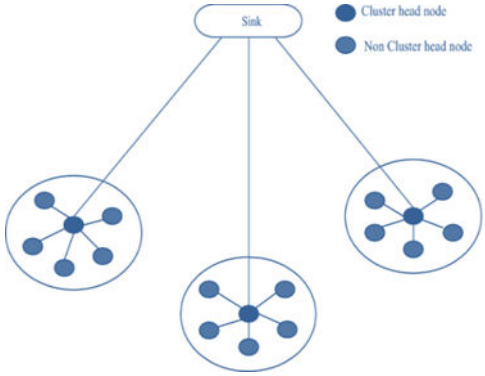

Fig 2. Theory Approach for CH

In the event that all adjustments are known to us, we can straightforwardly discover the Nash equilibrium utilizing the relaxation algorithm. Nonetheless ,in the event that we just approach one gamer result capacity and all gamers' previous activities, at that point at each stage in the constant cycle we pick the ideal reaction for that gamer, accepting that different gamers will participate as they had inthe past period. Thusly, convergence to the Nash standardized equilibrium will happen asq →∞. By considering adequately numerous emphases, it is our mean to decide the Nash equilibrium x1∗ with a predetermined accuracy. The following steps state the conditions of convergence for the relaxation algorithm. This condition may be restrictive but it can solve all types of games

In this algorithm focus the existing a unique normalized Nash equilibrium point if :

[1]. X_1 is a convex compact subset of Rm,

[2]. the Nikaido–Isoda function $\mathbf{\Phi : X_1 \times X_1 \rightarrow R}$ is a weakly convex-concave function and $\mathbf{\Phi(x_1, x_1) = 0 \text{ for } x_1 \in X_1}$,

[3]. the optimum response function $Z(x_1)$ is single-valued and continuous on X_1,

[4]. the residual term $rz(x_1, y_1)$ is uniformly continuous on X_1 with respect to z for all $x_1, y_1 \in X_1$,

[5]. the residual terms satisfy $\mathbf{ry_1(x_1, y_1) - \mu x_1(y_1, x_1) > \delta\, kx_1 - y_1k\ , x_1, y_1 \in X_1}$, where $\delta(0) = 0$ and δ is a increasing parameter**(i.e., δ(t2) >δ(t1) if t2 > t1),**

[6]. the relaxation parameters αs justisfy

a) $\gamma q > 0$,

b) $P\infty\ q=0\ \gamma\ q = \infty$,

c) $\gamma\ q \rightarrow 0$ **as** $q \rightarrow \infty$.

Notice that the convex set X_1 is able to represent coupled constraints and that the key condition may be satisfied in case of non-differentiable payoff function

EXPERIMENTAL RESULTS

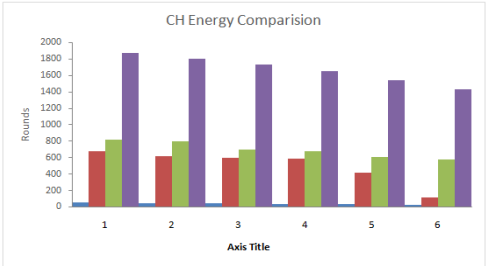

Fig. 3. CH Energy Comparison

Residual Energy	LEACH	PSO	GAME THEORY
50	675	812	1865
45	612	795	1800
40	594	693	1732
35	580	675	1653
30	413	603	1541
20	112	572	1427

Table 1 CH Energy Comparison

CONCLUSION

Clustering is an efficient approach in wsn. But the efficiency of the network depends on the cluster head. The proposed method uses a game theory approach to detect the cluster head. By using this approach the selfish node will get eliminated in being a cluster head. Moreover, the candidates of the cluster respond to the head in a timely manner. This method eradicates the problem created by data replication. The simulation results prove that the proposed game-theoretic approach performs well in various wsn environments.

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RESEARCH ARTICLE

Execution of Entropy Based Features for the Classification of Ictal and Pre-ictal Electroencephalogram Signals: A Comparative Study

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ABSTRACT

Our developed model is based on classification of ictal and pre-ictal Electroencephalogram (EEG) the biomedical signal of a fully or partially affected epileptic persons. Our research methodology is very much helpful for the analysis of epileptic abnormal EEG signals as differentiate to normal Electroencephalogram (EEG) signals. In this work, Six types of entropies (Approximate Entropy (AEn), Sample Entropy (SaEn), Spectral Entropies (SEn), Renyi's entropy (REn), and two numbers of Phase Entropies (PEnS1 and PEnS2)), are used in this approach for the feature extraction of the ictal and pre-ictal EEG signals. Detected EEG signals are separately classified using three types (Multi-Layer perceptron neural network (MLPNN), Radial basis function neural network (RBFNN), and Adaptive Neural Fuzzy Inference System (ANFIS)) of classifiers. The optimization algorithms like Map Reduce Quantum PSO (MRQPSO) are used for training and testing purposes of the classifiers. In the evaluation criteria, we have calculated the different statistical parameters such as Accuracy (ACC), Sensitivity (SEN) and Specificity (SPE) positive predictive value (PPV), negative predictive value (NPV), and Matthew's correlation coefficient (MCC). Performance analysis of the model can be estimated by the best-calculated values of the parameters. The best-calculated value of ACC 100% (MLPNN-MRQPSO-REn, RBFNN-MRQPSO-PEnS1, ANFIS-MRQPSO-AEn, ANFIS-MRQPSPO-REn) SEN is 100% (from MLPNN-MRQPSO-PEnS1, RBFNN-MRQPSO-REn, ANFIS-MRQPSO-REn), SPE 100% (MLPNN-MRQPSO-PEnS2, RBFNN-MRQPSO-SaEn, ANFIS-MRQPSO-PEnS2), maximum calculated value of PPV is 99.98% in (ANFIS-PEnS1-MRQPSO), NPV 98.66% (ANFIS-PEnS1-MRQPSO), MCC 99.95% in (RBFNN- MRQPSO-PEnS2) are yielded on the stated patient-specific EEG database. Comparison with other decomposition and classification methods, our stated methods provide better performance for the estimation of different statistical parameters, gives superior dimension to detect seizures in focal EEG signal.

Keywords: EEG Signals, seizure detection, Epilepsy, Entropy-based feature, classifiers.

INTRODUCTION

Epileptic condition detects and observes the disorder mental condition and function of the human being with the study of the irregular Electroencephalogram EEG signal flow [1]. As per the 2009 annual report of WHO near about 40 to 50 million people are affected with epileptic disorder across the whole world [2, 3]. EEG signals are recorded with the help of metallic electrodes from the human brain, used to analyzes and evaluate the condition of epilepsy [4–6]. Electrodes are placed with some specified areas of the brain these are, Frontal Lobe, Temporal Lobe, etc, details of the fixed positions are at [7]. One of the advanced analyses was mentioned by Babloyantz et al. [8] who used two non-linear parameters like Correlation Dimension (CD) and Largest Lyapunov Exponents (LLE) to study the nature of in sleeping stage EEG signal. Non-linear energetic techniques are based on the dimension of chaos utilized to different positions of biomedical signals [9, 10]. Diagnosis of epileptic EEG signals is the very fundamental application in bio-signal detection and classification area [11–13]. So many methods of classification are observed to detect Alzheimer's diseases [14]. A new approach mentioned as attention-deficit/ hyperactivity disorder (ADHD) is utilized for EEG signal diagnosis [15]. The diagnosis of autism and autistic spectrum disorders are classified as [16, 17]. Diagnosis of both normal as well as alcoholic EEG signals is compared in [18].

Wavelet transform and wavelet-chaos methodologies have been studied to detect seizures and study the disorder conditions of epileptic EEG signals [19, 20]. The multivariate empirical mode decomposition [MEMD] method is used to study the EEG signal to detect the Anesthesia conditions [21, 22]. Study of Epileptic condition is the basic method to analyze the neurological problem acts on the normal life of human being, that may meet of higher risk of death [23]. Guo et al. [24] proposed on seizure detection and transformation method related on approximate entropy for feature extraction. Some of the ideal parameters (Entropies) are used for the extraction of features and detection of seizures in EEG signals [25,26]. In this research work, we have implemented an composite methodology for the classification of ictal and pre-ictal states of observed Electroencephalogram signals. Six entropy features named as Approximate Entropy (AEn), Sample Entropy (SaEn) Phase Entropies (PEnS1 and PEnS2), Spectral Entropies (SEn), and Renyi's entropy (REn)) are used for feature extraction from the collected EEG signals. Three ideal classifiers such as Multi-Layer perceptron neural network (MLPNN), Radial basis function neural network (RBFNN), and Adaptive Neural Fuzzy Inference System (ANFIS) are used in this proposed model. Present research correlates to the epileptic disease basically used to classify between ictal (seizure period) and pre-ictal (seizure-free) EEG signals. The paper systemizes with the following modules: Module 2 represents the description of materials, module 3 describes the feature extractor and classifiers that were used. Module 4 discussed the evaluation criteria using the different statistical parameters to evaluate the performance of the classifiers. Module 5 represents the results and their discussion and comparative study with the reviewed literature-related results obtained. The conclusion section is discussed in module 6.

MATERIALS

Time series artifact-free Electroencephalogram databases are taken from the University of Bonn (Dept. of Epileptology) [27]. Three types of single-channel EEG signals such as normal, ictal, and pre-ictal with a time duration of 23.6 sec are collected. Bonn University database consists of 200 data sets where each one contains with 100 cases. In this database, seizure-free pre-ictal EEG signals are collected from five epileptic patients. 100 numbers of Normal EEG data are collected from five healthy volunteers in awake state (eye open and closed). The sample of the ictal database is taken from five epilepsy patients. Electroencephalogram signals are collected from a 128 channel amplifier system. The sample rate of the signals is 173.61 Hz, and are separated with 12-bit A/D resolution. Extracted data are filtered with the help of a band-pass filter arranged with 0.5340 Hz ~12 dB/octave. As an example, both Pre-ictal and ictal EEG signals are shown in Fig.1. Epileptic EEG signals are collected from electrodes that are placed in a specified zone [28].

METHODS

Processing (feature extraction) of the signals

Entropy-based features:

According to the concept of biomedical signal, processing Entropies are used for feature extraction and detection of epilepsy in EEG signal [29]. Nonlinear parameters are used to explain the comparison of the EEG signals in the ictal and pre-ictal nature.

Approximate Entropy (AEn).

Approximate entropy (AEn) is a complicated estimation of the time series function [30]. It is extensively utilized in many fields for EEG epileptic activity of seizure detection, [31], background activity of Alzheimer's disease patients [32], Linear, nonlinear, normal, and CAD-affected heart rate signals analysis are classified in [33], etc. A leading probability of high and low regularity produces lower and higher AEn values respectively. Approximate Entropy AEn, which is suggested by Pincus in [34], is scale and model liberated. Analyse of hormone fluctuation can be analyzed by an approximate entropy algorithm [35]. In our work, the method is given by Pincus et al. used for the detection of AEn from the data set. As per the above said method a time series expression x(n), n = 1,2...., N is considered. The length of the pattern is e which separates out the pattern from the intersection is derived from the equation x(n). Approximate Entropy AEn is given by [30].

$$AEn(e,r,N) = \frac{1}{(N-e+1)}\sum_{i-1}^{N-e+1} log C_i^e\ (r) - \frac{1}{(N-e)}\sum_{i-1}^{N-e} log C_i^{e+1}\ (r) \quad (1)$$

Index r is a stable specification that puts the permissive of the differentiation, $C_i^e(r)$ is the reciprocity integral. The reciprocity integral is plotted logarithmic-ally with respect to log(r).

$$C_i^e(r) = \frac{1}{(N-e+1)}\ N_i^r \qquad i = 1,2,\ldots\ldots\ldots\ldots N-e+1 \quad (2)$$

Here N_i^r computes the separation between vectors X(i) and X(j), whose value is less than the tolerance value r. Smaller values of AEn are more effective for self-similarity or effective regularity that represents the signal. If the values of the parameter 'r' is less, then the probability of estimation becomes poor and is more sensitive to noise [18]. In this proposed model, the value of r is selected as r = 0.2 times the standard deviation of the data, and the embedded dimension e is set as two [30].

Sample Entropy (SaEn)

Sample Entropy (SaEn), proposed by Richman and Moorman [36], which is based on negative natural logarithm used to estimate the conditional probability that maintains to match the length (point to point) of pattern e within a tolerance value r also match to attain the next point[37]. It can also estimate the data connectivity like AEn. However, SaEn independent of the recorded length and displays related constancy under the scenario where AEn does not [36]. Like AEn, larger values of SaEn related to more amounts of data irregularity and vice versa. Tolerance r is changed till the variation of point for the calculation of SaEn is carried out, estimation of template matched is stored in counters A(k) and B(k) for the variation of length k up to e. The Value of Entropy SaEn is represented by the following formula (3):

$$SEn(k,r,N) = \ln\left(\frac{A(K)}{B(K-1)}\right) \quad (3)$$

Here N is the length and k is the embedded dimension of the input series. The value of K is calculated using False Nearest Neighbor (FNN). In our work, the value of k is taken as 2 [38].

Phase Entropies (PEnS1 and PEnS2)

Higher-Order Spectra (HOS) is defined for both discrete and random processes of the signals [39]. Here two-phase entropies are calculated from the complex-valued function and product of three Fourier coefficients, which are

defined in Eq (4). HOS is correlated with the Fourier Transforms (FT) and with the method of non-linear signal processing. The function of this network consists of the higher-order moments (m3,m4….) and the cumulants (C1, C2).

$B(f_1,f_1) = E\,[A(f_1)A(f_2)A*(f_1 + f_2)]$ (4)

In equation (4), A(f) is the Fourier Transforms of the EEG signal a(nT). Nyquist frequency f can be normalized within the limits 0 and 1. Mentioned phase entropies (PEnS1 and PEnS2) are very similar to spectral entropy (SEn). The equations (5) and (6) are representing the two entropies (PEnS1 and PEnS2) [40].

Phase Entropy 1: $PEnS1 = -\sum_k P_k \, log P_k$ (5)

Where $P_K = \frac{|B(f_1,\ f_2)|}{\sum \Omega |B(f_1,\ f_2)|}$

Phase Entropy 2: $PEnS2 = -\sum_i q_i \, log i$ (6)

Where $q_i = \frac{|B(f_1,\ f_2)|^2}{\sum \Omega |B(f_1,\ f_2)|^2}$

Phase entropies and probability distribution function (pk and qi) are calculated from probability estimation. These estimations are focused on L^1 and L^2 norms of the square of the magnitude of the signal bi-spectrum (f1 and f2) calculated from the Ω region. Each norm is similar to the probability distribution function. As mentioned in equations (5) and (6) p_k and q_i are very similar to the probability distribution functions and Ω represents the non-redundant area inside the bi-spectrum.

Spectral Entropies (SEn)

The power spectrum of the signal is used to estimate the continuity of the time series in Spectral entropy (SEn). In the power spectrum amplitude components are utilized to calculate the probability in entropy. Spectral entropy (SEn) [41, 42] is estimated employing the normalized Shannon entropy that calibrates the spectral convolution of the time series. The power level of frequency elements of the signal that are calculated by Fourier transform is denoted by Pf. normalization of the power level is executed by calculating the gross power as ($\sum P_f$). Power level related to each frequency component is expressed as:

$p_f = \frac{P_f}{\sum P_f}$ (7)

Multiplication of power level of each frequency component with the logarithm of inverse power level computed the Spectral Entropies (SEn) using the following formula [43] as:

$SEn = \sum_f p_f \log(\frac{1}{p_f})$ (8)

Renyi's entropy (REn)

Renyi's entropy is used to measure the spectral complexity of time series explained detail in [43, 44, and 45]:

$REn(\alpha) = \frac{1}{1-\alpha} \log(\sum_f p_f^{\alpha})$ $\alpha>0, \alpha\neq1$ (9)

Renyi's entropy equivalent to $\alpha = 2$ is known as Renyi's quadratic entropy, defined as follows [43, 45]:

$REn(2) = -\log(\sum_f p_f^2)$ (10)

In our work, we have used (10) to calculate the REn. Both high entropy data (broad, flat probability distribution) and low entropy data (narrow, peaked distribution) are expressed in [43].

Classifiers

In our work, we have used three classifiers namely Multi-Layer perceptron neural network (MLPNN), Radial basis function neural network (RBFNN), and Adaptive Neuro-fuzzy inference System (ANFIS) which are briefly explained as.

MLPNN

Multi-Layer perceptron (MLP) is a three-layer feed-forward artificial neural network. Nodes of Each hidden layer are known as the neurons which can execute a nonlinear activation function. Now a days the most ideal methodology used for the smooth operation of nonlinear activation functions is Multilayer Perceptron Neural Network (MLPNN) [46]. In our proposed methodology, MLPNN Network has trained and test with the Optimization Algorithm (The MRQPSO Algorithm).

RBFNN

The RBF network is a feed-forward network with one hidden layer. The RBF network usually trains by a supervised training algorithm. The behavior of radial basis function used as hidden units in neural networks is more adoptive to use in the non-stationary data. The basic formula for the RBF network [47] can be presented in equation (11), where Gaussian function is used as the basis function.

$$y(x) = \sum_{i=1}^{M} w_i \, e^{\frac{(\|x-c_i\|)^2}{2\sigma^2}} \quad (11)$$

Where x is the input, y(x) is the output, c_i represents the center, σ represents the width, and Mdenotes number of basis function, similarly w_i denotes weights.

Adaptive Neural Fuzzy Inference System (ANFIS)

ANFIS network was designed by Jang in [48] established on the structure of an adaptive neural network. Takagi–Sugeno model based on fuzzy inference system [49]. In ANFIS, the neuro-fuzzy network is designed in an adaptive nature that can tune the parameters of a fuzzy inference system. Due to modification access of the ANFIS network, it can be used to classify the linear and non-linear EEG signals very effectively. Fuzzy layers are used to trap the random nature of the EEG signals. The study of the Takagi–Sugeno model depends on the ANFIS network shows that there is no restriction on the node functions of the auto-adjusted network except the piece-wise distinguishable. No restriction also on the designed network except it would be feed-forward type. Due to the above features, the adaptive and composite of ANFIS model in case of stationary, non-stationary signal like EEG.

Evaluation criteria

Method of K-fold cross-validation is used to calculate the test and observational performance of the classifiers (MLPNN, RBFNN, ANFIS), etc. In this evaluation criteria10-fold cross-validation method is used, accessible data are separated into 10 subsets [50]. Initially, 9 subsets are used to train the network, and the rest is used to test the network. The validation of the Multi-Layer perceptron neural network (MLPNN), Radial basis function neural network (RBFNN), and ANFIS classifiers are evaluated using sensitivity (SEN), specificity (SPE), accuracy (ACC), positive predictive value (PPV), negative predictive value (NPV) and Matthew's correlation coefficient (MCC). Decomposed parameter TP (true positive) shows the total number of ictal signals recognized as ictal EEG signals. Parameter TN (true negative) is the number of non-ictal EEG signals that are recognized same as non-ictal EEG signals. Parameter FP (false positive) is the number of non-ictal EEG signals identified as ictal EEG signals and Parameter FN (false negative) is the total number of ictal EEG signals recognized as non-ictal EEG signals.The mathematical expressions of the performance measure parameters (TN,TP,FN,FP) are in [51, 52]. The outputs are calculated in terms of different parameters as sensitivity (SEN), specificity (SPE), Accuracy (ACC), positive predictive value (PPV), negative predictive value (NPV), and Matthew's correlation coefficient (MCC). The evaluated parameters are classified by the expressions represented in equations (12-17).

$$\text{SEN (\%)} = \frac{\mathbf{TP}}{\mathbf{TP+FN}} \times \mathbf{100} \quad (12)$$

$$\text{SPE (\%)} = \frac{\mathbf{TN}}{\mathbf{TN+FP}} \times 100 \quad (13)$$

$$\text{ACC (\%)} = \frac{\mathbf{TN+TP}}{\mathbf{TN+TP+FN+FP}} \times 100 \quad (14)$$

$$\text{PPV (\%)} = \frac{\mathbf{TP}}{\mathbf{TP+FP}} \times 100 \quad (15)$$

$$\text{NPV (\%)} = \frac{\mathbf{TN}}{\mathbf{TN+FN}} \times 100 \quad (16)$$

$$\text{MCC (\%)} = \frac{\mathbf{TP \times TN - FN \times FP}}{\mathbf{T1 \times T2}} \times 100 \quad (17)$$

Where $\mathbf{T1} = \sqrt{(\mathbf{TP+FN})(\mathbf{TP+FP})}$ And
$\mathbf{T2} = \sqrt{(\mathbf{TN+FN})(\mathbf{TN+FP})}$

Epileptic and non-epileptic signals are estimated using the Matlab version of R2017a.

Optimization Algorithm (The MRQPSO Algorithm)

The particle swarm optimization (PSO) [53] is a simple and effective evolutionary algorithm. Focusing on the shortcoming of basic PSO, Sun et al. proposed a modified algorithm named quantum-behaved particle swarm optimization (QPSO) in 2004 [54]. The QPSO algorithm puts the search space inside quantum space to let the particle move to any location with a different probability. Through this strategy, the premature phenomenon could be solved to a certain degree. the landscape that is the randomly moving particles of the QPSO miss the narrow area where the global optimum present. To solve the Arises complex problems in QPSO, it is replaced by the Map-Reduce model named MRQPSO [55]. Detail operation of MRQPSO can be explained as mentioned in Algorithm 1, and the flowchart of this operation is shown in Figure 2. Algorithm 1 shows the pseudo-code of the map function of the used MRQPSO. For $(0 < i < n)$; and obtained sub-spaces are $m1 * m2 * \cdots * mn$ **[56].** The pbest is the position of particle with best value and $gbest$ is the position of solution with global best value. Both the pbest and gbest values are updated continuously with algorithm 2 **[55].**

Algorithm 1: The Framework of MRQPSO.
Step 1. Divide feasible space into several subspaces;
Step 2. Construct Mapper which performs QPSO on one subspace and outputs the obtained optimal solution on this subspace;
Step 3. Construct Reducer which selects the best optimal solution on different subspace from mapper; Step 4. Output the best optimal solution and its functional value **[55].**

Algorithm 2: MRQPSO map

```
function mapper (key, value)
{
initialize the positions of all particles
evaluate the function values of positions then select the pbest and gbest
// update the particle
while the termination condition is not met
{
calculate the mbest and α
for each particle
 {
update the pbest and gbest
for each dimension {
update position
```

```
 }
}
 calculation + 1
 } emit a message (ID of gbest, string of gbest and fitness)
}
```

MRQPSO Reduce Function

As mentioned in algorithm 2, the reducer of MRQPSO is used to select the minimum value from all sub-spaces. The mappers produced and transported the immediate key/value pairs which are received by the reducer after completion of all mappers function. At the reduce phase, all *g*best and corresponding fitness values of blocks are compared with each other. The minimum value of them is selected and finally, we get the output.

EXPERIMENTAL RESULTS AND DISCUSSION

Table 1. Shows the experimental results of some specified statistical parameters of the proposed methods. The estimated sensitivity is 100% of the (MLPNN-MRQPSO-PEnS1, RBFNN-MRQPSO-REn, ANFIS-MRQPSO-REn) methods, Specificity is 100% of the (MLPNN-MRQPSO-PEnS2, RBFNN-MRQPSO-SaEn, ANFIS-MRQPSO-PEnS2) methods, ACC is 100% from (MLPNN-MRQPSO-REn, RBFNN-MRQPSO-PEnS1, ANFIS-MRQPSO-AEn, ANFIS-MRQPSPO-REn) methods. The maximum calculated value of Positive Predictive Value is 99.98% of (ANFIS+PEnS1) method, Negative Predictive Value is calculated as 98.66% from (ANFIS+PEnS1) method, MCC is calculated as 99.95% (RBFNN+PEnS2). Table 2 represents the differentiation study of accuracy (between the proposed method and existing method) calculated from three classifiers with six different types of entropies. An estimated comparative study of the sensitivity and specificity of the proposed method with the existing methods is discussed in table 3.

Estimated accuracies from [57-67], [70], [71] and [73-81] are varies from 85.9% to 99.6% whereas [82] and [93] performs 100% accuracy. The experimental result of our proposed method shows 100% of accuracy with the combinations of decomposers and classifiers as (MLPNN-MRQPSO-REn, RBFNN-MRQPSO-PEnS1, ANFIS-MRQPSO-AEn, and ANFIS-MRQPSPO-REn). Calculated sensitivities of [82] to [93] varies from 86.20% to 99.21%. Results from our proposed method show 100% of sensitivity in the methods (MLPNN-MRQPSO-PEnS1, RBFNN-MRQPSO-REn, and ANFIS-MRQPSO-REn). Calculated specificity of [82-84] and [86-93] varies from 99.12% to 99.55%, [85] has specificity of 100%. Our proposed method performs 100% of specificity in the (MLPNN-MRQPSO-PEnS2, RBFNN-MRQPSO-SaEn, ANFIS-MRQPSO-PEnS2) methods. Figure 4 to 6 shows the Stock chart diagram of estimated SEN, SPE, ACC, PPV, NPV, and MCC of the three different specified classifiers. Fig 7. Shows the ROC Curve of the proposed models ANFIS, RBFNN, and MLPNN Classifier.

CONCLUSION

These experimental outcomes give an ideal approach for feature extractions and classifications of various seizure activities present in the partially affected epileptic patient. Six types of features such as AEn, SaEn, PEnS1, PEnS2, SEn, and REn are used on entropy-based feature extraction to characterize the behavior of the ictal and pre-ictal EEG signals. Three numbers (MLPNN, RBFNN, and ANFIS) of classifiers are employed for the EEG (both ictal and pre-ictal) signal classification. Maximum sensitivity is 100% from (MLPNN-MRQPSO-PEnS1, RBFNN-MRQPSO-REn, ANFIS-MRQPSO-REn) methods, Specificity is 100% from (MLPNN-MRQPSO-PEnS2, RBFNN-MRQPSO-SaEn, ANFIS-PEnS2) methods, ACC is 100% from (MLPNN-MRQPSO-REn, RBFNN-MRQPSO-PEnS1, ANFIS-MRQPSO-AEn, ANFIS-MRQSPO-REn) composite methods experimentally perform better result as compared to the existing work. The bar chart diagram and ROC curve representation in our proposed work give better performance. Estimated values are achieved from the partially affected epileptic patients which show its importance in clinical practice.

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Table 1. Calculated statistical parameters of the proposed method with different classifiers. The bolded values are the best-weighted performances by using the proposed methods.

Classifies	Optimization Algorithm	Entropies	SEN (%)	SPE (%)	ACC (%)	PPV	NPV	MCC
MLPNN	MRQPSO	AEn	98.42	92.84	98.26	97.4	92.43	97.26
		SaEn	96.33	97.28	98.61	99.33	97.65	98.43
		PEnS1	**100**	98.65	99.45	98.28	96.65	99.45
		PEnS2	99.26	**100**	99	97.26	96.16	96.93
		SEn	98.34	97.97	94.34	97.65	98.79	93.34
		REn	99.45	94.59	**100**	98.45	94.28	97.37
RBFNN	MRQPSO	AEn	94.56	93.84	97.26	99.04	94.43	98.46
		SaEn	96.33	**100**	98.42	95.33	98.65	98.61
		PEnS1	99.26	98.62	**100**	99.26	98.14	97.22
		PEnS2	98.26	96.34	99.11	98.29	97.16	99.95
		SEn	97.19	99.79	96.62	97.19	91.79	94.34
		REn	**100**	96.91	98.26	93.45	96.45	95.37
ANFIS	MRQPSO	AEn	97.24	91.84	**100**	92.43	94.82	98.26
		SaEn	99.33	98.46	98.61	95.33	96.65	99.61
		PEnS1	99.42	99.95	100	99.98	98.66	98.42
		PEnS2	98.32	**100**	99.45	95.26	96.79	96.93
		SEn	97.89	98.79	99.34	97.19	96.18	97.34
		REn	**100**	94.29	**100**	94.45	94.28	94.37

Table 2. Comparison of measured accuracy using the proposed method with existing methods having different classifier.

Reference	**Features/method Analysis/classification**	**Accuracy (%)**
[57]	Wavelet features and approximate entropy Neural networks	94 .00
[58]	Dual-tree, complex wavelets+inverse Gaussian SVM	96 .28
[59]	DWT,ANN	96.67
[60]	WT SVM	95.33
[61]	RWE ANN	95.20
[62]	DWT Based EA NNE	98.78
[63]	Non-linear preprocessing filter-diagnostic neural network	97.2
[64]	Time and frequency domain features – Recurrent neural network	99.6
[65]	Entropy Measures – ANFIS	92.2
[66]	Discrete wavelet transform – Adaptive neural fuzzy network	85.9
[67]	Discrete wavelet transform – Mixture expert model	95
[68]	Fast Fourier Transform – Decision tree	98.7
[69]	ApEn-Elman Network	100
[70]	Time-frequency methods – ANN	97.7
[71]	ApEn on DWT coefficients and classifier	96

[72]	DWT and PCA, ICA, LDA and SVM	98.75(PCA), 9.5(ICA), 100(LDA)
[73]	Lyapunov exponents – Recurrent neural networks	96.7
[74]	Mixed-band feature space – Back-propagation Network	96.7
[75]	Mixed-band feature space –Spiking Neural Networks	92.5
[76]	Mixed-band feature space –Principal component analysis-enhanced cosine radial basis function neural network classifier	96.6
[77]	Mixed-band feature space – Multi-Spiking Neural Network	90.7-94.8
[78]	Bi-spectrum entropies and bi-spectrum magnitude –Gaussian mixture model	93.1
[79]	Non-linear parameters – Gaussian mixture model	95
[80]	Four local maxima and four local minima values using Burg's method – SVM	93.3
[81]	Recurrence quantification analysis features – SVM	95.6
PROPOSED METHOD	MLPNN-MRQPSO-REn	**100**
	RBFNN-MRQPSO-PEnS1	**100**
	ANFIS-MRQPSO-AEn	**100**
	ANFIS-MRQPSPO-REn	**100**

Table 3. Comparison analysis of sensitivity and specificity of the proposed method with existing methods.

Reference	Methods	Sensitivity (%)	Specificity (%)
[82]	Stock-well transform and boosting algorithm	94.26	96.34
[83]	Fuzzy rule based system	86.90	97.80
[84]	WT and SVM Seizure detection	94.46	95.26
[85]	Wavelet transform, phase space reconstruction, Euclidean distance based on NEWFM	96.33	100
[86]	Support Vector Machine	92.4	98.6
[87]	RWE with ANN	98.17	92.12
[88]	Mixture of Expert	95	94
[89]	Fractional linear prediction, SVM	96	95
[90]	TQWT, Kraskov entropy and LS-SVM	97	99
[91]	WPT, Standard deviation, entropy and SVM	99.21	99.34
[92]	DTCWT, energy, standard deviation, entropy and General regression neural network	98.32	99.55
[93]	EMD and LS-SVM	97.68	98.07
PROPOSED METHOD	MLPNN-MRQPSO-PEnS1	**100**	98.65
	MLPNN-MUR-MRQPSO-PEnS2	99.26	**100**
	RBFNN-MRQPSO-REn	**100**	96.91
	RBFNN-MRQPSO-SaEn	96.33	100
	ANFIS-MRQPSO-REn	**100**	94.29
	ANFIS-MRQPSO-PEnS2	98.32	**100**

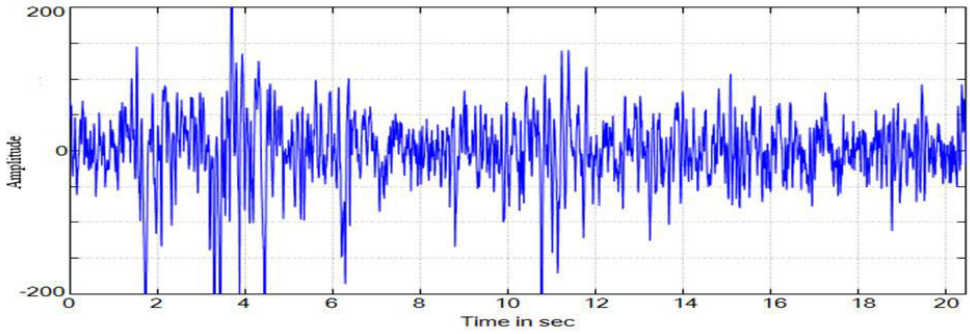

Fig. 1. (a) Ictal EEG Signal

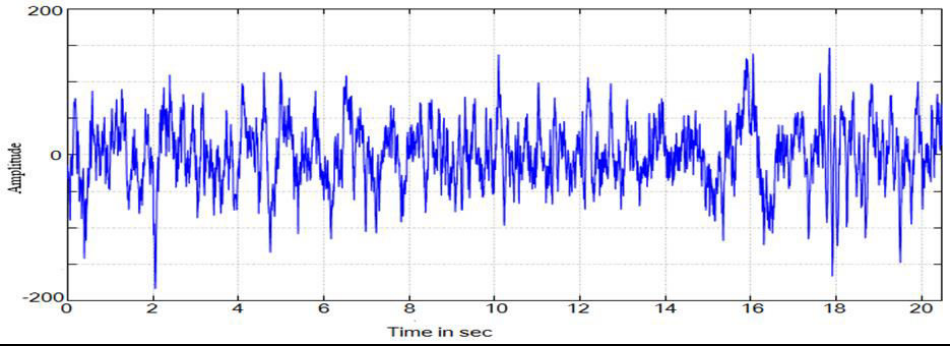

Fig. 1. (b) pre-ictal EEG Signal.

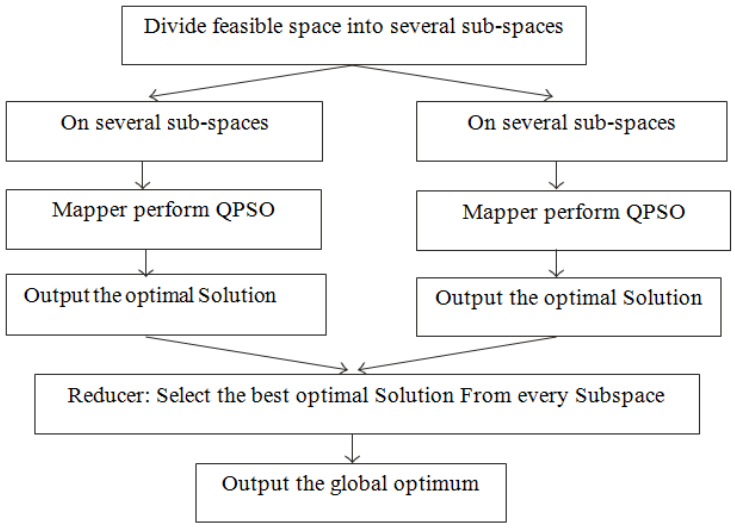

Fig. 2: Flowchart of MRQPSO [55]

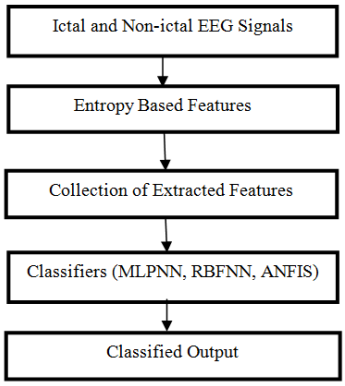

Fig. 3. Block diagram Proposed model

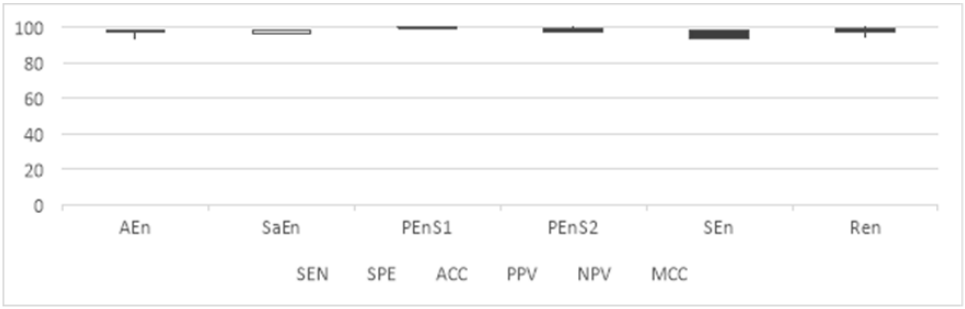

Fig. 4. Stock chart diagram of estimated SEN, SPE, ACC, PPV, NPV, MCC of the proposed method (MLPNN+ Entropies+ MRQPSO).

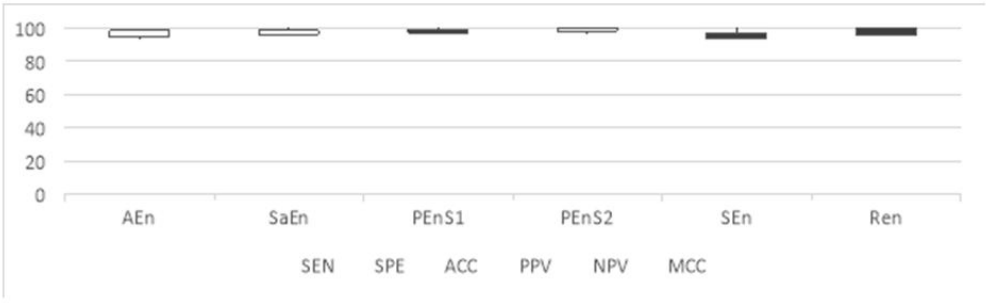

Fig. 5. Stock chart diagram of estimated SEN, SPE, ACC, PPV, NPV, MCC of the proposed method (RBFNN+ Entropies+ MRQPSO).

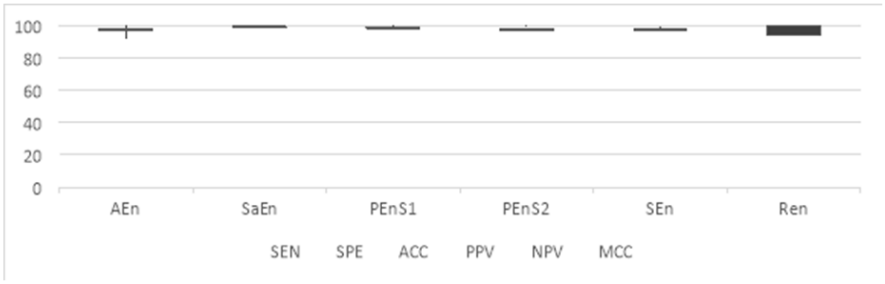

Fig. 6. Stock chart diagram of estimated SEN, SPE, ACC, PPV, NPV, MCC of the proposed method (ANFIS+ Entropies+ MRQPSO).

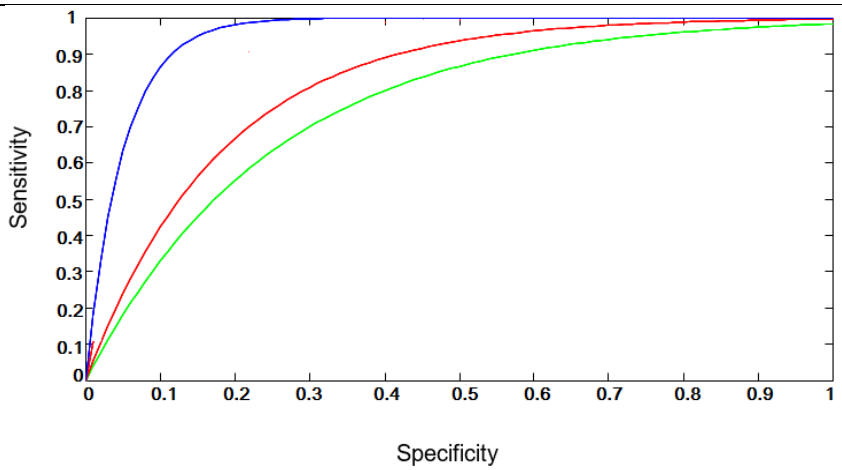

Fig. 7. ROC Curve of the proposed models (1)blue colour(--------) curve for ANFIS classifier (2) Red color (--------) curve for RBFNN classifier (C) Green color(--------) curve for MLPNN Classifier.

RESEARCH ARTICLE

Measuring and Maintaining the Data for frequency of Electrical Power Grid through AC Mains

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ABSTRACT

The paper presents a good economical method to measure electrical frequency of the single-phase power supply. Overcoming the drawbacks of the traditional frequency measuring devices and methods, a more reliable measuring device is designed using Arduino which use Atmega328 microcontroller which would be beneficial to farmers who use non-conventional energy sources for agriculture purpose, to check the electrical frequency of their system, so as to save their IM in low frequency conditions to avoid saturation. Arduino Uno is considered as it has good resolution. This study also provides the information about the traditional and normally used methods for frequency measurement and the pros and cons associated with it. The prototype will display and record the readings taken which will be useful for future analysis of the system. Algorithm implemented in the system is made so as to provide better computation speed and the margin of error is minimum. The measuring device is protected from disturbances happening in the input side whose frequency is to be measured with the help of an optocoupler, thus providing a smooth functioning.

Keywords: Measurement of electrical frequency, economical method, Arduinouno microcontroller

INTRODUCTION

Alternating current (ac) frequency is the number of cycles per second in an ac sine wave. It is measured in hertz (Hz). In India 50 cycle/sec i.e., 50 Hz, grid frequency is maintained. Grid operators controls the frequency by giving necessary instructions to generating stations. It is an important parameter in power systems as it deals with the stability of the system. The equipment in our home, factory or office is designed to operate at a 50Hz within a tight

tolerance of 1% (49.5Hz to 50.5Hz) therefore it's very important to keep the frequency of our power supply stable. For the synchronizing of generators with grid it is important that the frequency of the system and frequency of the grid should be equal otherwise it may lead to failure of synchronization.

While dealing with electricity and electrical devices measurement is the important factor to be considered so as to measure frequency of electricity of domestic consumers a frequency measurement device is needed. Instruments like multimeter and CRO are capable to measure frequency but they are very costly and have their own disadvantages, so to overcome those disadvantages a frequency meter using Arduinouno is introduced. As per the current scenario it is seen that the use of non-linear power system load is increased so that harmonic contamination in the power quality increases ,When the imbalance of the power supply and demand occurs between systems, it will result in system frequency variation [1], and thus the frequency is very important parameter as it deals directly with the stability of the system to keep generators of power grid in synchronization it is important to match and balance or maintain their frequency equal. Mismatch of frequency of grid and alternators, equipment's result in failure of system. Here Arduino is the heart of device and it has a better resolution which is useful for accurate measurement.

Arduino Uno is selected as it has many advantages over the other microcontroller. It is cheap, easy to maintain and can be programmed easily as per the desired results of the programmer. For programming the controller Arduino IDE is used. Also, the clear and easy programing environment is not limited to only windows operating system, the board is flexible to use and can modified using any system. The handiness of the Arduino board also provides a better hand in easy maintenance of the device. Now if the grid frequency fluctuated more than it is allowed, the power transmission system will become unstable and eventually collapsed. The drop in frequency at the grid indicates that the demand is higher than the supply, while the jump in frequency indicates otherwise. Hopefully the measurement device that is developed could assist the relevant stakeholders to monitor the quality of the grid frequency thus increase the awareness of the importance of understanding the behavior of the grid frequency [3].

Need to Measure Frequency

Most importantly frequency acts as a mediator between the device and the supply, so mismatch of the frequency will have its consequences on the device and also if the variation in frequency continues then that may cause permanent damage to the device. It can be avoided if a proper frequency measuring technique is implemented. Throughout times the measurement devices have always proven to act as a troubleshooting tool for engineers. The frequency also helps to understand the behavior of inductance and capacitance present in the system. Various measurement techniques and the effects of frequency are being discussed in here. Also, while measuring the grid frequency it has to be taken into consideration that the instrument used for measuring is accurate and has a good resolution as it should be able to measure the slightest change.

Effect of Variation in Frequency

Various effects due to variations in frequency are as follows:

Effect of Increase/Decrease of Supply or Demand in Power System

When the supply is decreased, or demand is increased beyond the generated power, then the speed of rotation of the generator is decreased which causes frequency to reduce, as the speed of rotation is directly proportional to the frequency. The stored Kinetic Energy of the alternator also reduces which results in affecting stability of the system.

Effect on Transformers

If the frequency increases, then the secondary voltage increases. Increase in frequency also affects the V/F ratio of the transformer which give rise to the core losses thereby reducing the efficiency of Transformer. Under changing frequencies, the transformer may get into saturation. The skin effect on the conductor is also proportional to the change in frequency.

Frequency Affecting Reactive Power

As inductive reactance is directly proportional to the frequency and capacitive reactance is inversely proportional to frequency and as Q=V2/X, where X may be inductive or capacitive reactance. Thus, change in frequency affects the reactive power of the system.

Effect on Electrical Appliances

Appliances such as TV set if operated at lower frequencies then a slight hum is observed on the set and also the picture in the display is disturbed which may result in instability of the device.

Methods to Measure Frequency

Various frequency measurement devices and algorithms are employed by the power supplier and distribution organizations to measure frequency accurately and in real time. These methods are proven to be usefulbut have drawbacks like high cost and difficult to employ them in the system. While taking considerations of only devices like CRO and frequency meters which are performing well but it requires some practice so as to use them.If we consider measuring the frequency of grid using CRO then we have to plug the CRO probes to the AC supply whose frequency is to be measured. Then by optimizing the signal and observing the AC wave on the CRO screen we are able to determine the frequency by counting no. of horizontal divisions and multiplying it by the respective scale. Then taking the reciprocal of the answer we are able to determine the AC frequency.

Now if we consider of measuring the frequency using a vibrating reed frequency meter then we have to have a close look on its working and construction. Now, as this frequency meter consists of an electromagnet comprising of a laminated armature and winding connected with a resistance. Other main thing in the construction is its reeds which are placed near the electromagnet. For measuring frequency, we have to have a close look on the reeds as they experience a force and the one with maximum vibrations is taken into consideration and then frequency is determined by taking the reading of that reed.

So, after discussing these methods it is sure that these methods have disadvantages which need to overcome. Measurement using oscilloscope requires keen observation and also it needs a good operator who will determine the results accurately and also it needs manual calculations to finally calculate the frequency also for the frequency meter discussed above has a big disadvantage that if the observation is not done properly then the results may vary from accurate results and also in normal working also the accuracy of the device is not proper. To overcome these drawbacks a device is made which measures the frequency easily and precisely. It uses the principle of zero crossing of AC wave which is mostly used in many frequency measurement algorithms. This zero crossing is detected by the Arduinouno controller as on and off pulses which determines the total time of one cycle of input wave. The algorithm so developed requires minimum time calculations which are processed fully automatically by the device and gives the real time data logging. This real time data helps to analyze the variations in frequencies. This analysis is required to have a better understanding of faults or misbalance in the grid. The measurement technique explained here is designed such that it will sense and record the data even under major fault conditions.

Components Details

Resistor: The property of circuit that opposes the flow of current is called resistance. The electronic device is commonly used to reduce the power or current in an electronic device. Resistors operate on the principle that energy can be neither created or destroyed, only changed from one state to another. A resistor is made of a material that has a specific amount of resistance to current flow. Resistors are selected for the amount of resistance they possess. This value is measured in Ohm's (Ω).

Diode: A diode is a device which allows current flow through only one direction. That is the current should always flow from the Anode to Cathode. The 1N400x series is a family of popular one ampere general purpose silicon rectifier diodes commonly used in AC adapters for common household application. For 1N4001 diode the maximum current carrying capacity is 1A it withstands peaks up to 30A.

Optocoupler: An optocoupler is basically an interface between two circuits which operate at (usually) different voltage levels. The key advantage of an optocoupler is the electrical isolation between the input and output circuits. With an optocoupler, the only contact between the input and the output is a beam of light. This is especially necessary for the coupling between high-voltage information-gathering circuits and low-voltage digital logic circuits. A current is first applied to the optocoupler which makes the infrared LED emit a light that's proportional to the current. When the light hits the photosensitive device, it switches on and starts to conduct a current as any ordinary transistor might.

Arduino SD Card Module: The module (Micro-SD Card Adapter) is a Micro SD card reader module, and the SPI interface via the file system driver, microcontroller system to complete the Micro-SD card read and write files. Arduino users can directly use the Arduino IDE comes with an SD card to complete the library card initialization and read-write. This is the primary storage unit of our device which will store the data up to 16 gigabytes.

Arduino UNO: The Arduino Uno is a microcontroller board based on the ATmega328 (datasheet). It has 14 digital input/output pins (of which 6 can be used as PWM outputs), 6 analog inputs, a 16 MHz crystal oscillator, a USB connection, a power jack, an ICSP header, and a reset button. It contains everything needed to support the microcontroller; simply connect it to a computer with a USB cable or power it with a AC-to-DC adapter or battery to get started. The Uno is the latest in a series of USB Arduino boards, and the reference model for the Arduino platform.

LCD 16*2: The term LCD stands for liquid crystal display. It is one kind of electronic display module used in an extensive range of applications like various circuits & devices like mobile phones, calculators, computers, TV sets, etc. These displays are mainly preferred for multi-segment light-emitting diodes and seven segments. The main benefits of using this displaying custom characters, special and even animations, etc. The 16×2 liquid crystal display contains two horizontal lines and they are used for compressing the space of 16 display characters. This module will receive direct commands from the Arduino and will display the frequency.

Potentiometer: A potentiometer is defined as three terminal variable resistors in which the resistance is manually varied to control the flow of current. The potentiometer is a simple device used to measure the electrical potentials between the end of the wire and any point along it will be a potential proportional to the length of wire to that point.

Circuit Diagram

The above figure shows the actual connection and circuit of the hardware to be employed. The supply is firstly connected to the optocoupler through the half wave rectifier circuit. The half wave rectifier circuit is employed so that the AC voltage gets converted into the DC voltage and one cycle of the input is eliminated and it becomes easier for us to correctly measure the on and the off time of the supply signal which will be useful for calculating the frequency of the supply. The circuit employs an optocoupler which makes it safer to use in any case of faults in supply. With help of our algorithm and Arduino UNO board we are able to determine the frequency and the results are stored in a memory unit connected it. The data is transferred from the Arduino UNO to the memory unit through serial communication.

Algorithm and Working

Below shown represents the algorithm of the device:

It is clear from the above flowchart that for the programming part of the device first the initialization of variables is done and all the libraries are included in the Arduino IDE after which the help of half wave rectifier ckt implemented the Arduino UNO is able to sense the ON and OFF time of the input cycle. Electrical frequency is calculated by taking the reciprocal of the time measured. This value is recorded on the SD card which is used as a memory storage element and the interaction of SD card and Arduino is made via the serial data communication and the data is printed on the LCD screen as shown below.

Application

The novel and lesser cost frequency measurement technique proposed may be used for the following applications.
It will benefit the farmers who use solar power for agriculture purpose, to check the output frequency of the inverters so as to save their IM in low frequency conditions. Hostel owners who have solar rooftops can check whether their operating frequency is within tolerance limit or not. It can be used in laboratories for experiments as it directly measures frequency and no calculations are required to be done. It can be used as a good alternative for the normally used devices for frequency measurement. The range of the meter can be extended by adding external circuits.

CONCLUSION

It is required and is essential to measure and monitor the grid frequency continuously to avoid any kind of grid failures and misfunctioning of the power system. By not maintaining the frequency as per standard rules designed by the national authority of the specific country could lead to serious problems on both consumer and the supplier side. The measurement technique should also provide a well-structured report of the on-going variations in the frequency and also the operator who is monitoring will have to cross check the data with the manual readings which he records in his register to check whether the device is properly functioning or not.

Also, as for the Arduino used for measuring purpose should not be restricted only as per the algorithm displayed there can be many modifications to the circuit for various other purposes. This Arduino helps us and ease the problems of designing the complex circuits which are present for performing this job. As for the device explained it has given accurate results and the margin of error is also very less. It displays and also maintains the data for future use while consuming less power. The safety of the device is also excellent as the optocoupler isolates the main functioning parts from the ac mains. The device gives the data keeping all as per the standards mentioned by the governing authority. The device so designed gives no sign of damage or degradation even after long use.

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Table 1 : Components Table

Components	Ratings
Resistor	220 ohms(Ω)
Diode 1N4001	1 A, 50V
Optocoupler PC817	100mA, 400V
Arduino SD Card Module	16 GB (micro)
Arduino UNO	5V
LCD 16 *2	4.7V -5.3V
Potentiometer	10 KΩ

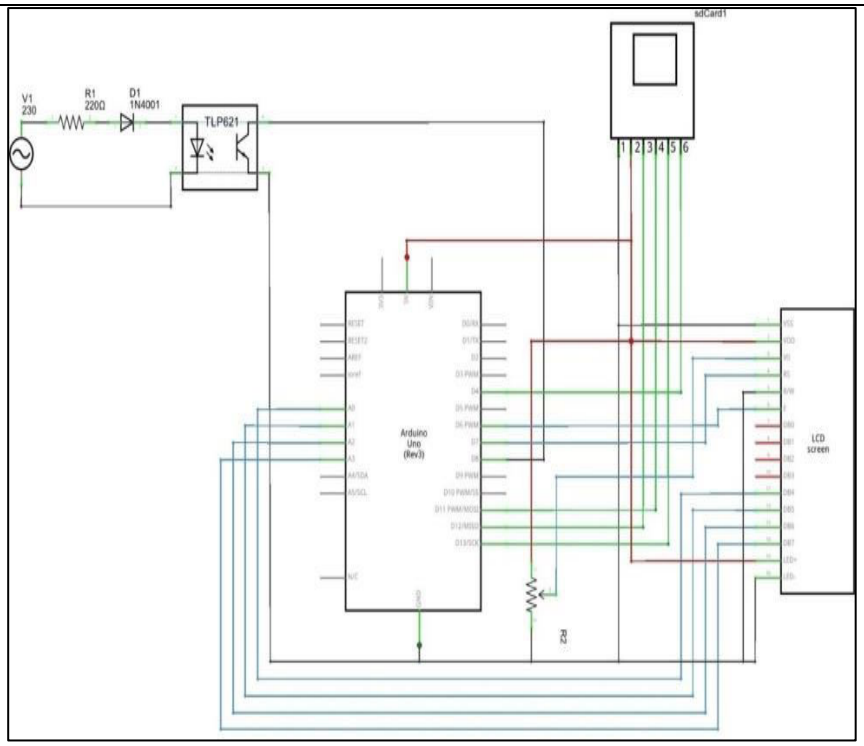

Fig.1 : Circuit Diagram

Fig.2 : Algorithm of the device

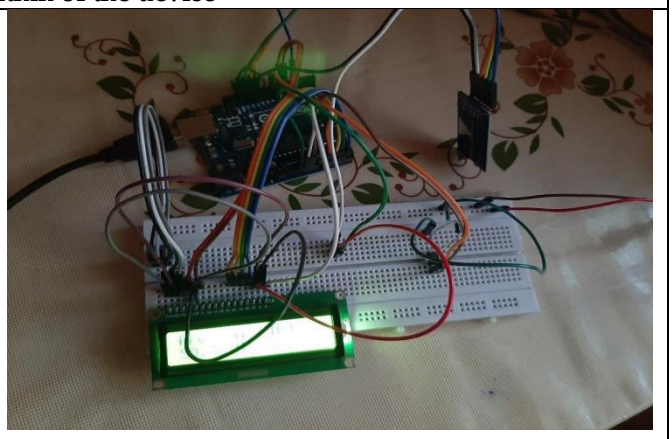

Fig.3 :The hardware setup of the circuit for testing on breadboard

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RESEARCH ARTICLE

Image Classification and Super Sampling using Generative Adversarial Network

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ABSTRACT

In today's rapidly evolving era, high resolution digital data has become all but a necessity, especially when it comes to media. With the exponential increase in on-demand media consumption around the world, there has been an increasing requirement for higher quality. The content being produced these days are natively high resolution, but what about the content that has already existed for years? One option is to remaster them into high-definition but we rarely see it done, especially for niche media such as animation. This is because remastering process takes a lot of time and effort, and consequently, a lot of investment. However, with the recent developments in the field of deep learning and neural networks, it has now become possible to automate most of the remastering process. The latest technology in use for this purpose are called Generative Adversarial Networks, or GANs. In this paper we analyze the process of super resolution image upscaling from the ground up, along with the challenges it comes with, and find new ways to improve GANs by making them more efficient and enhancing the quality of their output using image classification.

Keywords: Generative Adversarial Networks, Super Sampling, High Resolution Image Upscaling, Digital Media Remastering.

INTRODUCTION

Image categorization is a overseeing learning problem, where we can determine a bunch of specific classes, objects to recognize in images, and teach a model to identify them using labeled photos. Pixel data(raw) alone doesn't provide a abundantly solid portrayal to enclose the multitude of differences of an object as expressed the image. The orientation of object, camera angle, background , lighting, and camera focus can all produce variations in raw pixel

info; these dissimilarities are significant enough that they cannot be amended by taking weighted averages of pixel(RGB) values. Computer vision models put on new property obtained from pixel data for modeling. This required a lot of work and there were too many inputs to tweak. It made the system less accurate and made building models even more difficult. Building models for image classification was made a lot easier with a major development: the discovery that a convolutional neural network, may be used to successively draw out high level portrayal of the image. A convolutional neural network gets the image's raw pixel data as input and learns how to bring out these features, and eventually infer what object they account for. It ended up saving a lot of processing time and reduced the need for manual input or tweaking of parameters.

However, the type of Image Classification we're applying in this research is slightly different from the usual. The aim of classification here is to recognize all the artifacts that are present in the image. The most common ones of these artifacts are noise, detail loss, haloing, aliasing and banding and blocking. They will be explored in detail in later sections, but they each require different kinds of processing, called filtering, to remove them. Applying image classification to this process will result in better pre-processing of image by taking into account the specific type of issues that need to be fixed. If the input image can be improved by filtering, then consequently the output quality will increase too. Using Image Classification with Generative Adversarial Networks will improve their efficiency too. Models for GANs are required to be trained for every particular type of media, which is a time taking process. However, by using Image Classification prior to modeling, we can reduce the modeling time since all the common artifacts have already been accounted for. The common artifacts present in images to be upscaled are noise, detail loss or removal of grain, haloing, aliasing and banding and blocking. We will now take a slightly more in-depth look at each of them.

Literature Survey

We studied the methodologies of techniques that are currently in use for this purpose of classification and upscaling of images. Our research led to the following conclusions about each of them.

Traditional Upscaling

The easiest way for upscaling an image is to put it through a decent upscaling algorithm, such as Spline36, Lanczos, or Bilinear upscale. This results in a blurry output but it is still the most commonly used upscaling method. That is because it's easy, cheap and can be done by anyone. In fact, as far as animation is concerned, it is almost always made at a low resolution, of around 720p to 900p and is then upscaled to 1080p or even 2160p when it is put on Blu-ray. This process creates its own set of artifacts which can be fixed via descaling, that is, reversing the upscale, but that discussion is beyond the scope of this paper.

Remastering

The classic way of converting standard definition to high definition is rescan the source digitally, which takes several minutes to digitize each frame in the best resolution possible. It can easily take a few days to even a week to complete. From there, the new digital master had some film grain removed is restored and color corrected. Removal of film grain is a contentious issue, but it's frequently a necessary evil. If the camera negative cannot be found, other film elements will kick into place, but the quality will deteriorate. Since those film elements are irreplaceable, a lot of restoration work has to be done. Usually, creators are not willing to risk putting them through international shipping and customs for outsourcing.

Convolutional Neural Networks

CNNs have been around for years and have recently exploded in favor mostly thanks to its achievements in the field of image classification. Most important elements of this process can be summarized as:

1. Using modern and powerful GPUs for systematic training.

2. Preserving good quality while still working faster thanks to Rectified Linear Unit.
3. Having access to large sets of data such as ImageNet for training bigger models.

Deep Learning for Image Restoration

Many studies have been done about the utilization of deep learning methods for reconstruction of images. In multi-layer, all of them are fully-linked in comparison to convolutional. Learning a deep CNN for image SR is put in for denoising and post-deblurring. Upon a closer look, they are connected to our work, the CNN is added for denoising image naturally and removed for noisy patterns like grain. Restoration problems such as these are driven by denoising. Whereas the SR image problem has not observed much utilization of deep learning as far as we're aware.

Research Papers

We also studied the following paper published in reputed journals and we have tried our best to summarize their research work in the following paragraphs.

In the paper "The relativistic discriminator: a key element missing from standard GAN", we see the use of relativistic generative adversarial network (RGAN) and relativistic average generative adversarial network (RaGAN) that gauge the possibility that the given data is more realistic than random data that is fake. RGANs and RaGANs are notably more stable and create better quality data samples than their non-relativistic equivalent, Standard RaGAN with gradient penalty create data of higher quality than WGAN-GP while only needing a sole discriminator update per generator update and finally RaGANs are able to create high resolutions images (256x256) from a very limited sample that also becomes a limitation or a disadvantage.

The paper "Image Super-Resolution Using VDRCAN (Very Deep Residual Channel Attention Networks)" we see the use of Convolutional neural network (CNN) with an improved and better deeper network called very deep residual channel attention networks (RCAN) it forms very deep network, which incorporates various residual groups with long and short skip connections, LSC and RSC respectively. All remaining group holds some residual blocks with SSC. RIR permits plenty of less-frequency info to go around through many skip connections, having the focus of the main network on training high-frequency data this deep neural network permits it to have increased or better accuracy than their counterparts but it also makes them more complex. In "Residual Dense Network for Image Super-Resolution" we also see the use of an upgraded version of CNN that uses hierarchical features from LR image, In this they use residual dense network and residual dense block, that is, RDN and RDB to withdraw ample local properties via dense linked convolutional layers. RDB then permits direct links from preceding RDB to all layers of the current RDB, getting to a contiguous memory mechanism, called CM mechanism. Fusion of local features in RDB is then used to evolutionarily learn more efficient attributes from previous and local features and balances the training of bigger connections; they attain great performance against other methods this also makes it more heavy on the system.

In Human Parsing with Contextualized Convolutional Neural Network" it uses Contextualized Convolutional Neural Network (Co-CNN), inputting the image of a human, it makes classification taking in each pixel in a thorough way. The cross-layer conditions is seized by the LGL(local-to-global-to-local) structure at first, which structurally merges the global semantic form and the native details in the cross-layers. The GILLP(global image-level label projection) is used as the additional goal in the median layer of Co-CNN, the results further is utilized for leading the feature learning of the following convolutional layers that leverages the factors affecting GIL(global image level).To use LSC(local super-pixel contexts), the WSPLO(within super pixel leveling out) and CSAV(cross-super-pixel area voting) are put together as ingenious sub-parts of Co-CNN. To attain the domestic label stability in the testing and training method the

F-1 scores of the large datasets obtains 76.95% produced by Co-CNN that is higher than the rest Due to its pixel wise categorization higher resolution inputs need more processing power.

The "Color image identification and reconstruction using artificial neural networks on multimode fiber images: towards an all-optical design" uses structures that implement artificial neural network(ANN) concepts that need hardware of a new kind which can bear the required conditions of the HSAC(high speed associative computing) while preserving low energy utilization are needed to fit the design of the optical imaging process that is based on ANN and has the capacity to grasp the image prompts from an unclear light origin in variety of colors. The design includes a amalgam of multimode fiber and a multi-core optical fiber discerning a neural network but this system needs a large investment to properly set it up and run.
The DeepLab: Semantic Image Segmentation(DSIS) with Deep Convolutional Nets(DCNs), its Convolutions, with Fully joint CRFs" the spatial pyramid pooling (ASPP) is used to greatly separate items at several scales, the ASPP inquires a CFL(convolutional feature layer) that has filters at subsequent sampling rates, thus seizing objects at several scales of image context. by merging methods from PGM (probabilistic graphical models) and DCNNs. The frequently stationed down sampling and mix of max-pooling in DCNNs fulfils the invariances that leads to downsides on local accuracy. While all these papers focus on different aspects of the result that we are trying to achieve, they all had something to contribute towards our research.

METHODOLOGY

We used the image classification part of the previous work and applied it into our image upscaling method. The classification done here is very different from the usual ways, though. Instead of classifying the contents of the image, we classify the artifacts present in the image. Using this classification, our upscaling algorithm gets a better idea on how these issues can be fixed. Before we get into fixing and upscaling, we must first identify these artifacts. They are generally classified as follows.

Grain: Aside from film grain, grain is added to videos for a few different reasons. It can be added to create an effect or for a change the atmosphere, or it can be added to protect against more harmful artifacts from occurring like banding and blocking. In excess, it may be considered an artifact, but for modern sources, it needs to be preserved.

Noise: Visually, noise looks worse and more out of place than grain. It's less specific and can look blocky, blotchy, or consist of small dots, wherein grain has a proper texture. heavy random grain might be added and encoded with low bitrate, resulting in blocky, large, unstable, noisy, grain. This is frequently impossible to remove without noticeable detail loss, and in this case scene filtering and heavy detail loss are the only two options.

Haloing: Also knows as Ringing, it is something of a blanket term for edge artifacts, including mosquito noise, edge enhancement artifacts, overshoot, or actual ring-like ringing caused by the Gibbs phenomenon. It is most likely caused due to bad upscaling or heavy compression.

Aliasing: It happens because non-identical signals become identical, or aliases of one another, when sampled. In imaging, it's regularly perceived as 'jaggies', which pop up as steps along what should be a uninterrupted line or edge. It has a few main sources: bad sharpening , low bitrate, bad upscaling, and interlacing. To reduce it, we take into account how much an ideal edge overlaps adjacent pixels and smoothen it.

Blocking: Blocking is known by various names, like quilting, checkerboarding, mosaicking, tiling, pixelating, and jaggies; and it takes place at any moment a complicated and highly comped image is sent over a low bandwidth link., the output of some deciphered blocks makes neighboring pixels seem merged together to look like bigger blocks At decompression. This artifact is often found in MPEG2 TV sources or in DVDs that are from the previous decade.

Banding: Due to with its many flat areas and smooth gradients, banding is a frequent problem in animated media, which is caused by the limits of 8-bit color depth and truncation, especially in low bitrate sources.

Apart from these artifacts, the issue with using GANs is that it requires a model to be trained for every specific type of source which is a time taking process. Applying Image Classification prior to modeling, can give it a boost in efficiency as it will already have ways to deal with most of the commonly occurring visual artifacts.

Implementation

We propose a system which can best be described by the above architecture diagram.
The aim of classification here is to recognize all the artifacts that are present in the image. The most common ones of these artifacts are noise, detail loss, haloing, aliasing and banding and blocking. They each require different kinds of processing, called filtering, to remove them. Applying image classification to this process will result in better pre-processing of image by taking into account the specific type of issues that need to be fixed. If the input image can be improved by filtering, then consequently the output quality will increase too. Using Image Classification with Generative Adversarial Networks will improve their efficiency too. Models for GANs are required to be trained for every particular type of media, which is a time taking process.

However, by using Image Classification prior to modeling, we can lessen the modeling time since all the usual artifacts haves o far been calculated for. We readdress the key parts of SRGAN and better the structure in three ways:

- Refine the network architecture by initiating the (RDDB)Residual-in-Residual Dense Block, which is of bigger capacity and simple to train. We also take off (BN) Batch Normalization layers as in and make use of To make training a very deep network easier, residual scaling and smaller initialization are used.
- Refine the discriminator using RaGAN, that can judge ‘if one picture is more logical than another' instead of judging on the basis of 'if a particular picture is genuine or isn’t'. Our testing show that this development helps the generator recuperate more realistic texture details.
- Enhance perceptual loss by making use of VGG characteristics before activation instead of after activation as shown in SRGAN. We objectively find that the adjusted perceptual loss gives us better and sharper edges which are more visually appealing.

Post-up sampling SR is when SASR models grasp The majority of mapping functions are performed in LR, with very few of the upsampling layers applied during the network part. Training of the upsampling layers is done along with the preceding convolution layers. This is done in an end-to-end manner and they are made discoverable. Earlier approaches called pre-up sampling SR, and then using the upsampled original image with a pre-defined up sampling before learning to map them in the HR output. One major disadvantage is that it necessitates a higher number of parameters for each and every layer, which increases cost of computation, time required and restricts the development of neural networks. The majority of data present in LR image gets to be retained in SR. Identity information is transmitted through skip connections, while high frequency detail is reconstructed on the network's main route, making residual network designs extremely significant. As a result, SR models learn primarily thanks to the residuals of LR and HR. As in Res-Net or specialized variants, these layers are frequently residual blocks Beforelearning the mapping in HR space, the LR image was sampled with a predefined up sampling operation. allowing deeper networks to be built. The global skip layer is depicted in the following diagram. This article's up sampling layer is a sub-pixel convolution layer. The sub-pixel convolution layer produces a representation of size HxWxs2C It then reshapes it to sHxsWxC using a convolution operation. Completing the up sampling operation, given an input of size HxWxC and an up sampling factors. The result is a factored output that is spatially scaled. Transposed convolution layers are another choice. Convolutions that are transposed can also be learned, but their receptive area is smaller than sub-pixel convolutions, because of which, they can process fewer contextual data, resulting in less accurate predictions.

EDSR Model

The EDSR paper, describes the super-resolution model following this high-level architecture. Here's a quick rundown of its structure: Its residual block architecture is different from Res- Net's. Layers of batch normalisation have been eliminated. As can be seen on the right side of the figure, the final ReLU activation has also been removed. EDSR model creators claim that batch normalization loses scaling data from images and decreases activation range. It uses a one upsampling layer for SR scales, that is, for factors of two, three and with two upsampling layers for four times the upscaling. EDSR function below uses TensorFlow 2.0 to implement the EDSR model. Removing the batch normalization layers improves SR presentation while reducing GPU memory usage by almost half, allowing for the training of much larger models. The default claims are the same as those in the paper's EDSR baseline. The following sections go into model training in more detail.

WDSR Model

EDSR model tweaks residual block architecture even further while holding the total number of parameters the same, by dropping channel count on identity mapping and raising channel count in all residual blocks. The following diagram depicts their residual block designs: As we increase the channel count inside the residual blocks until ReLU permits more information to be passed in the process of activation, according to the authors. Improving model efficiency even more. They also discovered that implementing weight normalization simplifies training and convergence of deeper models, allowing them to use orders of magnitude higher learning rates than in EDSR training.

This is understandable, because EDSR removes the weight normalization layers and makes training deeper models difficult that before. It's simply a reshuffling of parameters of neural network weights which identifies the direction of weight vectors using their magnitudes, making optimization problem training simpler and faster. The weight normalization layer parameters are not set using data-dependent initialization. It would rescale features in the same way that batch normalization does, as seen in EDSR paper, which was further confirmed in WDSR paper, lowering model performance. Weight normalization without data-dependent initialization, on the other hand, increases the accuracy of deep WDSR models.

Data

The DIV-2K dataset will be used to train EDSR and WDSR models. LR images may be used for a variety of downgrade functions. It's a set of LR and HR picture pairs with a wide range of material. Preparation is done using 800 HR images, and validation is done with 100 HR images. Augmentation requires random crops, flips, and rotations are used to generate lots of training images. Bicubic down sampling will be used in this situation. A DIV-2K data loader automatically downloads DIV-2K images and provides LR and HR image pairs for a given scale and downgrade functionality.

Pixel Loss

Training SR models requires the pixel wise L2 and L1 loss functions. These are the most commonly used methods. Between IHR and ISR, the pixel wise mean square error is calculated along with the absolute error, using the following formula:

$$\mathcal{L}_{pixel,L^2}(I^{HR}, I^{SR}) = \frac{1}{HWC}\|I^{HR} - I^{SR}\|_2^2 \quad (1)$$

$$\mathcal{L}_{pixel,L^1}(I^{HR}, I^{SR}) = \frac{1}{HWC}\|I^{HR} - I^{SR}\|_1 \quad (2)$$

The image's height, width, and number of channels are represented by H, W, and C, respectively. PSNR, a widely used measurement metric in super-resolution competitions, is explicitly optimized by the pixel-wise L2 loss.

Throughout our tests, we've discovered that pixel-wise L1 loss can often achieve even better results, so it's used to train EDSR and WDSR models.

Perceptual Loss

Pixel wise loss functions have the downside of resulting in low perceptual consistency. SR images that have been created lack high frequency textures, and are blurry. Perceptual loss functions are used to solve this problem. Photo-Realistic Single Image Super-Resolution Using a Generative Adversarial Network is a pioneering paper for producing SR images with higher perceived quality. Authors used a material and adversarial perceptual loss feature. Content loss collates features from SR and HR into VGG that has already been conditioned.

$$\mathcal{L}_{content}(I^{HR}, I^{SR}; \phi, l) = \frac{1}{H_l W_l C_l} \|\phi_l(I^{HR}) - \phi_l(I^{SR})\|_2^2 \quad (3)$$

Where H is height, W is width, and C is the number of channels respectively, of the function map at layer l. The GAN discriminator D is used to differentiate between SR and HR images. While generator is designed to generate more realistic SR images so it can easily deceive the differentiator.

$$\mathcal{L}_{perceptual} = \mathcal{L}_{content} + 10^{-3}\mathcal{L}_{generator} \quad (5)$$

They use a pixel wise loss to pre-train the super-resolution mode, which is the generator in a GAN, and a perceptual loss to fine-tune the model. rather than training it from scratch. SR Res-Net, a precursor of EDSR, is used as a super-resolution model in the SRGAN paper. Experiments have shown that the SRGAN method is also effective for fine-tuning EDSR and WDSR models.

RESULTS

The research papers we used for our base focused on different aspects of the result that we have achieved. While the previous work only did image classification, we modified and applied it in our image upscaling method. The classification done here was very different from the usual. Instead of classifying the contents of the image, we classified the artifacts present in the image. Using this classification, our upscaling algorithm was able to efficiently fix these issues. In the following figures, we can see exactly how big of an improvement our method makes over the traditional ones.

A s compared to practicing with loss pixel-wise, tuning with perceptual loss produces more natural textures in the SR videos. The SR images that have more realistic textures are also generated by the fine-tuned WDSR-B model. The images above, from the resized progressive section of practicing, demonstrate how well tech deep learning-based super resolution improves detail, removes watermarks, and imprints missing information. The same trained model performed super resolution on the next three image, demonstrating that a deep learning SR model could be used uniformly.

CONCLUSION

Deep learning based SR model that uses function loss like these can be very effective in the super resolution in a variety of situations, including removal of watermarks, enhancing the quality of an image and increasing its resolution, removal of all JPEG and other compression artifacts, magnification low-res images to high-res images and removing artifacts from images.

We can apply these techniques to a range of image subjects and industries. Our main purpose with this research was to enhance the quality of low-resolution media. However, with some modifications, this method can be used in the medical field, for enhancing minor details, or even in astronomy, to get a clearer picture of faraway objects. In the future, we want to create an efficient universal super resolution model that works well with all types of images. It's also possible to train the model on a greyscale version of the dataset and then colorize the images. We also intend to transform this model into a web application and maybe even a mobile app used via a webservice.

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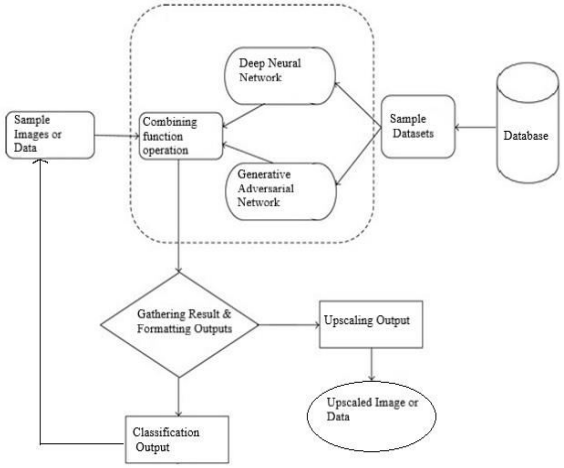

Figure 1. Workflow Diagram

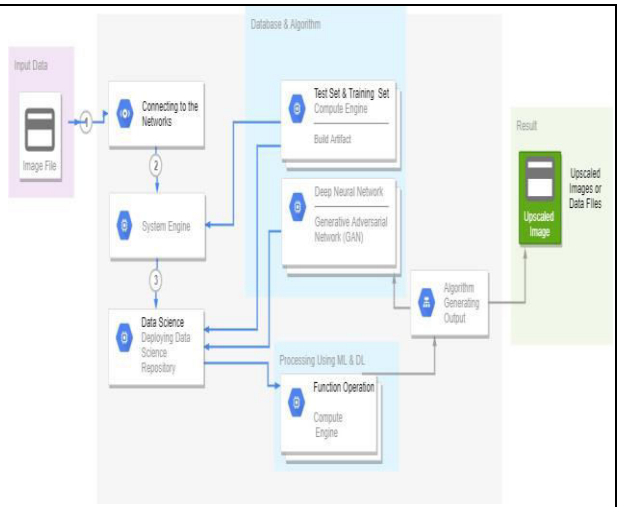

Figure 2. Architecture Diagram

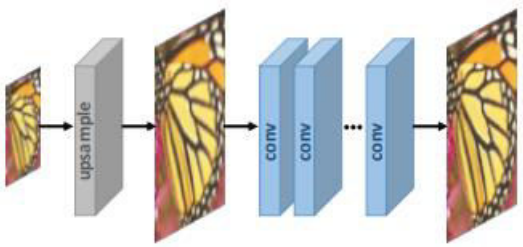

Figure 3A: Pre-upscaling SR

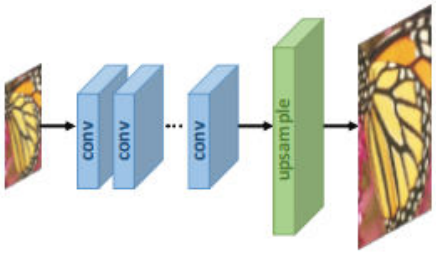

Figure 3B: Post-upscaling SR

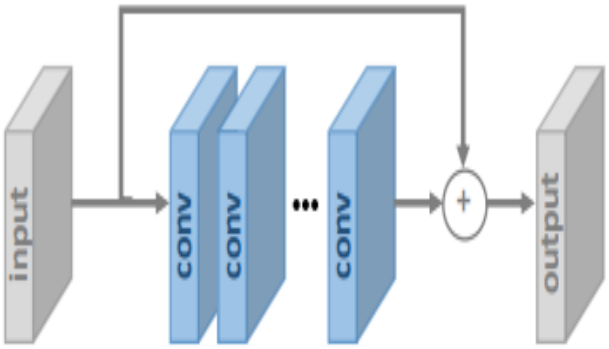

Figure 4: Global Skip Connection

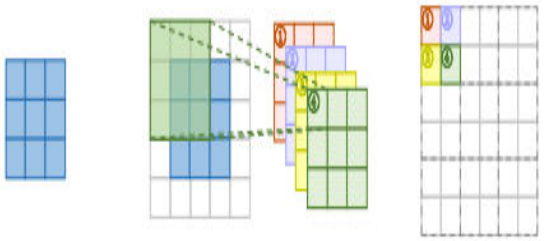

Figure 5A: Starting Figure 5B: Convolution Figure 5C: Reshaping

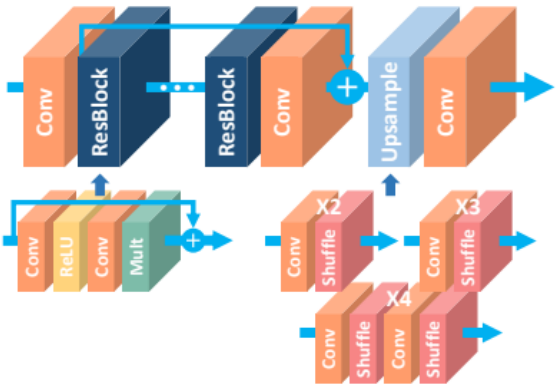

Figure 6: EDSR architecture

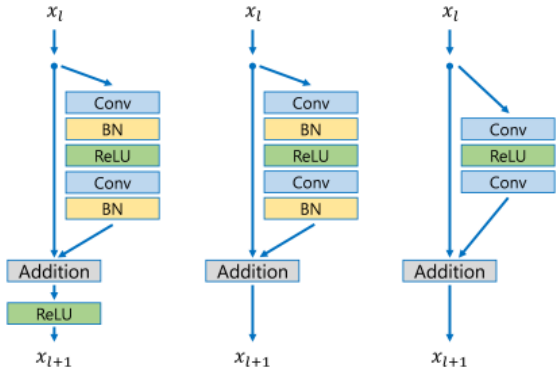

Figure 7: Res-Net and EDSR Residual Block Designs

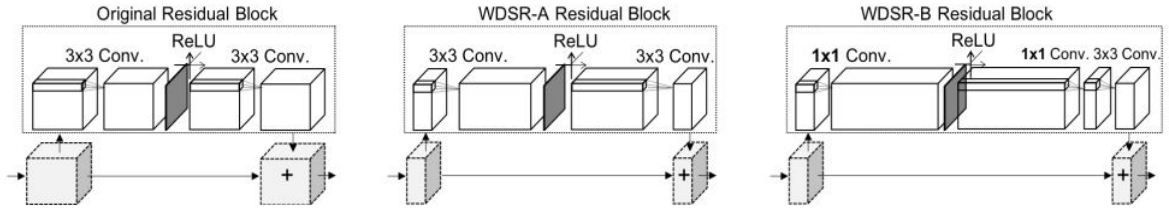

Figure 8: WDSR Residual Block Designs

Figure 9: Comparison Between Input and Output Images

Figure 10: Comparison Against Other Methods

Figure 11: A picture from the validation dataset with super resolution.

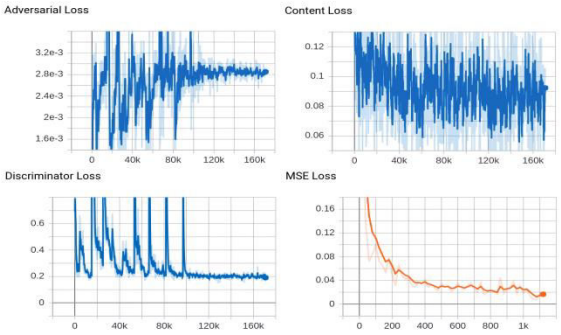

Figure 12: Graphs showing reductions in various artifacts

REVIEW ARTICLE

Successful Aging: A Review on Its Relationship with Hand Function and Cardiorespiratory Fitness

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ABSTRACT

A complex and a naturally occurring phenomenon, aging, is influenced by and correlated to numerous factors. As the world is going through a major changeover in the number of elderly people alive, it becomes necessary to review the relationship of various factors both physiological and physical, which can affect the aging process. The current review has made a perspective on the correlation of hand functioning and cardiopulmonary fitness with successful aging process. This review shows that not only cardiopulmonary endurance is a major physiological factor, but it also correlates importantly with aging and the effect of aging on hand function has also been established clearly in this review. Finding this relationship can showcase a predictor which can lay out parameters of successful aging, allowing independent living for a longer time period, thereby reducing healthcare sector workload. With this established correlation we can indulge into planning of certain intervention to improve the rate of successful aging.

Keywords: health, aging, elderly, cardiopulmonary fitness, hand function, hand grip strength

INTRODUCTION

Aging is an invincible part of life and while it is not itself debilitating, it can still go with by an expanded association of debilitating physical and metabolic sequences. We live in a worldwide aging society [1]. According to census

generated by The World Health Association (WHO), in the year 2000, there were 600 million individuals aged 60 years and more. This number will show an increase to as high as to 1.2 billion by 2025 and again by 2050 this number will rise up to 2 billion aged people (≥60 years) [1]. Aging can be seen to be a societal achievement, but it is additionally a challenge in terms of wellbeing care and people's perception. Hence, it is vital to assure the aged population a freedom not only from major infection and disorders. Along with the physical attribute there is a necessity to uplift the mental and physical functioning of elderly. Achieving this will diminish the large social and financial responsibilities to about half of what is spent in a life time for health care[2], [3]. Ideally, successful aging should mean a state of wellbeing through most of one's life particularly for those individuals who are aged 50 years and more, those who wish to know the ways for and imply them for effective maturing [3].Aging, an uninterrupted physiological process is autonomous of gender[1].It implicates a dynamic decrease within the proficiency of a few physiological processes[1]. A person starts to age from early adulthood to middle aged group and after that to the early elderly stage, there's the progressive increment in physical, physiological, and cognitive decay.

Physical fitness, a very important aspect in aging process, is inclusive of two main things: cardiorespiratory fitness (CRF) and muscular strength [3]. CRFis characterized as the capacity of the circulatory, respiratory, and strong vascular system to supply oxygen in spite of diminished physical exercise [4]because of aging, cancer, diabetic mellitus, depression, and all- cause mortality [2]. The possibility of respiratory and musculoskeletal disorder increase with age and this isn't constrained to the elderly population (≥60 years) only. The decrease in muscle quality begins at around 30 years of age and gets to be more visible after the age of 65 years[5]. The vital hand grip strength (HGS) decreases from 45.5 kg to 23.2kg for males, and from 27.1kg to 12.8 kg for females between the ages of 25 and 95 years[6]. Respiratory function declines when proper care is not being taken of and based on evidences available it has been marked as a free indicator of mortality [7]. A decreased CRF is an efficient and strong predictor of numerous outcomes of health specifically in elderly population. Supporting its efficiency as a predictor, low muscular strength also can very easily stand out for early morbidity in elderly patients [8].

The aging parameters have found to be in a remarkable relationship with the hand function and CRF. There exists strong evidence behind the fact that aging has the great impact in the hand function and cardiopulmonary fitness performance. These both can help in prediction of healthy and successful aging and can be used as a marker of any impending abnormality. The main aim of this review was to outline the relationship of aging with the hand function and cardiopulmonary fitness. Cardiopulmonary endurance has the great influence on the hand function and presence of lifestyle disease risk factors is an important affecting factor as this study will reveal the correlation between them. The association will set up a base for the future prediction for physiotherapy intervention to support the multidisciplinary approach in the field.

MATERIALS AND METHODS

Criteria for considering studies for this review:
For formulating this short review the PICOS (population, intervention, comparison, outcome and study design) criteria was used and was kept broad deliberately to capture all the relevant articles. The articles were made sure comprised of elderly population (aged ≥60 years) with no morbidities attached and also did not had recent previous surgery or illness. No limitation was placed on the type of studies included in this short review.
Search strategy for identification of studies:

The primary literature search was done using PubMed database, Medline, Excerpta Medica Database (EMBASE), the Cochrane, and Controlled Enlist of Trials (CENTRAL) and the Aggregate Record to Nursing and United Wellbeing writing (CINAHL), Google researcher, National library of medication using following terms: "successful aging," "cardiopulmonary fitness", "hand function" and "aging" in the period of 2015 – 2020. Language barrier was placed as it was kept only English. Ten articles were found which were all within the recent advance, evidence based and were

ethically supported articles. Last research was completed on January 2021. As a result of search strategy the titles and abstracts generated were again assessed for eligibility and full text articles which were completely relevant were retrieved. Duplicate publications, if any, were excluded. Table 1 talk about the methodological extraction of evidences and their inclusion in the study.

RESULTS AND DISCUSSION

Through the literature search 1099 titles were screened after removal of duplicates. Out of these 1071 studies were excluded on the basis of irrelevant abstracts and titles. The reviewers were left with 28 studies (full text). In the next step n = 10 articles were found to have wrong population age selection, so they were also excluded and finally 10 articles were included for formatting this short review. Table 2 is depicting the characteristics of the included articles in details.

This review shows a clear and conceptualized relationship between hand function and cardiorespiratory fitness in individuals growing old. Aging is an inevitable phenomenon associated with the functional decline of different organs which in turn is accompanied with the increase in age-related illnesses [9]. The elderly body which can be characterised as healthy should possess certain components such as: diminished muscle mass and decline in muscle quality amid the maturing phase, and this downfall actually begins at around 30 years of age [5]. Amaro-Gahete FJ *et al.* 2017, concluded that even though maturing includes a dynamic affliction of functionality, it is possible to delay or restrict this decrease in functionality, making elderly in all round wellbeing through increase in physical health [9].

Serving as the most important and critically relevant component of physical wellbeing, cardiopulmonary fitness, has been very effectively characterized customarily by the value of VO2max[9]. In a review done by Schmidt D Leitzmann, (2015) it was observed that individuals with high cardiopulmonary fitness have a lower mortality chance (45%) less for any sort of cancer when compared to cardiorespiratory fitness [10]**.**It clearly states that individuals who have a good cardiorespiratory fitness strive to live longer. The support for HGS factor was also evident with another recent review done by R.zhu *et al.* (2020) it was stated that good HGS was associated with proper vital capacity, forced expiratory volume (FEV_1) and maximal vital volume in both elderly genders [11]. HGS has been a very much emphasized factor by many reviewers and it is clearly evident by this review also that it can correlate very well with healthy aging properties.A researcher Grontved et al, emphasised moderate correlation of muscular strength, an important parameter of successful ageing, to cardiorespiratory fitness and HGS and it also reflected the cardiopulmonary function to some extent, relationship with pulmonary function (VC, r=0.44 in males and r=0.46 in females) was also established [12].

With formulation of this short review, we got evidence background that there is the positive and identical influence of hand function with cardiopulmonary fitness in aging population. Hand function, an inevitable representative of peripheral muscle strength, is also an important issue to be addressed because of the reason that most daily activities require efficient use of the hands. Physiological decline in hand functions because of biological aging is an important observation which can predict many health outcomes [12]. Age-related decrease in manual dexterity may be especially a vital issue to address since most everyday activities require effective utilize of the hands and this even makes it more necessary for elderly people [7]. Another research done by Richard A. Winet and Ogletree A.M in 2009 for evaluating the effect and contribution of other factors like exercise types, and addition of resistance on promoting the development of active aging in elderly beyond age ≥ 60 years. They found a good correlation between these two factors, emphasizing on CRF and general body strength more [13].

The reviewers were able to reach to a complete definition of manual dexterity defined by Poirier as "a manual aptitude that requires fast co-ordination of net and fine intentional developments based on a certain number of capacities, which are created through learning, preparing and experience"[14].An effective work out session utilizing

handgrip dynamometer is a kind of isometric exercise where voluntary muscle action is related with a considerable surge to the cardiovascular system, demonstrating high heart rate and blood pressure. The rise in heart rate is additionally due to parasympathetic withdrawal and the enactment of another central command [8]. Handgrip strength equitably employing a dynamometer is prescient of different results among a varied group of subjects. The utilization of this lower arm aspect is quite often throughout the day [15].The general utilization of hand and its musculature by the day in certain useful activities prioritizes that handgrip quality can be utilized as an indicator of general muscle quality and has been detailed to exceedingly anticipate functional incapacity associated with aging [15]. Hyun Iee Shin *et al*, 2017 proved with their study that respiratory muscle strength, an important predictor of CRF is very effectively correlated with skeletal muscle mass and specifically Hand grip strength in aged population which are otherwise healthy [16].

Furthermore study done by Lesser I.A *et al.,* 2015, at different geographical location assessed the association of levels of CRF and other fitness parameters like BMI and abdominal fat and peak VO2 in older population. They found that these variables are correlated inversely and have a strong association [17]. However the other set of researchers Lin PS et al., 2016 inferred from their study that independence in ADLs in elderly phase of life has got a great contribution from CRF parameter, and thus is correlated to an efficient fitness level of individual [18].

The improvement of physical functions increases the functional capacity related to aging. The correct evaluation and physical assessment and measures, can improve both hand function and cardiopulmonary function which can make the concept of healthy aging a verifiable thing to be considered.

CONCLUSION

In summary of the evidence collected it is almost clear that successful aging has to be adjusted and kept up from beginning itself as we age, the deterioration and loss of capacity start within the physical and cardiopulmonary function as we are growing up. These two capacities are exceptionally imperative to urge effective maturing in an individual's life. All the later surveys concluded that physical wellness is a perfect indicator of health. Further evaluations can be done on finding out a single marker for successful ageing.

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Table 1: Flowchart for included studies

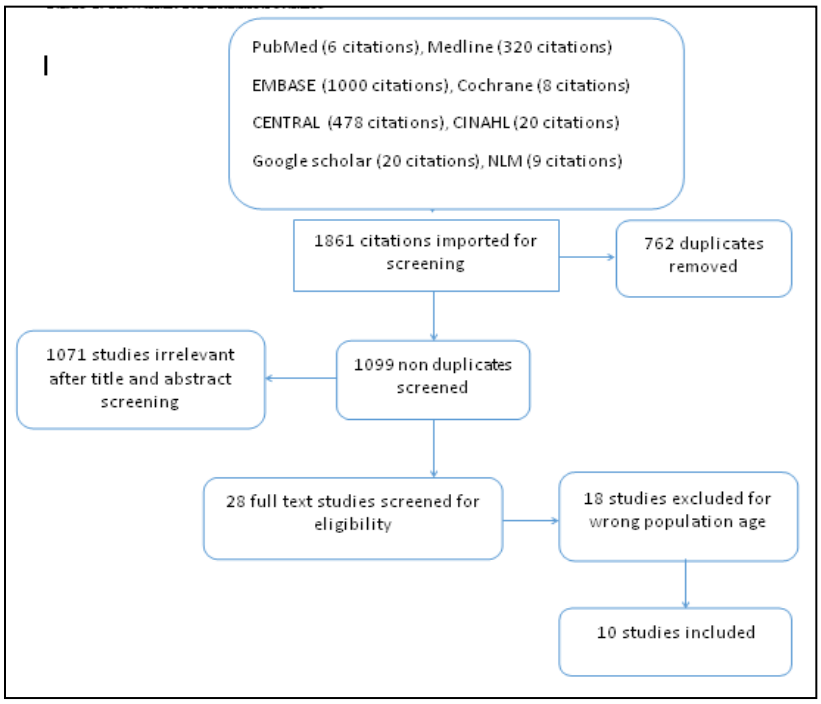

Table 2: Characteristics of the Included Studies

S. N	Author name/ year	Title	Methodology	Conclusion
1.	Chen lingnei *et al* [8]. 2020	Better pulmonary function is associated with greater hand grip strengths in a healthy Chinese population.	Cross sectional study with hand grip strength and pulmonary function was tested.	It shows both Pulmonary function and handgrip strength were inversely correlated with age, and better pulmonary function was associated with a greater Handgrip strength.
2.	Amaro- Gahete *et al* [9]. 2017	Fitness assessment as an anti- aging maker: A Narrative Review	A narrative review with the cardiopulmonary function.	It concluded that the gradual aging of the population in the last decades suggests the importance of the promotion of a healthy aging based on the good physical and mental condition.
3.	R. Zhu *et al* [11]. 2020	Hand grip strength is associated with cardiopulmonary function in Chinese adult's results from a cross- sectional study.	Cross- sectional survey of the national physique health in shanti province. 908 participants with cardiac function test and 380 participant with pulmonary function test.	It concludes that the greater HGS was associated with favourable cardiopulmonary function in Chinese adult, thus HGS might be an indicator of cardiopulmonary function.
4	Richard A. Winet [13] 2019	Evidence based high-intensity exercise and physical activity for compressing morbidity in older adults: A narrative review	A narrative review with recent research in high intensity interval training and sprint interterval training with evidence based	Concluded that they focused on the exercise components of intervention and emphasizing the effectiveness of higher intensity training for increasing healthy quality of life.
5.	Shin Hyun *et al* [16] 2017	Relationship between respiratory muscle strength and skeletal in the healthy elderly	65 volunteers over the age of 60 years was measured with skeletal muscle mass index using bioimpedence analysis and limb muscle function was assessed with handgrip strength, SPPB & gait spreed. RMS was addressed by maximal inspiratory pressure and maximal expiratory pressure using a spirometer.	This study suggest that respiratory muscle, inspiratory muscle, are significantly related to limb muscle strength and skeletal muscle mass. The clinical significance of MIP & MEP should be further investigated with prospective study.
6	I.A. Lesser *et al* [17] 2015	The association between cardiorespiratory fitness and abdominal adiposity in postmenopausal, physically inactive South Asian women	Associations between VO2 peak and inner-abdominal fat variables remained significant after adjustment for body fat percentage but were	Compared to women in the lowest tertile of VO2 peak, women in the middle tertile had significantly lower BMI (0.039) and women in the highest tertile compared to the middle tertile had significantly.

			no longer significant after adjustment for BMI.	
7	Pay-Shin Lin *et al* [18] 2016	Association between Physical Fitness and Successful Aging in Taiwanese Older Adults	Among the physical fitness variables tested, cardiopulmonary endurance, mobility, muscle strength, and balance were significantly associated with SA in Taiwanese OAs.	Early detection of deterioration in the identified functions and corresponding intervention is essential to ensuring SA.
8	Maria Fernström *et al* 2017	Aerobic fitness is associated with low cardiovascular disease risk: the impact of lifestyle on early risk factors for atherosclerosis in young healthy Swedish individuals – the Lifestyle, Biomarker, and Atherosclerosis study	Food habits did not differ However, aerobic fitness measured as VO2 max (mL/kg/min) differed; 47% of the subjects at risk had low aerobic fitness compared to 23% of the non risk subjects.	The high prevalence of young adults observed with unfavourable levels of high-density lipoprotein cholesterol and homeostasis model assessment of insulin resistance raises concerns about future CVD risk.
9	Sally Whelan *et al* 2020	Fostering the Resilience of People With Dementia: A Narrative Literature Review	The interventions impacted resilience by reducing the adversity of stigma and social isolation; increasing personal and social resources, providing stigma-free space and reciprocal support. Interventions empowered people with dementia, increasing their self-esteem and self-worth.	Interventions need facilitators to ensure they are strength-based, person-centered and they enable reciprocal social interactions.
10	Maria Teresa Tomas *et al* 2018	Functional capacity and levels of Physical activity in aging: a 3-Year Follow-up	The loss of functional capacity must be more related with qualitative variables than morphological (for example, SMM) since we could not find any relationship between changes in body composition and physical function variables.	This 3-year follow-up study confirmed the relevance of endurance and strength capacities, which may be improved across physical activity levels in combination with other body composition and physical function variables.

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RESEARCH ARTICLE

Phytochemical Estimation of Some Ethnomedicinal and Ethnoveterinary Plants in Dang Region of District Dholpur, Rajasthan

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ABSTRACT

The present study was undertaken to estimate the phytochemical compounds present in the leaf, stem and roots of medicinal plants in Dang region of Dholpur district. Extracts were prepared from Aqueous and organic solvent like Petroleum ether, Chloroform, Ethyl acetate and Ethanol. Medicinal plants have bioactive compounds which are used for curing various human ailments and also play an important role in healing. To estimate the presence of tannins, flavonoids, phenolics, steroids, and alkaloids, screening of the plants performed by standard methods. It is expected that the important phytochemical properties recognized in the present study in the indigenous medicinal plants of dang region of Dholpur district will be definitely useful in the curing of various diseases of the region.

Keywords: Medicinal plants, Phytochemicals, Estimation, Treatment, Compounds , Agents .

INTRODUCTION

The ethnomedicinal and ethnoveterinary plants are useful for healing as well as for curing of human diseases because of the presence of phytochemical compounds (11,12,13 and 14). Phytochemicals are naturally occurring in the medicinal plants, leaves, vegetables and roots that have defense mechanism and protect from various diseases(1,2,3,4,5). Phytochemicals are primary and secondary compounds. Chlorophyll, proteins and common sugars are included in primary constituents and secondary compounds have terpenoid, alkaloids and phenolic compounds. Terpenoids exhibit various important pharmacological activities i.e. anti-inflammatory, anticancer, anti-malarial, inhibition of cholesterol synthesis, anti-viral and anti-bacterial activities. Terpenoids are very important in attracting useful mites and consume the herbivorous insects. Alkaloids used as anesthetic agents are found in medicinal plants. Plant chemicals are regarded as secondary metabolites because the plants that manufacture them may have little need for them. They are synthesized in all parts of the plant body like bark, leaves, stem, root, flower,

fruits, seeds etc. i.e. any part of the plant body may contain active components . These chemical substances are called secondary metabolites. The most important of these bioactive groups of plants are alkaloids, terpenoids, tannins, steroids and phenolic compounds (6,7,8,9 and 10). Dang region is one of the most suffering a damaging lack of the basic necessities for life and arid region of Rajasthan state marked with degraded ravines, barren land and severe water shortage. All these factors together have created challenges for the community to even engage with basic livelihood activities such as agriculture and livestock rearing. Most farmers in the Dang region struggle hard even to fight hunger. Phytochemical estimation of several species of medicinal plants and allelopathic activities of the crude chemical compounds on crops and plants have yielded positive results (15,16,17 and 18) . In these days herbal medicine are demanding in all over world because of their low cost and higher safety margins. The present study revealed the qualitative phytochemistry of eight medicinal plants used by the peoples of Dholpur district, Rajasthan in curing dreadful ailments of human on one hand and cattle on the other hand.

MATERIAL AND METHODS

Collection of Plant Materials

Plant materials (leaf, stem, roots and Fruits) was collected from Dang region of Dholpur District, Rajasthan, India.
(A) The plants were identified by villagers of tribal communities about different aspects.
(B) Interviewing with common people to know about ethnomedicine and plants used for treating diseases in cattle.
Eight ethnomedicinal plants were collected locally from the Dang region Dholpur (Rajasthan). The plants were used for the purpose of their phytochemical analysis or estimation. The plants collected were identified in Herbarium Department of Botany, Rajasthan University, Jaipur. The present study included plant species which were *Achyranthus aspera, Asparagus race mosus, Balalmites aegyptiaca, Citrullus colocynthis, Desmostachya bipinnata, Pedalium murex, Solanum xanthocarpum, Tridax procumbens.* (Table 1, Figure 1)

Preparation of plant extract

Collected plant materials like leaf, stem, root and fruits were washed with distilled water and shade dried for a week. When plant materials complete dried then sample were ground by pulverizer and passed through 40 mesh sieve to make fine powder and stored in air tight containers. The dried powder was taken in a test tube and distilled water was added to it and shaken well. The solution was then filtered with the help of filter paper and filtered extract of the selected plant samples were taken and used for further phytochemical analysis.

Preliminary chemicals

Fehling solution A and Fehling solution B, Ethanol, distilled water, aqueous HCl, Methanol, Chloroform, concentrated sulphuric acid, Ammonia solution, Lead acetate.

Test for Tannins (Braemer's test)

Plant powder sample was mixed with distilled water in a test tube and shake well and filtered to take plant extract. Then to each plant extract, 1-2 drops of lead acetate was added. If turned out red color of precipitate, it confirmed a positive result.

Test for Steroids (Libermann Burchard test)

0.5 ml of the extract, add 2ml of acetic anhydride and 2ml of concentrate H_2SO_4 along the sides of the tube. The formation of green color indicates the presence of steroids.

Test for Terpenoids (Salkowski's test)

1ml. of extract was taken in a boiling tube and 2 ml of concentrated sulphuric acid was added slowly and red violet color was observed which indicate the presence of terpenoids.

Test for Flavonoids

For the confirmation of flavonoid in the chosen plants, 0.5 gm of each chosen plant extract were added in a test tube and 10 ml. of distill water, 5 ml of dilute ammonia solution were added to a portion of the aqueous filtrate of each plant extract followed by addition of 1 ml. concentrated H_2S0_4 . Evidence of yellow color shows the presence of flavonoid in each extract.

Test for Alkaloids (Mayer's test)

The plant extract was evaporated to dryness and the residue was heated on a boiling water bath with 2% hydrochloric acid. After cooling the composite was filtered and treated with a few drops of mayer's reagent. Existence of yellow color precipitate indicates the presence of alkaloids.

RESULTS

This study disclosed the presence of phytochemicals deliberated as active medicinal chemical constituents. Important medicinal phytochemicals such as terpenoids, steroids, flavonoids, alkaloids and tannins were present in the samples. The result of the phytochemical analysis shows that the eight plants are rich in at least one of alkaloids, flavonoids, terpenoids, steroids and tannins. The phytochemical screening and qualitative estimation of seven medicinal plants studied showed that the leaves were rich in tannins, terpenoid, flavonoids, alkaloids and steroids (Table 2).

DISCUSSION

The research work was carried out on the eight selected medicinal plants which showed that phytochemical constituent's i.e., terpenoids, flavonoids, alkaloids, steroids and tannins are either present or absent in these plants and the results were summarized in Table 2. Present study deals with qualitative phytochemical analysis of leaves, roots and fruits extract of *Achyranthus aspera, Asparagus racemosus, Balanites aegyptiaca, Citrullus colocynthis, Desmostachya bipinnata, Pedalium murex, Solanum xanthocarpum, Tridax procumbens L.* shows the presence of tannins, alkaloids, flavonoids, terpenoids and steroids. These plant parts extensively used in traditional medicine due to the presence of several phytoconstituents. Flavonoids have been recommended to as nature's biological response modifiers because of prominent experimental evidence of their natural ability to modify the body's reactions to antipathetic, virus and carcinogens. Flavonoids and tannins are phenolic compounds that are a major group of compounds that act as primary antioxidants or free radical scavengers (6,21). Plants steroids are known to be important for their cardio tonic activities, possess insecticidal and antimicrobial properties. They are also used in nutrition, herbal medicine and cosmetics (19,20). Plants derived natural products such as flavonoids,terpenoids and steroids etc. have received considerable attention in recent years due to their diverse pharmacological properties including antioxidant and antitumor activity(22).

CONCLUSION

The selected eight plants are the source of the secondary metabolites i.e., alkaloids, flavonoids, terpenoids, tannins and steroids. ethnomedicinal and ethnoveterinary plants play a vital role in preventing various diseases in human and cattle. The antidiuretic, anti-inflammatory, anti analgesic, anticancer, anti-viral, anti-malarial, anti-bacterial and anti-fungal activities of the medicinal plants are due to the presence of the above mentioned secondary metabolites. Medicinal plants are used for screening of the phytochemical constituents which are very helpful for the manufacturing of new herbal drugs. The previous studies on phytochemical analysis and present study show nearly the similar results due to the presence of the phytochemical constituents. The phytochemical analysis of the important medicinal plants are also important and have commercial interest in both research institutes and pharmaceuticals companies for the manufacturing of the new drugs for treatment of various deadly diseases. Thus

we hope that the important phytochemical aspects identified in present study in the local plants of Dang region Dholpur will be helpful in copping different diseases of this particular region. Thus plants studied here can be a potential source of useful drugs, if these plants are involved in further research.

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CONFLICT OF INTEREST

Author declare no conflict of interest.

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Table-1 Plant species selected during present investigation

S.No.	Plant Species	Local Name	Part Used
1.	*Achyranthus aspera*	Oonga	Roots
2.	*Asparagus racemosus*	Shatavari	Roots
3.	*Balalmites aegyptiaca*	Heengota	Root, Bark
4.	*Citrullus colocynthis*	Tumba / Indrayan	Fruits
5.	*Desmostachya bipinnata*	Daab	Roots
6.	*Pedalium murex*	Bara gokhru	Leaves
7.	*Solanum xanthocarpum*	Phal cateli	Fruits
8.	*Tridax procumbens*	Ghamra / Khoonbandhi	Leaves

Table - 2

		Name of Phytochemicals				
S.No	**Plant species**	**Tannins**	**Steroids**	**Terpenoids**	**Flavonoids**	**Alkaloids**
1.	*Achyranthus aspera*	+	-	-	-	+
2.	*Asparagus racemosus*	-	+	+	+	+
3.	*Balanites aegyptiaca*	+	+	+	+	+
4.	*Citrullus colocynthis*	-	+	+	+	+
5.	*Desmostachya bipinnata*	+	+	+	-	+
6.	*Pedalium murex*	+	+	+	+	+
7.	*Solanum xanthocarpum*	+	+	+	+	+
8.	*Tridax procumbens* Linn.	+	+	+	+	+

+ : denotes presence of phytochemicals - : denotes absence of phytochemicals

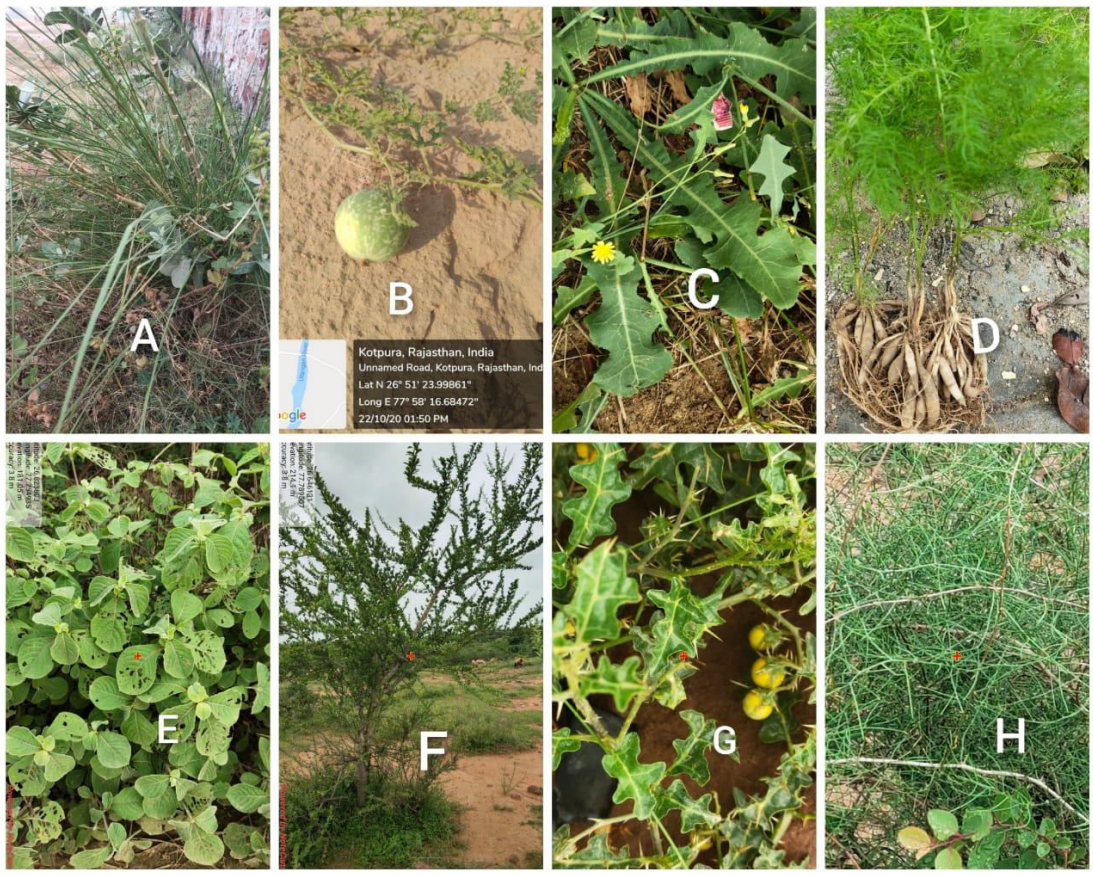

Figure 1: Images of (A- ***Desmostachya bipinnata,*** **B-** ***Citrullus colocynthis,*** **C-** ***Tridax procumbens*** **,D-*Asparagus racemosus,* E-** ***Achyranthus aspera,*** **F-** ***Balalmites aegyptiaca,*** **G-** ***Solanum xanthocarpum,*** **H-** ***Asparagus racemosus*****)**

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RESEARCH ARTICLE

Corrosion Inhibition by usage of Iso Leucine as Inhibitor on Mild Steel, Analysed by Experimental and Theoretical Methods

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ABSTRACT

This study is involves the usage of amino acid as corrosion inhibitor, as amino acids are natural compounds and are non-hazardous to environment. Amino acid Iso-leucine is picked up as an inhibitor for inhibiting corrosion on mild steel by using well water as a medium. Iso-leucine depicts the inhibition efficiency of 83% in 250ppm of Iso -leucine in well water and 30ppm of zinc, which is outlined by Gravimetric method. The contents of the inhibitor are revealed by FTIR spectral studies and polarization study insist that Iso-leucine is an anodic type of inhibitor.

Keywords: Inhibitor, corrosion, Amino acids, mild steel and Iso-leucine.

INTRODUCTION

Corrosion of metals is an electrochemical phenomena where immediate destruction of metal takes place. A good example for corrosion is rusting of steel and iron, but corrosion is also observed in ceramics and plastics. In case of metals it's a change of meta stable condition to stable condition of the mineral , where there is a decrease in free energy of the system. Corrosion can be wet and dry, wet type is due to the contact of metal with any type of solution or water and dry corrosion happens due to a touch of metal with air, moisture or oxygen in the atmosphere. As we can see a vast of steel due to its durability and strength is used in automobile industries and transportation purposes and this process of corrosion reduced the life of steel. So it has become a national issue spending lakhs of money on getting back the metal. Therefore this study relies on using environmental friendly and easily available materials as inhibitors. As we can see that these amino acids [6,7,8] are easily available and is also environmental friendly. The usage of these amino acids and its inhibition efficiency has proven to be used under normal atmospheric conditions where the metal is in direct contact with air and moisture. And further the fact also lies that these amino acids are

also unreactive to water or air and also remains as such on metal surface also forming a protective coat preventing it from atmospheric deterioration.

MATERIALS AND METHOD

Mild Steel Specimen Preparation

A mild steel specimen having a composition of carbon-0.0104%, Sulphur-0.026%, phosphorus-0.035%, Manganese-0.58%, Iron-99.287% and dimension of 1.5cm X3.5cmX0.2cm is used. The surface of the specimen is polished before use[13].

Inhibitor

Iso-leucine was employed as an inhibitor, which is a type of amino acid having α-amino acid, α-carboxylic acid and a hydrocarbon side chain with a branch.

Preparation of Stock Solution

Iso-Leucine (Iso-Leu)

Iso-Leucine of 1 gm was dissolved in distilled water and made up to 100ml in a SMF and 1ml of the solution is made up to 100ml in another SMF yielding 100ppm of Iso-leucine.

Preparation of Zinc Sulphate Solution

1.09g of zinc sulphate was dissolved in double distilled water and 10ppm of Zn^{2+} ion concentrations is made up.

Gravimetric Method

The weighed specimens were allowed to stand in 100 ppm of Well water containing various concentrations of the inhibitor in the absence and presence of $Zn^{2+}$for one day of immersion. After a day of immersion, the specimens were taken out, and weighed. By change in weight of the specimen, corrosion rates were calculated using the following relationship [1,25,29,].

Corrosion Rate (mmpy) = $\frac{\text{87.6 x weight loss in mg}}{\text{D xAxT}}$

D = Density of the Specimen
A = Surface area of the Specimen
T = Time (hr)

The inhibition efficiency (IE) was then calculated using the equation:

$$IE\ \% = \frac{W_1 - W_2}{W_1}$$

W_1 is the weight loss value in the absence of inhibitor and
W_2 is the weight loss value in the presence of inhibitor.

Electrochemical Measurements

This study was undergone by a 3 electrode cell assembly, where working electrode was carbon steel, platinum electrode was the counter electrode and saturated calomel electrode is fixed as the reference electrode. The time interval given to reach the steady state open circuit potential is around 5-10 minutes. With the help of the results , we can get E_{corr}(corrosion potential) and I_{corr}(corrosion current) values[41,43,48,50].

Tafel slopes anodic = ba and cathodic = bc and LPR value. The scan rate (V/S) was 0.01.Hold time at (Efcs) was zero and quiet time (s) was two.

AC Impedence Measurements

The AC impedence is calculated in the frequency range of 105 KHz to 101 KHz . This cell impedence gives us information about processes such as electronic or ionic conduction in electrode and electrolytes, interfacial charging at surface films or double layer. Z'(real part) and Z" (imaginary part) of cell impedence is measured in ohms. Here, $E_{(v)}$ =0, high frequency (Hz) =1x105, Low frequency (Hz) =1, Amplitude =0.005, quiet time (s) =2,

Rt=(Rs+Rt)-Rs

Rt-Charge transfer resistance

Rs= solution resistance

$C_{dl}=1/2\Pi IRt\ f_{max}$

f_{max}=maximum frequency

FTIR Spectra

FTIR spectra is used to find out chemical bonds in a molecule by producing IR spectrum[37,39], producing a molecular finger print, with which samples of different components are studied. Here, FTIR spectra enlightens about the presence of protective layer present on the metal surface. It gives out information's about various functional groups present in inhibitor and type of complex formed as a result of interaction between iron and Iso-Leucine.

RESULT AND DISCUSSION

Gravimetric method (Iso Leucine-Zn^{2+})

Corrosion rates and inhibition efficiencies of mild steel in the absence and presence of Iso-Leucine+Zn^{2+}(under 1 day suspension)

The carbon steel immersed in well water of 300ppm of Iso-Leucine without zinc , shows inhibition efficiency of 33% and by adding zinc , the inhibition efficiency is raised to about 83%for 30ppm zinc and 250ppm of Iso-Leucine. This proves the existence of synergistic effect between zinc and iso-leucine.

Synergism Parameter (S1)

The synergism parameters are used to find the interaction between inhibitors. If S1 is greater than 1, it indicates the presence of synergistic effect. If its equal to 1, then there is no interaction between the inhibitors and in case of less than 1. Then there is a negative interaction between the inhibitors.

Synergism parameter are calculated by

$$S_I = \frac{1 - I_{1+2}}{1 - I'_{1+2}}$$

Where,

I_1 is the surface coverage of inhibitor (Iso-Leucine),

I_2 is the surface coverage of inhibitor (Zn^{2+}) and

$I'_{1+2}$is the combined surface coverage of inhibitors (Iso-Leucine) and (Zn^{2+}).

The synergistic effect prevailing between 250ppm of Iso-Leucine and 30ppm of Zn2+ are around 2.5716, that is greater than 1, reveals the synergistic effect between inhibitors.

Analysis of Variance ANOVA

F-test is used to investigate synergistic effect existing between 2 inhibitors. The analysis of variance of ANOVA is for the influence of 15ppm and 30ppm of Zn^{2+} on inhibition efficiencies of 50ppm, 100ppm, 150ppm, 200ppm, 250ppm of Iso-Leucine. For 15ppm of Zn^{2+} , F-value is 1. 6664, which is not significant as F-value is less than 5.32 for 1,8 degrees of freedom at 0.05 level of significance . Therefore, for 15ppm of Zn2+,the inhibition efficiency for various concentration of Iso-Leucine was not significant.

But in case of 30ppm of Zn^{2+}F-value is 0.0337which is also not significant, as the F-value is less than 5.32for 1,8 degrees of freedom. So various concentrations of Iso-Leucine for 30ppm of Zinc is also not significant.

Analysis by Polarization Technique

1. Well Water
2. 300 ppm of Iso-Leucine + 30 ppm of Zn^{2+} + Well Water

The carbon steel is immersed in well water [22] , the corrosion potential is around -580mV vs SCE. The shift of corrosion potential is observed in -603mV vs SCEm for 300ppm of Iso-Leucine and 30ppm of zinc. This shift is on negative side, and anodic Tafel (ba) slope for 300ppm of Iso-Leucine and 30ppm of Zn2+ was been shifted anodically 60mV/decade than cathodic Tafel (bc) slope 11mV/decade. From this observations ,its clear that Iso-Leucine –Zn^{2+} is anodic type of inhibitor.

The above result also suggest corrosion current value to be $5.5432x10^{-5}$ and LPR value was $963\Omega cm^2$ for well water . And for inhibitors, corrosion current value has decreased to $1.0250x10^{-5}A/cm^2$ and LPR value has increased to $3130\Omega cm^2$. The presence of inhibitor is retrieved by increase in LPR value and decrease in corrosion current value.

Analysis of AC Impedence Spectra

Fig.6.1 AC impedance of carbon steel immersed in
1. Well Water
2. 250 ppm of Iso-Leucine + 30 ppm of Zn^{2+} + Well Water

Fig.6.1 exposes AC impedence spectra [25,26,27,28,31,32,33] of carbon steel immersed in well water in presence and absence of inhibitors.

In the above Table 6.1, we can retrieve the values of Rct which is $743.22\Omega cm^2$ and C_{dl} value is $5.3262x10^{-8}$ $\mu F/cm^2$. In the presence of Iso-leucine and Zn^{2+}[3]R_{ct} value increases to 1489.16Ωcm2 and C_{dl} value decreases to 0.4875×10^{-8} $\mu F/cm^2$. These results indicate the existence of thin layer of the inhibitor with zinc on the metal surface.

Analysis by FTIR Spectra

Fig.7.1. FT-IR spectra of
1. Pure Iso-Leucine
2. Protective film formed on the surface of the metal immersed in Well Water containing 300 ppm of Iso-Leucine and 30 ppm of Zn^{2+}.

The above figure insists us to believe on the existence of Iso-Leucine on the metal surface. FTIR spectra of the inhibitor Iso-Leucine dried on a glass plate, gives CN stretching frequency at $1129cm^{-1}$, CO and NH stretching frequency at $3449.25cm^{-1}$. Now, the spectral analysis of presence of Iso-Leucine on metal surface frequency shift from $1129.69cm^{-1}$ and $1109.17cm^{-1}$ for CN. Stretching frequency of CO is shifted from $1603.28cm^{-1}$ to $1631.19cm^{-1}$ and there is also a shift of frequency for NH from $3449.25cm^{-1}$ to $3469.77cm^{-1}$. These spectral details indicate that nitrogen atom of Iso-Leucine coordinated with Fe^{2+} is formed on metal surface, leading to formation of Fe^{2+}-Iso-Leucine complex on anodic sites of the metal surface[39].

CONCLUSION

Iso leucine shows good inhibition efficiency in well water and the presence of inhibitor is confirmed by FTIR and weight loss method . The type of inhibitor is analysed by electrochemiscal studies.

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Gravimetric method (Iso Leucine-Zn^{2+})

Table 1. Corrosion rates and inhibition efficiencies of mild steel in the absence and presence of Iso-Leucine+Zn^{2+}(under 1 day suspension)

Iso-Leu (ppm)	IE %			CR (mmpy)		
	Zn^{2+} (ppm)			Zn^{2+} (ppm)		
	0	15	30	0	15	30
0	-	8	16	0.1051	0.0963	0.0903
50	8	33	58	0.0963	0.0700	0.0438
100	10	41	66	0.0876	0.0613	0.0350
150	25	33	75	0.0788	0.0700	0.0262
200	25	41	75	0.0788	0.0613	0.0262
250	33	41	83	0.0700	0.0613	0.0175

Table 2. Synergism parameter for Iso-Leucine-Zn^{2+} (15ppm) system in carbon steel immersed in well water for a day

Iso-Leu (ppm)	Zn^{2+} (ppm)	I_1	I_2	I''_{1+2}	S_I	IE%
50	15	0.8	0.8	0.33	2.2089	33
100	15	0.16	0.8	0.41	1.5050	41
150	15	0.16	0.8	0.33	1.3253	33
200	15	0.25	0.8	0.41	1.4745	41
250	15	0.33	0.8	0.41	1.0677	41

Table 3. Synergism parameter for Iso-Leucine-Zn2+ (30ppm) system in carbon steel immersed in well water for a day

Iso-Leu (ppm)	Zn^{2+} (ppm)	I_1	I_2	I''_{1+2}	S_I	IE%
50	30	0.8	0.16	0.58	2.1142	58
100	30	0.16	0.16	0.66	2.0752	66
150	30	0.16	0.16	0.75	3.8224	75
200	30	0.25	0.16	0.75	2.5200	75
250	30	0.33	0.16	0.83	2.5716	83

Table 4. Distribution of F-value between inhibition efficiency of various concentration of Iso-Leucine and inhibition efficiencies of Iso-Leucine in the presence of 15ppm and 30ppm

Zn^{2+} (ppm)	Source of Variance	Sum of Squares	Degree of freedom	Mean Square	F-value	Level of Significance of F
15	Between	6466	1	6466		P> 0.05
	Within	31046	8	3880	1.6664	
30	Between	4727	1	4727		P< 0.05
	Within	111947	8	13993	0.0337	

Table 5. Corrosion parameters of carbon steel immersed in well water in the presence and absence of inhibitor obtained by polarization method

Concentration		Tafel Parameters				
Iso-Leu (ppm)	Zn^{2+} (ppm)	E_{corr} (mV vs SCE)	I_{corr} (A/Cm²)	ba (mV/dec)	b_c (mV/dec)	LPR (Ω cm²)
0	0	-580	5.5431×10^{-5}	116.23	110.88	963
250	30	-590	0.6897×10^{-5}	185.89	180.32	3671

Table 6. Corrosion parameters of carbon steel immersed in Well Water in the presence and absence of inhibitor obtained by AC impedance spectra:

L-Proline (ppm)	Zn^{2+} (ppm)	R_{ct}(Ω cm²)	C_{dl} (μF/cm2)
0	0	391	1.3137×10^{-6}
250	30	3018	0.0253×10^{-6}

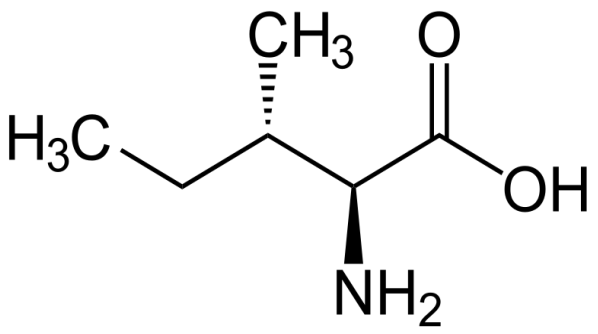

Fig. 1. Structure of Iso-Leucine

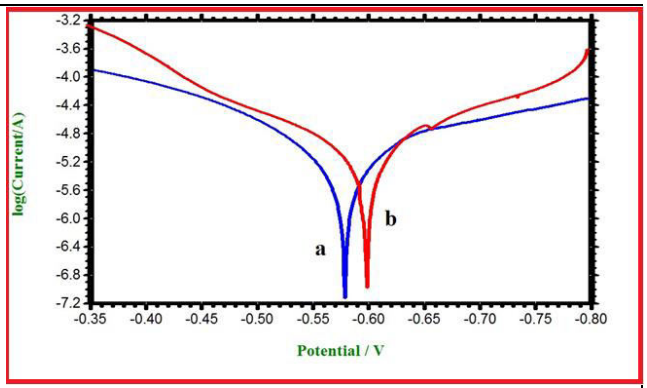

Fig.2. Analysis By Polarization Technique

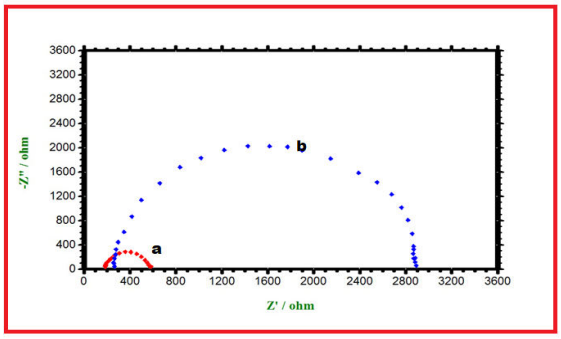

Fig.3. Analysis of AC impedence spectra

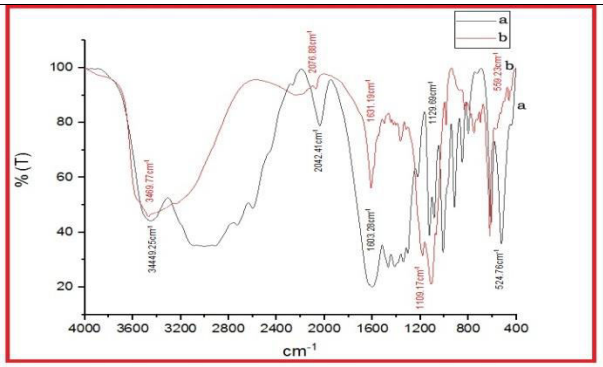

Fig.4. Analysis by FTIR spectra

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RESEARCH ARTICLE

Stabilization of Expansive Subgrade Soil using Waste Ceramic Powder (A Case Study on the Road Segment in Jaleswar to Chandaneswar Road, SH-57)

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ABSTRACT

Subgrade materials are expected to have basic desirable characteristics related to strength, stiffness and swelling. If these properties are not fulfilled, engineers are expected to come up with ground improvement methods. The growing cost of traditional stabilizing agents and the need for the economical utilization of industrial and agricultural wastes for beneficial engineering purposes have prompted an investigation into the stabilizing potential of waste ceramic powder in highly expansive clay soil. This research work is aimed to evaluate the suitability of waste ceramic powder for stabilization of expansive clay soil. The preliminary investigation of the soil to be stabilized shows that it belongs to A-7-5 class of soil in the AASHTO soil classification system. Soils under this class are generally of poor engineering use. Atterberg limits, free swell, free swell index, free swell ratio, compaction and CBR tests were used to evaluate properties of stabilized soil. The soil was stabilized with waste ceramic powder in stepped concentration of 5%, 10%, 15%, 20%, 25% and 30% by dry weight of the soil. All stabilized soil samples were also cured for 7 days for Atterberg limits, compaction and CBR tests. Analysis of the results shows that slight improvement on the geotechnical properties of waste ceramic powder stabilized soil. Waste ceramic powder reduces plasticity index, swelling and CBR swell and it increases MDD with decrease in OMC and CBR. Curing has an insignificant effect on the geotechnical properties of waste ceramic powder stabilized soil. From this study it was found out that waste ceramic powder stabilized soil do not show significant change for both index and strength property. Additional study is also incorporated as a supplementary work to investigate the effect of applying 3% lime as an activator in combination with 15% waste ceramic powder on the geotechnical properties of the soil for uncured and cured soil samples.

The results indicate that lime in combination with waste ceramic powder is suitable for improving the plasticity index, swelling and CBR. The strength values (CBR) also increased with curing ages, thus indicating that the blend has a potential for time-dependent increase in strength that will reduce the quantity of stabilizer needed for the construction of roads over the expansive soil. Therefore, this study shows that lime in combination with/plus waste ceramic powder can be effectively used to improve expansive soils with low soaked CBR value and high plasticity.

Keywords: Expansive Soil, Soil Stabilization, Waste Ceramic Powder, Atterberg limit, Compaction and CBR value.

INTRODUCTION

The need to bring down the growing cost of soil stabilizers and the cost of waste disposal has lead to intense global research towards economic utilization of wastes for engineering purposes. The safe disposal of industrial and agricultural waste products demands urgent and cost effective solutions because of the debilitating effect of these materials on the environment and to the health hazards that these wastes constitute. In order to make deficient soils useful and meet geotechnical engineering design requirements researchers [5,6] focused more on the use of potentially cost effective materials that are locally available from industrial and agricultural waste in order to improve the properties of deficient soils. Sub grade is the native material underneath a constructed road or pavement. It is the foundation of the pavement structure and called formation level [7, 10]. Sub grade function is to prevent excessive rutting and shoving during construction, provide good support for placement and compaction of pavement layers, limit pavement rebound deflections to acceptable limits and restrict the development of excessive permanent deformation (rutting) in the road structure during its service life. The quality of the sub grade will greatly influence the pavement design, performance and its service life [2].

Roads constructed on expansive soils areas are known for bad condition and unpredictable behavior for which the nature of the soil contributes to some extent. The failures of pavement, in form of heave, depression, cracking and unevenness are most likely to happen by the expansive soil in the sub grade. To eliminate the danger from such these soils, a technique of soil stabilization needs to be taken out. Soil stabilization is a collective term for any physical, chemical, or biological method or any combination of such methods employed to improve or change certain properties of natural soil to make it serve adequately an intended engineering purpose. There are many techniques of soil stabilization like mechanical, chemical and physical stabilization. Stabilization waterproofs the soil improves its strength, workability and durability and helps to reduce its volume change due to temperature or moisture DIYUANN CERAMIC PLC is over 400,000 m^2 in Eastern Industrial Zone, India. The production capacity is 60,000 m^2 per day. They use the resource material which comes from around Mojo like Talk, Feldspar, Calcite, Quartz, Muscovite and other material which are important for the ingredient of ceramic production. It has been estimated that about 30% of the daily production in the ceramic industry goes to waste. These discarded materials, most of which cannot be recycled within the plant, constitute industrial waste which is often land filled. Meanwhile, the waste has been categorized under pozzolana with about 3.13 % calcium oxide (CaO), 0.75% iron oxide (Fe_2O_3), 1.82% magnesium oxide (MgO), 67.51% silicon oxide (SiO_2) and 16.92% aluminumoxide (Al_2O_3) (from Balasore, Odishapian geological survey). The utilization of this pozzolana as a replacement for traditional stabilizers, such as cement and lime, will go a long way in actualizing the dreams of most developing countries of scouting for cheap and readily available construction materials. Waste ceramic powder has been used in concrete as a partial replacement material for cement Expansive soil refers to a soil that has the potential for swelling and shrinking due to changing moisture condition. Expansive soils cause more damage to structures particularly pavements and light buildings than any other natural hazard, including earthquakes and floods. It has been reported that the damage caused by these soils contribute significantly to the burden that the natural hazard pose on the economy of countries where the occurrence of these soils is significant. Balasore, Odisha is amongst the list of countries where the occurrence and spatial

distribution is recognized as significant. Expansive soils can be found anywhere in the world but they are basically confined to semi–arid and arid regions. These areas are naturally characterized by marked dry and wet seasons with low rainfall, poor drainage and exceedingly great heat. The climate condition is such that the annual evapo-transpiration exceeds the precipitations [9]. Two groups of parent materials have been associated with the formation of expansive soils. The first group comprises sedimentary rocks of volcanic origin which can be found in North America, South India and Israel, while the second groups of parent materials are basic igneous rocks found in India and Southwestern [10]. The most well- known example of expansive soils is the black cotton soil which is dark grey to black in color and the name originated from India where locations of these soils are favorable for growing cotton.

Objectives of the Research

The general objective of this study is to evaluate the suitability of waste ceramic powder as a stabilizing agent for expansive soil. This is achieved through the following specific objective:

Specific Objectives

The specific objectives of this study are:

1. To evaluate the effect of waste ceramic powder on the properties of the expansive soil using Atterberg limits, free swell, free swell index, compaction and CBR as measuring parameters.
2. To compare the changes in properties of expansive soil with respect to waste ceramic powder stabilized soil.
3. To investigate constituents of the waste ceramic powder.
4. To come up with a recommendable optimum proportion by weight of the waste ceramic powder required to improve expansive soils to meet the specification requirement of sub grade material.

RESEARCH METHODOLOGY

In order to achieve the above objectives of the study the following methodologies were adopted:

1. Literature review: pertinent literature pertaining to expansive soils has been identified andreviewed.
2. Sampling and testing: material sampling and testing methods are undertaken as per ASTM, AASHTO and IS standards. Soil samples were collected from Jaleswar, Kamarda, Chandaneswar. The chemical additive, waste ceramic powder taken was collected from East Industry.
3. Sample preparation of the experimental work involved air drying, pulverization and sieving of the natural soil sample to the required particle sizes. Classification of soil was made by running grain size distribution and Atterberg limit tests. Then Atterberg limit, free swell, free swell ratio, free swell index, compaction and California bearing ratio tests are carried out on natural soil as well as on soil- waste ceramic powder mix to study the effect of the stabilizer (waste ceramic powder).
4. Analysis and discussion of test results: based on the theories and laboratory tests performed, the results obtained have been analyzed and discussed thoroughly.

EXPERIMENTAL RESULTS

These days sustainability plays the major role in every aspect of human activities. Many technologies came to end because they were not in harmony with the idea of sustainable development. Sustainability is concerned about the world we will be leaving behind for future generations. It focuses on the social, environmental and economic issues of human activities. Therefore it requires every activity to be environmental friendly, economical and safe for the social. Waste ceramic powder contains large amount of silica which is the most important component of cement

replacing materials. Despite this abundance and silica content, relatively little has been done to examine the potential of this material for soil stabilization.

Sample Preparation

Prior to treatment and testing, the soil samples were prepared in accordance with the method described in AASHTO T87-86. This method involves:

- Air drying of samples and/or oven drying at 60ºCorless;
- Breaking up the soil aggregates by rubber covered mallet. Then, sieve analysis is performed to separate the dried soils into two groups. The first group involves preparing uniform samples for Atterberg limits, free swell, and free swell index and free swell ratio tests. And the other for compaction and California bearing ratiotests.
- Then, soil and waste ceramic powder are mixed manually to get uniform mix ratio for each.

TEST RESULTS AND DISCUSSIONS

CBR-values	Quality of Subgrade
0 – 3%	very poor sub grade
3 – 7%	poor to fair sub grade
7 – 20%	fair sub grade
20 –50%	good sub grade
> 50	excellent sub grade

Hence, the soil was found to be highly plastic expansive clay with low bearing capacity when it is soaked and high swelling potential and fell below the standard recommendations for most geotechnical construction works especially highway construction. Therefore, the soil requires initial modification and/or stabilization to improve its workability and engineering property. From the two test station I used station one for taking soil sample for stabilizing with waste ceramic powder because station one is slightly higher expansive than station two by controlling swelling test.

CONCLUSION

The following conclusions can be drawn from the results of the study/investigation carried out within the scope of the study.

1. The plasticity index slightly reduced with increased in waste ceramic powder content and curing has also an insignificant effect on the plasticity of the expansive soil.
2. The optimum moisture content decreased while the maximum dry density values increased with increment of waste ceramic powder content.

3. Free swell, free swell index and free swell ratio of the stabilized samples decreased with increasing waste ceramic powder content.
4. CBR values slightly increased with the addition of waste ceramic powder. The change in CBR value is not significant for both cured and uncured samples. Addition of waste ceramic powder alone does not improve the strength of soils due to presence of only reactive silica with low amount of calcium content in waste ceramic powder.
5. The plasticity index significantly decreased with addition of waste ceramic powder combined with lime and increased curing period. However, the addition of waste ceramic powder alone has a minor effect on the plasticity index of expansive soil.
6. The addition of lime and waste ceramic powder together led to a more decrease of the maximum dry density and increase in optimum moisture content compared to the addition of lime and waste ceramic powder separately.
7. The addition of waste ceramic powder in combination with lime improved the CBR value. The improvement is more significant when the sample is cured. Hence, combination of waste ceramic powder and lime can strongly improve the strength of the expansive soil.
8. Unlike lime in combination with waste ceramic powder the improvement achieved by waste ceramic powder alone on the poor geotechnical properties of expansive soil was limited because lower amount of calcium in the waste ceramic powder. Hence, improvements achieved with up to 30% waste ceramic powder content were not satisfactory. However, the rate of swelling and heave decreased with increasing waste ceramic powder content of stabilized expansive soil.

In this investigation waste ceramic powder stabilized expansive soil does not bring significant change for use it as a sub-grade material. Therefore, waste ceramic powder is not an effective standalone stabilizer for highly plastic expansive soils. However, waste ceramic powder plus/in combination with lime can effectively stabilize this soils. The expansive soil stabilized with waste ceramic powder plus/in combination with lime can be used as a good sub grade material. So, combining two local materials (waste ceramic powder and lime) can effectively improve the poor geotechnical properties of this soils and help in increasing land resources availability for construction projects and reduce the amount of lime needed for the stabilization purpose.

Recommendations

Based on the findings of this research, the following recommendations are forwarded: The results obtained during this investigation as discussed in the previous sections showed.

1. Waste ceramic powder as investigated in this research work can be used as a soil stabilizing material in combination with lime with economic and environmental benefits. Therefore concerned bodies different ceramic industries and government entities should be made aware about this potential soil stabilizing material and promote its standardized production and usage.
2. The Ceramic industry in collaboration with higher education organizations in the country should work together and establish a research team to further study the use of waste ceramic powder as a soil stabilizing material on different types of soils.
3. When pavement layers are treated with cementations stabilizers in Balasore, Odishapia, good quality materials should be used and attention needs to be given to construction procedures such as compacting pavement layers and curing properly.

The following topics are recommended for future studies

The stabilizing potential of waste ceramic powder from different sources like Tabor ceramic, Balasore, Odisha-ceramic, Arerty industrial park and the coming new industries should be studied.

- Stabilizing soils with cement and waste ceramic powder on different types of soils.

- Stabilizing soils with cement kiln dust and waste ceramic powder on different types of soils.
- Stabilizing soils with waste ceramic powder and marble waste dust on different types of soils.
- Stabilizing soils with cement, lime and waste ceramic powder on different types of soils.

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Table 1 Index and Engineering Properties of Stabilized Soil.

WCD (%)	LL (%)	PL (%)	PI(%)	FS (%)	MDD (g/m^3)	OMC (%)	CBR (%)
0	71	32	39	117	15.6	20.4	1.6
5	65	29	36	108	15.8	19.8	1.8
10	54	26	28	101	16.1	19.4	2.1
15	51	24	27	67	16.5	19	2.5
20	47	22	25	52	17.2	18.5	2.8
25	43	20	23	44	17.5	18.2	3.5
30	35	18	17	36	18.1	17.6	4.1

Table 2: Geotechnical properties of the natural soil for station 1.Below 1m from NGL

Property	Quantity for Station one
Percentage passing No.200 sieve, %	90.5
Liquid limit, %	106.5
Plastic limit, %	44
Plasticity index, %	64.5

AASHTO soil classification	A-7-5
Specific gravity	2.70
Free swell, %	140
Maximum dry density, g/cm3	1.29
Optimum moisture content, %	32.5
Soaked CBR value, %	1.02
Unsoaked CBR value, %	19.5
CBR-swell,%	9.2
Colour	Grayish black

Table 3: Geotechnical properties of the natural soil for station 1.Below 1m from NGL

Property	Quantity
Percentage passing No.200 sieve, %	88.74
Liquid limit, %	100
Plastic limit, %	43
Plasticity index, %	57
AASHTO soil classification	A-7-5
Specific gravity	2.7
Free swell, %	127.5
Maximum dry density, g/cm3	1.32
Optimum moisture content, %	36
Soaked CBR value, %	1.4
Unsoaked CBR value, %	18.4
CBR-swell,%	9.2
Colour	Grayish black

Figure 1: Soil Sample from Station One.

Figure 2: Soil Sample from Station Two.

Figure 3: Location of Study area and source of Waste Ceramic Powder. (Source Balasore, Odisha)

Figure: 4 overview of thesamplestation

Figure:5 Views from waste ceramic powder from disposedsite.

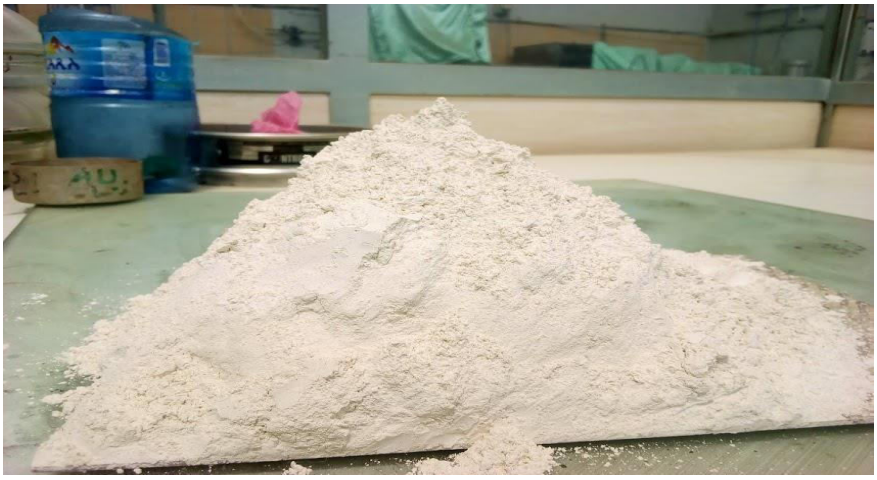

Figure 6: Lime Powder.

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RESEARCH ARTICLE

A Semantic and Shared Prospects Neural Network based Energy Consumption Prediction

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ABSTRACT

The growth of development inside the world, in the field of production, economy and growth over recent years has provided surplus amount of energy exchange between the communities combining all the natural resource power exhibitor. In this span of time humans are dependent upon energy exchange between the products and environment. Natural source of energy has been exploited over ages. So, in this paper we have come up with an idea of energy exchange and consumed prediction system through neural networks via industrial statistical data. The output shown here states all the results of prediction model and its validation. To clarify the uncertainty in the prediction model; vector regression in terms of nonlinear data regression problem is often used. The prediction model can access 24 hours ahead energy consumption and production by natural resources and provide the surplus amount of energy to the industrial sector and society based on the prediction.

Keywords: Bagging Technique, Bootstrap Technique, Root Mean Square Technique, Support Vector Regression, Neural Network.

INTRODUCTION

The good thing about renewable energy (RE) in energy production is growing differentiated to the various proposed submissions received from various energy producing sources like oil and coal [2] [3]. World renewable energy production capacity increased by 170 GW (growth of 10%) to 2,350 GW globally, by the last of 2018. Other renewable energy sources (PV) accounted for about two hundred (485 GW) of renewable energy generation at the end of 2017 [4] [5], with an increment of nine GW (+ 25%). The module, with the competitive acquisition of Star PV systems, also seems to have a potential law for national power generation from the power supply. It is shown that the speculative models of the unambiguous base are the same, the higher the predictable accuracy of the coefficient effect is often obtained [1]. Many strategies are considered in the literature to identify differences between integration models, such as using distinctive types of prediction models. Adopting the similar type of prediction model but with completely

distinct parameters settings, or building / training an entire predictive model with completely distinct coaching sets, using these approach such as Bootstrapping Aggregating(BAGGING TECHNIQUE), Boosting, and Ad boost during this work, the dismissal process (relying on training for maltreatment of many basic models, its square measurement settings are poorly sampled by replacing the initial training database) used as shown is able to improve the performance of the forecast and is easy to use. for eg . If the lower prediction models of the ensemble square measure have been developed, an effective strategy to consolidate their predictive results is required. In general, these recent methods provide completely distinct (powerful) instruments for all basic models in accordance with the function of native predictions calculated by considering the same input patterns as well as input pattern under research, such as the closest neighbour patterns in the verification database. during this process, a mathematical strategy is adopted by enabling speculation on individual basic models because it is better to develop and better know that when a PV star prediction of a square measure has been found, this activity focuses on calculating the uncertainty that contributes to the prediction. Specifically, 3 sources of square uncertainty were analysed during this activity:

1) Uncertainty by reason of the inclusion of the model, i.e., measuring climate change errors.

2) Thanks to the uncertainty of the natural variability / theoretical of the visual process, and

3) Unpredictability arising from within the model structure and parameters.

Related Work

During this work, it is presumed that climate information (W) and therefore the corelative power generation (PE) of the Y-year PV star system are available. Accessible weather information contains approximate temperatures close to 1m and therefore international radiation. The goal of this project is to produce a brand-new way of combining 24h power forecasting in front of the PV star system, with a number of concurrent uncertainties. Specifically, the systematic approach aims to take advantage of the planned parameters, e.g. Timestamp (hours) from the beginning of the year information, that is, the written account of your time **T** on day **D** of the year [6], that the ability to predict and therefore the uncertainties associated with it can be calculated, and therefore historical weather values, collected during T on all previous days of the day D (i.e., henceforth referred to as embedded magnification), for the following 2 purposes:

i. To produce a count of PV star energy production on day D (i.e., 24-hr in advance). Specifically, this method finds input and provides output 24h pre-star PV power output, measuring the general uncertainty affecting PV star power forecasts, within the Prediction Interval (PI) style, that time relative to lower and higher power output parameters and separately, among which a certain amount of energy production is expected to have a previously defined opportunity.

ii. The enhancements within the predictive accuracy and therefore the correct measurement of the uncertainty, which shows the difference between the real / real and therefore the expected product, are important and teach the maker to choose the right plan, plan and manage the production of accessible energy sources, ensure reliable power supply, complete system, a reduced correlation of energy market performance.

The Proper use of predictable data databases, details are pre-processed as follows.

i. Negative radiation values (e.g., negative) and corresponding production values are recognized at the beginning and end of the hours; that may be an offset within the radiation sensors and a failure to convert electricity, in excess. Accordingly, the emission and as a result the values of production are set to zero.

ii. A small amount of lost radiation, temperature and productivity are recognized in other hours of the middle days; this may be due to a failure of solar radiation and heat and failure to convert electricity or the network pattern disruption, respectively. Hence, these values are kept out from the evaluation.

iii. General information is accustomed to a variation of [0 or 1] to increase the pace of training and maintaining the interaction between the given inputs and thus, to ensure the enduring integration of Neural Networks inner boundaries. Over the past few Years, many data-driven methodologies have been developed and strongly used in Photo Voltaic star power production forecasts. For Eg, Izgi et al. use the ANN degree in a low-power solar system

(6750Watt) to find out the maximum length of time that additional short / medium power forecasts are available; Malvoni et al., Has organized the Least-Square Support Vector Machine (LS-SVM) to obtain exact Solar energy power forecasts related to those which is obtained by the Radial Basis operating Neural Networks (RBFNN) literature; anatomist et al., used k-NN conversion and Support Vector Regression (SVR) astronomical Photo Voltaic power to predict in each calculated and predicted Climate condition[7] [8].

Whereas the completely distinct data-driven methodologies have been able to adequately provide PV power generators adequately, ANNs have been adopted during this work to represent an organized group, because of their simplicity, direct understanding, and because of their ability to successfully solve offline issues. However, a more integrated integration approach can also be produced by looking at other data-driven approaches such as basic models, ELM and SVM. This could be a corresponding degree of future analytical work. ANN can be a process model, originally designed and impressed by neural networks. The ANN contains many hidden neurons that are somehow connected by a limited connection that is structured in the correct input, encrypted (via H-secreted neurons) and output layers. ANN aims to capture a hidden input / output relationship (an anonymous priority), that is, the current Temperature and the past climatic condition values and therefore the corresponding Photo Voltaic energy production, respectively: provided training, X train. ANN must be produced / prepared based on the findings. In contrast, performance-based methods, such as International Weight Loss and traditional weighted weight, the weight of ANN models based on the accuracy of its prediction included in the verification data for input patterns. for example, the global weighted scale assumes that the ANN ensemble types of arches are bound (equal or not), as opposed to looking at the input pattern, based on their performance on the verification database [9][10].

Proposed System

In recent years, with the advent of the energy crisis and the ongoing environmental crisis, the structure of energy use is changing dramatically. The rate of renewable resources decreases year by year, and the rate of renewable energy will increase steadily. Therefore, it is necessary for the city to accurately predict the formation of power, to create affordable development. With growing limitations supporting energy demand forecasting and future energy planning, this paper introduces Neural Network to integrate Associate in Nursing to develop a power forecasting model. The connection between these elements and the power structure is complex. Therefore, it is very difficult to determine the Nursing Meeting the right relationship between those influential factors and the power structure. The tendency of the energy structure is studied by the Neural Network theory, in line with the historical knowledge of the structure of energy consumption. In this paper is given the concept of abuse NN Model technique for predicting electricity consumption. Predicting the use of force is an important function of mercantilism power organizations. Guessing should be as accurate as possible as the accuracy of the forecast translates directly to the company's profits. With this paper we have a practice of comparing the Associate in Nursing accommodate the linear model with evolving model.

Data Evaluation

Analysis of experimental information is highly dependent on explicit visual perception and interpretation. whereas applied mathematical modelling provides a "simple" low-level image of the relationship between variables, often requiring high-level data on the mathematical strategies used and mathematical principles. Visualization and graphs of a local unit are often descriptive and easy to come up with, so you will quickly explore many other aspects of the database. The goal of the last word is to find simple summaries of information that inform your questions. it is not the conclusion within the pipeline of information science; however, it is still relevant. Features of alpha graphs are produced with the local unit of EDA different from the final graphs [14] [16]. You may generate multiple alpha graphs, if not, during the data analysis period. In these graphs, you will find yourself publishing one or two in the final format. One purpose of the EDA is to improve the confidential understanding of data, so all your code and graphs should be included in that purpose [11][12]. The required information that you can simply add if you would publish graph seems unnecessary in the graph degree alpha graph. Alpha information analysis can be a way of analysing.

If natural law supports, the distribution of certain information. Alpha knowledge Analysis (EDA) abuses the visual methods of obtaining the structure of content within the information. The methods of visual analysis used in large-scale selections can be traced back many centuries, because of which the human eye and brain have a strong cognitive ability to acquire such a right in the experiment of knowledge. And visual analysis to play a range of human models within the process of special thanksgiving process to show information. Analysts regularly perform alpha data analysis, and then the location is sure to select a property value mode or random quantity; Alpha information Analysis can also show sudden deviations from the standard model that is not possible. The main purpose of alpha analysis Information not only applies a lot of elements to the knowledge structure but additional flexible reactions to the open mode of the latest analysis step [10].

Feature Engineering

Engineering Feature Data that gains human gamma globulin live with bow many details contributes to the presence of the or the absence of the classification call in any class. Human gamma globulin also calls its value once the roll is for each category and the gift name is a number. The Separate Feature Methods the feature gives bigger scores to different options and reduces scores to flexible options. Ambiguity live (AM) selection strategies can assign the following points to options that appear to be organized in one category. The AM rating is calculated for each factor [13]. This method assigns points to one if the feature is clear; otherwise, it gives points up to zero. Given one limit and supported by this threshold, options with AM points below that threshold those square options are filtered and therefore options with AM points above that square boundary used for the study component. Feature data gain calculates the entropy difference whether reflected in the text or not, Great data gain, great contribution to text symbols [13] [15]. High-gain data features are selected as a feature. Space reduction is widely used in advanced data analysis, visual imagery, and modelling. Only one in between ⌈ best ways} to reduce space through feature design; the person selects only those input values that contain the relevant data for the exact resolution.

Feature Extraction can be an additional standard procedure when a person attempts to bring in a change of input location to a lower mathematical space that stores most relevant information. Output feature and techniques for selecting a square measure used alone or together for the purpose of improving performance such as countless accuracy, visual imagery and comprehension of the information being studied [20]. Generally, options will be categorized as appropriate, non-essential, or undesirable. In feature choice method set from offered square measure information options selected method of reading law. The most efficient set that has the smallest various sizes that all contribute to accurate reading.

Model Prediction & Evaluation

The formula creates an error in restoring the neural network to the supervised reading using the descending gradients method. This type of NN is made up of neuron-like substances, called nodes. The node area unit is organized by layers. Through the operation of the input and encrypted layer, the hidden and exit layer, NN transmits the installation details to the hidden layer notes, as well as the hidden layer details to the output nodes. Results will be available in the output layer [19] [22]. NN networks consist of 2 items, that area unit forward and backward distribution. The unit of data location measured in the network in the installation layer. At the beginning of the study, the unit of weight for the connection area was started with a little random information. Within a further diffusion study, the state of neurons in each layer will only affect the future coating layer.

There are no connections between neurons within the same layer. If the output layer does not receive the expected output, that is, there are local unit errors between the expected output and the output, then the course of education changes the distribution return method [17][18]. Analysis of the forecast model to predict future unknown power consumption. So, we tend to take 1-week data as a coaching set, as well as a different week's information as a test set, the number of training and testing samples, respectively. And before training details, they must get used to being separated [19]. As we tend to show, the importance of a planned planning approach lies in its capacity to provide additional 24h-forward prediction of PV star for power generation and to provide intermittent periods of PV power

generation to stabilize uncertainties that affect PV star prediction. Effective, enhancements within the accuracy of the forecast and the correct measurement of the unpredictability, which shows the dissimilarity among the real and the predicated product, are often important and teach the maker to choose the right setting, planning and management of accessible energy production, ensure we have shared the degreed of the operation of the energy market.

The effectiveness of the planned approach in relation to:
i) The prediction of production area, is indicated in terms of 3 well-known performance metrics, mainly Root Mean Square Error (RMSE), Mean Absolute Error (MAE), and Minimum Mistake Error (MME); and
ii) Uncertain price calculations related to institutional assumptions, indicated in relation with two known performance metrics, in particular the probability of PI Coverage and PI dimension.
For comparative relation, logical perseverance model and two different square measurement models seek to ensure the appropriateness of the systematic approach in providing appropriate predictions of power generation PV for the ASU star PV system.

RESULTS AND DISCUSSION

The formula creates an error in restoring the neural network to the supervised reading using the descending gradients method. This type of NN is made up of neuron-like substances, called nodes. The square measure of nodes is arranged in layers. With active activation between the input and hidden layer, the hidden and exit layer, NN transmits the insertion details to the hidden layer notes, as well as the hidden structural details to the output nodes. Results will be available in the output layer. Once the system has been provided the train database will use many image process techniques for that. Accuracy has greatly improved. The accuracy has been achieved exactly ninety achieved with a sample set of ten models and exactly seventy-five by twenty models within the sample. This set model predicts the prediction of electrical power (PV) before 24 hours which can be used to predict the maximum amount of potential energy. Therefore, we will conclude because the size of the sample set will increase the accuracy decreasing. We will obviously challenge that by training the system on a much larger database can use them in the future so that the work can reap the rewards. This structured model is of great benefit to large industries in that renewable energy is used more frequently and therefore has made less expensive profits in industry and crop production. This proposed model has produced a test graph of the PI intervals of photon particles responsible for power forecasting. The graph below shows the time of Photon vs EST by hours indicating how many photon particles are produced in the observed hours, indicating that between 10 a.m. to 3 p.m. the graph shows the height of the generation of photon particles. During this period of time, it produced more photon particles. Several distortions occurred at the same time period as shown in figs, that the multi-line constraints are shown when the photon value depends on the expiration time. As time goes on the photon particles also increase depending on the sunlight source.

CONCLUSION AND FUTURE WORK

In this paper, compile an advanced building guessing models planned. 1st model used to predict energy demand. Based on the result, an improved residual model was developed to modify it into a more accurate prediction.

- Excessive use of unstructured information
- Completion of feature engineering
- Ability to Deliver High Quality Results

After that supported by the analysis of the power supply system, the misalignment of the NN element, the power structure is expected. Finally, with increasing margins supporting the prediction of energy demand and therefore the future energy development, the model for the proposed improved infrastructure is approaching. In addition, a strategy for calculating the potential for flexible matrix variables is planned [21]. Taking power generation and the use of power as a mathematical analysis, not only recognized the connected problem of speculation and problems,

but the function of simple integration, precise balance, has shown that neural networks have a remarkable ability to function. Extensions to separate servers for information candles in directing the energy saving algorithm system to save energy consumption. Best offered at this stage of the event is a re-engagement approach to a comprehensive integration approach to provide accurate predictions of 24h star PV power output up front and to measure related uncertainties within the forecast period.

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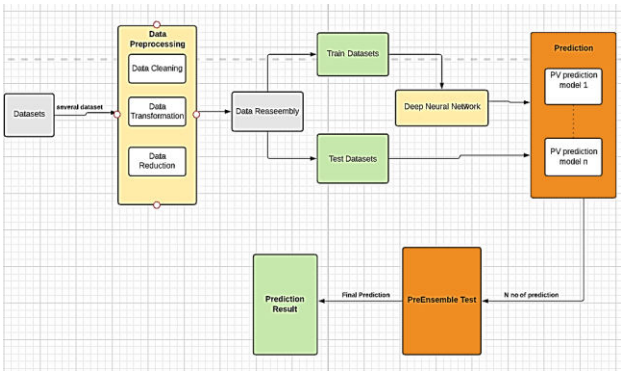

Figure 1. Workflow of Proposed System

	FR10	year	month	week	day	hour	time
0	0.0	1986	1	1	1	0	1986-01-01 00:00:00
1	0.0	1986	1	1	1	1	1986-01-01 01:00:00
2	0.0	1986	1	1	1	2	1986-01-01 02:00:00
3	0.0	1986	1	1	1	3	1986-01-01 03:00:00
4	0.0	1986	1	1	1	4	1986-01-01 04:00:00

Figure2. Pre-processed Longitude Dataset

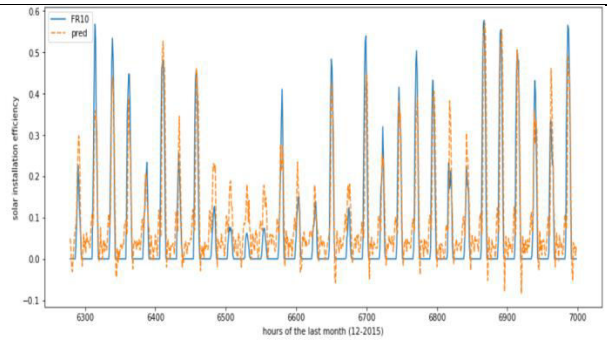

Figure 3. Base Line Prediction vs Real Values

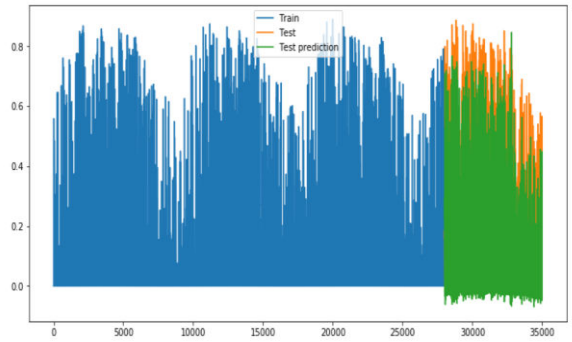

Figure 4. Exploratory Graphs of PI interval

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RESEARCH ARTICLE

Possible Steps to Enhance Battery Cycle for Electric Vehicle

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ABSTRACT

This paper discusses completely different ways to improve the efficiency and life of an electric vehicle. In electric vehicle, lithium-ion batteries play a major role and are extremely useful. This paper describes different energy storage techniques with battery management system in lithium-ion (Li-ion) battery configuration of parallel battery, battery charging with simulation and approaches to enhance the overall battery efficiency, capacity and lifespan. we have a tendency to describe the structure and implementation of an innovative BMS and sensors shall monitor every battery cell by measurement of voltage and temperature. Within the future the sensors will be applied in lithium batteries for electric or hybrid vehicles. Battery cycle check results are used for initial model structure and it is transferred to the look & simulation of BMS with the help of Simulink. The simulation results are valid by experimental results and MATLAB/Simulink simulation.

Keywords: Electric vehicle, Li ion battery, efficiency, battery management system (BMS) , Matlab.

INTRODUCTION

The global pollution is on rise and so as to shield human living environment and source of our energy. One among the trouble is that introduction of Electric Vehicles (EV). The battery is the elementary component of EV. Li-ion chemistry is the battery technology of selection because of its good energy density, good power rating and charge discharge efficiency in periodical energy flow system. The battery management system is answerable for monitoring and controlling the practicality of every single cell continuously to stay whole battery in best condition all the time. The acquisition watching includes the voltage, current and temperature. It additionally monitors its state of charge (SoC) and state of health (SoH).

But with all this benefit comes the necessity for careful BMS to make sure safe operation and accepatable durability for example temperature and voltage ought to stay inside acceptable limits to avoid premature degradation as ought to power delivery and acceptance.

This review includes the battery cell monitoring, state estimation, charging and discharging control, temperature control, fault analysis and protection schemes to boost the performance of battery for EV applications and can be simulated with MATLAB/SIMULINK. The complete model of BMS and every one purposeful block of BMS are enforced in Simulink toolbox of MATLAB.

Battery Cell

The battery cell is in the form of battery pack that is employed in the EVs. The battery cells combining to form a module and such modules collectively form a battery pack. As the batteries are fundamentally a storage medium consisting of two electrodes in an electrolyte. This electrolyte provides a medium for the exchange which produces the electricity. Each battery has their own advantages and disadvantages, though recent innovations in Li-ion batteries have propelled them to become the market leader for use in most handheld and portable electronics as well as EVs. This is because of their specific energy (Wh/kg), cycle life, high efficiency and safe as compare to batteries. They have their drawbacks which include their high cost, the need of complex safety and the monitoring systems. There are various battery technologies available for EVs.They are summarized as follows:

Lead Acid Battery

Lead acid battery is the earliest type of rechargeable battery. It having a very low energy- to - weight ratio and a low energy- to- volume ratio, it has ability to supply high surge currents means that the cells have a large power- to-weight ratio. These features and having low cost, make them attractive to use in motor vehicles to provide the high current required by motors.

Nickel-Metal Hybrid Batteries

Nickel-metal hydride batteries are now considered a relatively mature technology. While less efficient (60–70%) in charging and discharging than even lead- acid, they have a specific energy of 30–80 Wh/kg, far higher than lead-acid. When used properly, nickel- metal hydride batteries can have exceptionally long lives, as has been demonstrated in their use in hybrid cars and in the surviving first- generation NiMH Toyota RAV4 EVs that still operate well after 100, 000 miles (160, 000 km) and over a decade of service.

Zebra or Sodium Nickel Chloride Battery

The sodium nickel chloride battery which uses a molten sodium chloroaluminate ($NaAlCl_4$) salt as the electrolyte. A relatively mature technology, the Zebra battery has a specific energy of 120 Wh/kg. Trials with the first sodium-nickel chloride or zebra batteries in vehicles indicates that the pulse power capability of the battery needed to be improved towards the end of the discharge. A research program led to several design changes to improve the cell which is in combination, has improved the power of the battery to greater than 150 W kg at 80% depth of discharge.

Lithium-ion Batteries- 1)Lithium Cobalt Oxide (LCO)

The battery consists of a cathode as cobalt oxide and a anode as graphite carbon. The cathode has a multi-layer structure and during discharge lithium ions move from the anode to the cathode and also the flow reverses on charge. Batteries produced with $LiCoO_2$ cathodes which has very stable capacities, but have lower capacities and power than those with cathodes as compare to nickel- cobalt- aluminum (NCA) oxides. Issues with thermal stability are better for $LiCoO_2$ cathodes than other nickel- rich chemistries although not significantly. This makes $LiCoO_2$ batteries are very sensitive to thermal runaway in cases of abuse such as high temperature operation (>1300 C) overcharging.

Lithium Nickel Cobalt Aluminium Oxide (NCA)

The most important manufacturer of NCA batteries is Panasonic or Panasonic' s cooperation partner Tesla, as Tesla uses NCA as active material in the traction batteries of its car models. The usable charge storage capacity of NCA is about 180 to 200 mAh/g. However, the capacity of NCA is significantly higher than that of alternative materials such as lithium cobalt oxide LiCoO2 with 14 mAh/g, lithium iron phosphate LiFePO4 with 165 mAh/g and NMC with 170 mAh/g. Like LiCoO2 and NCA belongs to the cathode materials with layer structure.

Lithium Iron Phosphate (LFP)

The energy density of $LiFePO_4$ is lower than that of lithium cobalt oxide(LCO), and also consisting of a lower operating voltage. In general, lithium iron phosphate batteries do not explode or ignite. LiFePO4 batteries are safer in normal use, but they are not absolute and can be dangerous in some extreme cases. LFP contain neither nickel nor cobalt, both of which are supply- constrained and expensive. Human rights concerns have raised concerning for the use of mined cobalt in batteries for the distributed energy, home storage and also for EVs. The nominal cell of 3.2 V output, four cells can be placed in series to obtain a nominal voltage of 12.8 V. This comes close to the nominal voltage of six-cell lead-acid batteries along with the good safety characteristics of LFP batteries.

Lithium Battery Challenges

To determine the performance of the lithium-ion cells the important parameters are the operating temperature and voltage. Figure 1-1 and 1-2 shows that the cell operating voltage, current and temperature must be maintained within the area indicated by the green box labeled "Safe Operation Area" (SOA) at all times. The cell could be permanently damaged if it is operated outside the safety zone. The batteries could be charged and discharge in its distinct voltage. If the recommended voltage i.e., 4.2 V was exceeded during charging, excessive current would flow and result in lithium plating and overheating. On the other hand, overly discharging the cells or storing the cells for extended periods of time may cause the cell voltage to fall below its lower limit, typically 2.5V and this could progressively break down the electrode.

The operating temperature of lithium-ion cells should be carefully controlled because the excessively high or low temperatures could damage the battery cell. Figure 1-3 shows that the lifecycles of the battery cell would be reduced if its operating temperature falls below approximately 10°C. Similarly, their lifecycles would be reduced if the cells were operated above 40°C. Furthermore, thermal runaway would occur when the temperature reached 60°C. The thermal management system, one of the parts of BMS, must be designed to keep the cells operating within its limitation at all time. Hence, it is clear that the BMS helps to keep the operating cells within their safety zone. This could be achieved using safety devices such as protection circuits, integrated circuit (ICs)and thermal management systems.

Methods to Measure Frequency

The battery management system (BMS) could be a combination of sensors, controllers, communication, and computation hardware, with computer code algorithms designed to choose the most charge/discharge current and period from the estimation of state-of-charge (SOC) and state-of-health (SOH) of the battery pack. BMS can be outlined within the following manner:

- It need to make sure that the energy of the battery is optimized to power the product.
- It ought to make sure that the chance of damaging the battery is reduced.
- It ought to monitor and management of the charging and discharging method of the battery.

Battery management system (BMS) is that the crucial system in electric vehicle as a result of batteries utilized in electric vehicle must not be get overcharged or over discharged. If that happens, it ends up in the injury of the battery, rise in temperature, reducing the era of the battery, and generally additional to the persons exploitation it. It is additionally boost to maximize the vary of vehicle by properly exploitation the quantity of energy holds on in it.

There are different kinds of BMSs that are used to avoid battery failures. The foremost common sort may be a battery observance system that records the operational factors like voltage, current and therefore the interior temperature of the battery in conjunction with the close temperature throughout charging and discharging.

Battery management system is necessary for following reasons:

i. Maintain the protection and the reliableness of the battery.
ii. ii)Battery state observance and analysis.
iii. To control the state of charge.
iv. For reconciliation cells and dominant the operation temperature. v)Management of regenerative energy.

Functions of the BMS

Discharging Management

The main function of BMS is to stay the battery in operation in its island. The BMS should defend the cell anyplace impact throughout the discharging. Otherwise, the cell may operate out of its limitations.

Charging Management

Most batteries tend to induce broken or get reduced in lifetime once charged not suitably. For lithium battery charger a 2-stage charger is used. The first stage is termed the Constant Current (CC) during that the charger outputs a continuing current to charge the battery. Once the battery gets nearly full the second stage is known as Constant Voltage (CV) stage is employed throughout that continuing voltage is provided to the battery at awfully low current. The BMS ought to confirm each voltage and current.

Cell Leveling

Cell balancing could be a methodology of compensating weaker cells by equalizing the charge on all cells within the chain to increase the general battery life. chained of multi-cell batteries, tiny variations between the cells than to production tolerances or in operation conditions tends to be increase. Throughout charging weak cells could also be overstressed and become even weaker till they eventually fail, inflicting the battery to fail untimely. To trot out this downside the BMS needs to implement one thing known as cell leveling. In passive leveling the concept is that the cells with excess voltage are going to be forced discharge through a load like resistance to achieve the voltage price of the opposite cells. whereas in active leveling the stronger cells are going to be wont to charge the weaker cells to equalize their potentials.

State-of-Charge (SOC) Determination

We can consider SOC because the fuel gauge of the work unit. It actually tells the battery capability of the pack in proportion. The voltage and charge/discharge current of the pack should be monitored to predict the capability of the battery. Once the voltage and current is measured there are a great deal of algorithms which will be utilized to calculate the SOC of the Battery pack. the foremost ordinarily used methodology is the coulomb tally capability.

In the coulomb-counting methodology, this going into or initiating of battery is integrated to provide the relative value of its charge. this is often like tally the currency going into and out of a checking account to see the relative quantity within the account.

SOC = Total Charge Input / most capability

State-of-Health (SOH) Determination

The capability of the battery not solely depends on its voltage and current profile however additionally on its age and operative temperature. The SOH measurement activity tells United States concerning the age and expected life cycle of the battery based on its usage history. this manner we are able to shrewdness abundant the mileage (distance coated once full charge) of the work unit reduces because the battery ages and additionally we are able to grasp once the battery pack ought to get replaced. The SOH ought to even be calculated and unbroken in track by the BMS.

Thermal Control

The life and potency of a Li battery pack greatly depends on the operative temperature. The battery tends to discharge quicker in hot climates compared with traditional room temperatures. Adding to the current the consumption of high current would any increase the temperature. This entails a Thermal system (mostly oil) in an exceedingly battery pack. This thermal system ought to solely be able to decrease the temperature however ought to even be able to increase the temperature in cold climates if required. The BMS is accountable for measurement the individual cell temperature and management the thermal system consequently to take care of the temperature of the battery pack.

Communications

The communications perform of a BMS could also be provided through a knowledge link utilized to monitor performance, log data, give set system parameters. The perform might also be provided by a communications channel carrying system management signals. The choice of the prescript isn't determined by the battery; instead, it's determined by the appliance of the battery. The BMS utilized in electrical vehicles should communicate with the higher vehicle controller and also the motor controller to make sure the correct operation of the vehicle. There are 2 major protocols utilized by the BMS to communicate with the vehicle: through the data bus or the controller area network (CAN) bus. Data buses have the RS232 affiliation and EIA-485 (also known as the RS485connection). The trade normal for on-board vehicle communications is that CAN bus, that is a lot of ordinarily utilized in vehicle applications.

Building Blocks of Battery Management System

Power electronics takes care of the assorted power conversion processes from the plug to wheel. The various power electronics converters utilized in EVs

AC-DC converter- The EVs conventionally charged from an associated AC outlet. However, the batteries charge solely with dc power. Hence, the AC-DC converter helps in changing the ac power to dc power, not only batteries, dc power is needed by several electronics loads like lights, heater within the EVs and therefore it is a large network of power.

DC-DC converter- The dc power from the AC-DC converter is commonly variable and unsteady. Hence, it is essential to create the dc power constant and stable. In a DC-DC converter, it is necessary to supply the isolation between input and output. This makes sure that the power electronics converters are safe from any reverse flow of current.

DC-AC converter- The ac power is important to drive the electric motors in EVs. Hence, another DC-AC converter is important to convert the dc power from DC-DC converter to ac power. The ac power may be single-phase or three-phase relying upon the kind of motor used.

AC-AC converter- This converter needs to adjusting the frequency of ac power. The electric motors once needed to operate with variable speed supported frequency may use this converter. There are wide areas of analysis in power electronics to be used in EVs. The converters should be compact and occupy terribly less area. This helps in providing additional interior spacing inside the vehicle; the converters should be lightweight. A heavier converter burdens the electric motors to hold more current to gain high speed. The heat management in power electronics is also very vital and process of ventilation facility has to offer.

Simulation

The Simulink model has been designed and implemented to overcome the challenges mentioned above. Equivalent circuit to represent the dynamic behavior of battery call this is important since BMS have any controller needs to be tuned to the dynamic of plant it is connected to. The circuit also provides safe operation, performance and also monitors cells voltages, balances the SOC of individual cells and estimates the overall SOC of the battery. The behavior of the thermal and the electrical circuit has been examined relating to that the nature temperature of

temperature change and the SOC of the battery have been plotted against various intervals of time. It helps to determine the current state and life span of the battery. Results obtained are as shown below:

The above graphs show the result of process taking place during the passive cell balancing of the battery which is connected to the system. A battery is a collection of cells. Each cell of the system is connected to a separate SOC and a separate subsystem from where we get the different variation in temperature. In this system the subsystem is consisting of three temperature sensor which is connected to three different converters giving three different curves of temperature with respect to time. Similar is the case of SOC which is connected to three different SOC's. The graph of SOC shows the result of three different SOC's i.e., SOC1, SOC2 and SOC3 which is indicated by blue, pink and red color respectively with respect to time. The temperature graph has three graphs of T1, T2 and T3 indicated by orange, blue and indigo color respectively with respect to time.

CONCLUSION

In this way we are developing the system model for battery management in electric vehicle by controlling the crucial parameters such as voltage, current, state of charge, state of health, state of life, temperature. It is every important that the BMS should be well maintained with battery reliability and safety. This present paper focuses on the study of BMS and optimizes the power performances of electric vehicles. Moreover, the target of reducing the greenhouse gases can greatly be achieved by using battery management system.

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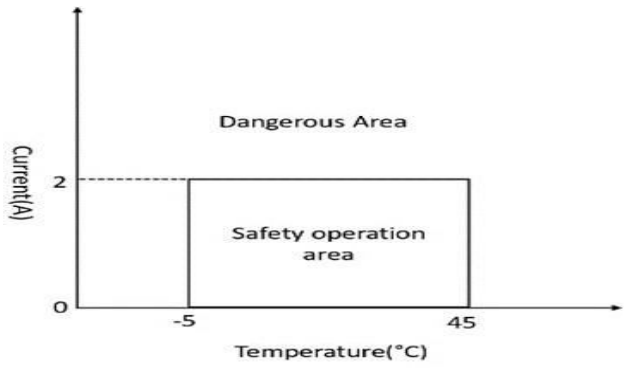

Fig.1.Lithium ion cell operation window (current)

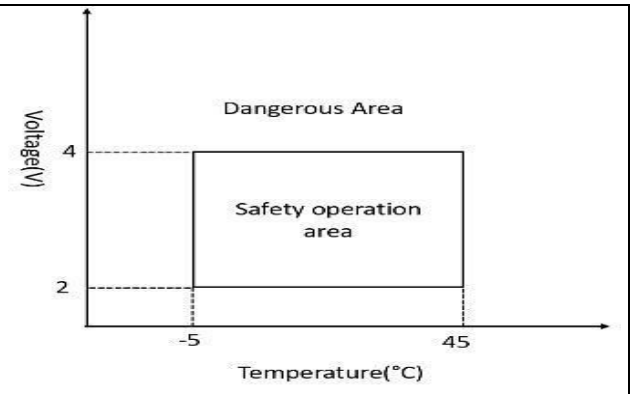

Fig.2.Lithium ion cell operation window (Voltage)

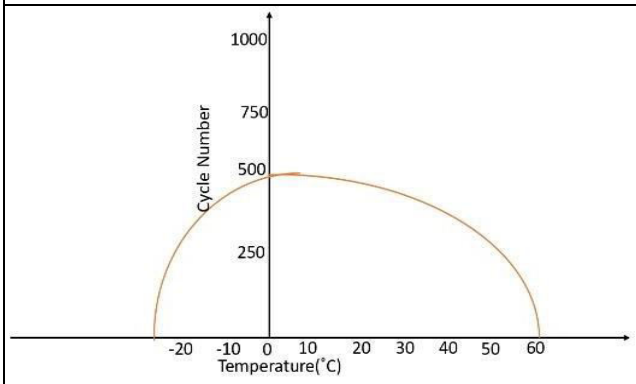

Fig.3.Lifecycle versus operating temperature in Li-ion cells

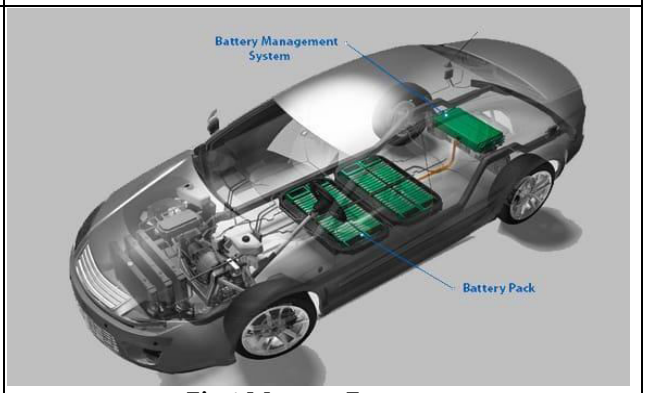

Fig.4.Measure Frequency

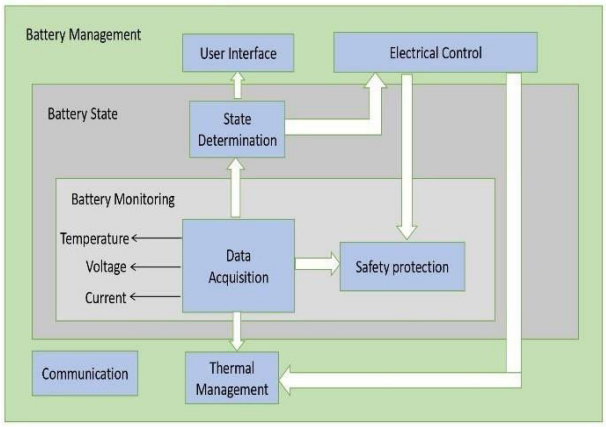

Fig.5.Battery Management system

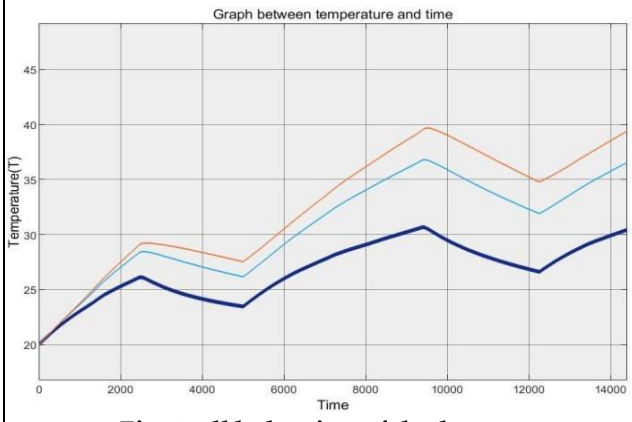

Fig.6.cell balancing of the battery

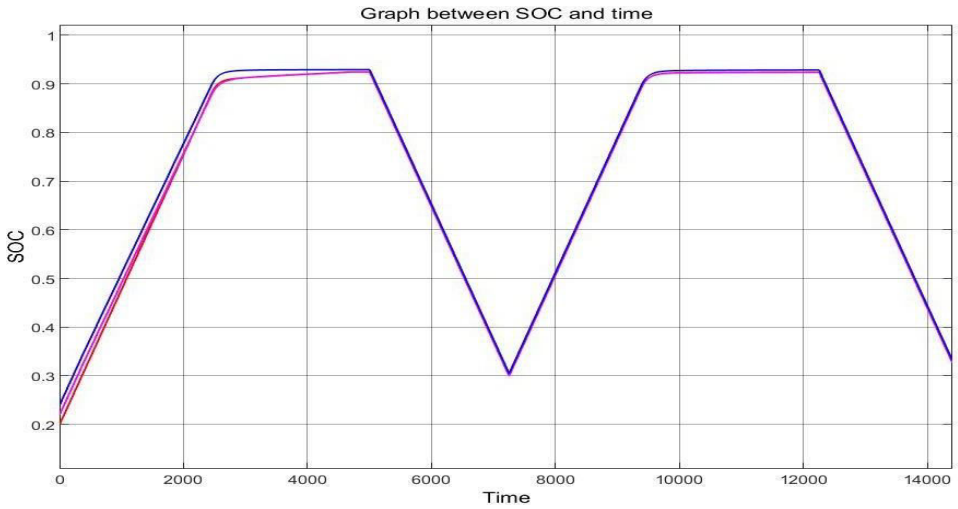

Fig.7.cell balancing of the battery

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RESEARCH ARTICLE

Study on Impact of Photoperiodic Regimes on Rhythmic Changes of Selected Bio-Molecules during Embryonic Developmental Stages of *Bombyx mori L*

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ABSTRACT

The photoperiodism is a sensitive indices stimulating the active synthesis of the metabolic reserves to facilitate the developmental progression of the embryonic stage. In the present investigation, the bivoltine silkworm breeds SK6XSK7 (single hybrid) was selected to study the impact of photoperiodic response during the embryonic stages and to understand the changes in the total carbohydrate and total protein content. The quantum of carbohydrate and protein content showed favourable response in the photoperiodic schedules. However, LD 16:08 revealed greater impact and proportionately more in quantum protein content compared to LD 14:10. The level of synthesis of protein under imposed photoperiodic schedules were limited from day 1 to day 5 compared to 6th to 7th day showed active accumulation for the sequential stages of embryonic development.

Keywords: Photoperiodism, Silk worm, Metabolicand Embryonic stage

INTRODUCTION

Sericulture, in India today, is being identified as a component of integrated rural occupation. Sericulture has several advantages over other integrated agriculture practices and is expected to improve upon the living standard of the marginal and middle order farmers. India is one of the oldest countries practicing sericulture and rearing of multivoltine silkworm as a tradition of the country. The mulberry silkworm, *Bombyx mori* L has been the source of row silk since time immemorial. Thus, its cultivation and domestication too dates back to that period.

Therefore, there is a large scope for the increased production of quality silk to cater to the need of power loom which could be possible only through the successful introduction of bivoltine sericulture on large scale coupled with large scale modern reeling unit. The evolution of bivoltine breeds suited to farmer's conditions, i.e., inferior management levels, poor quality mulberry leaves and fluctuating microclimatic conditions thus become necessary (Asoke Banerji 2011-12). Newly laid eggs of silkworm are composed of protein (10%), lipid (8.5%), glycogen (2.55), chorion(18%) and water (60%) (Yamashita and Irie, 1980). More than 95% of the total protein is yolk protein, vitellin 40%, 30kDa protein 35% and egg specific protein (ESP) 20%.These proteins are quite different from each other in their physiochemical and biological properties (Zhu *et al.,* 1986).

From its earliest origins, life on earth has evolved in the presence of a daily cycle of daylight and darkness. This environment rhythm of recurring of alternation of illumination and darkness is the earth's natural photoperiod. Photoperiod has played an extremely important role in biological history; virtually every major group of eukaryotic organisms has evolved the ability to utilize the daily cycle and seasonal progression of day length as source of environment information. The effects of photoperiod on the organism have to do not only with the temporal organization of the internal processes that characterize the living system. The diverse ways in which organism are influenced by photoperiod are the subject matter of the biological field known as photoperiodism.

Watanabe (1918, 1919, 1924, 1928) and Kogure (1933) reported that the quantitative characters of silkworms such as cocoon weight, shell weight, shell ratio, pupal weight, silk weight, filament thickness and survival rate of larva in a known environment are of paramount importance in sericulture. Many of these characters are not only controlled by genes but also influenced by environmental factors such as nutrition, incubation, temperature and photoperiod.

MATERIALS AND METHODS

For the present investigation two popular single hybrid races namely (SK6×SK7) and double hybrid races (FC2×FC1) were used. The required silkworm eggs were obtained from the germplasm bank, DOS in sericulture science, university of Mysore, Manasagangothri, Mysore. Disease free laying of each race was maintained in separate plastic trays provided with wet foam rubber pads to provide required temperature (25-28^{0}c) and humidity (80%) to the developing eggs. The eggs are then subjected to different photoperiodic schedules in a BOD incubator with LD 14:10 and 16:08. The eggs were used to estimate the level of carbohydrate and protein and compared from the day of release till the day of egg hatching.

Protocol for Estimation of Total Carbohydrate Level

The carbohydrate content in the silkworm eggs were estimated according to anthrone method (Sadasivam and Manickyam, 2008). Theknow quantities of eggs were homogenized using mortar and pestle in 5ml of 10% TCA solution. The mixture was then centrifuged. For 1ml of supernatant 5ml of anthrone reagent was added and subjected to boiling water for 10-15 minutes for colour development. The test tubes were cooled at room temperature. The intensity of the colour was read at 440nm against blank in a spectrophotometer.

$$\text{Amount of carbohydrate in mg/ml} = \frac{\text{Optical density} \times \text{mg of standard}}{\text{Optical density of std.} \times \text{mg of sample taken}} \text{x1000}$$

Protocol for the Estimation of Protein Level

The protein content in the silkworm eggs were estimated according to Lowry *et al.'s* (1951) method. The known quantities of eggs were homogenized using mortar and pestle in 10ml of tris buffer. The mixture was then centrifuged. To 1ml of the supernatant 5ml of protein reagent is added and contents are mixed well and kept for a10 min at room temperature. After 10min 0.5ml of follin's reagent is added and kept for 30 min at room temperature for

colour development. The intensity of the colour was read at 660nm against blank in a spectrophotometer. BSA was used as reference standard.

$$\text{Amount of protein in mg/ml} = \frac{\text{O.D of sample} \times \text{mg of standard}}{\text{O.D of std.} \times \text{mg of sample}} \text{x1000}$$

RESULTS

Results of the investigation on **"**The Impact of photoperiodic regimes on rhythmic changes of selected bio-molecules during embryonic developmental stages of *Bombyx mori L"*are presented in the following paragraphs:

The present study was conducted in relation to the development stages in the carbohydrate and protein content during the embryonic stage imposed to different photoperiodic schedules under an incubator from the day of release of the disease free layings from the refrigerator till the day of hatching. There are two longer photoperiodic schedules namely LD 14:10 and LD 16:08 under controlled condition at temperature of 25^0 C maintained throughout the developmental period.

Impact of Photoperiod on Selected Bio-Molecules: The impact of the photoperiodic regimes augmented during the sensitive indices of the light influenced a maximum extent over a period of a progressive consistent development in protein and carbohydrate.

Proteins

In single hybrid (SK6×SK7):

The pattern changes in the expression of protein level in the embryonic stage of single hybrid race maintain more or less stable concentrations with a marginal difference of 1% from 1st day to 4thday (1.82, 1.25, 1.20 and 1.05 in LD 14:10 and 2.07, 1.60, 1.91and 1.22 in LD 16:08) but on 5th and 6th (7.01 and 12.46 in 16:08 and 5.81 and 1.05 in LD 14:10) day a proportional level of protein arose almost 2 folds as influenced by 16:8compared to 14:10. A reversible change of decrease in the synthesis of protein level was observed in 16:8 and 14:10 from 7th to 10thday (6.06, 5.80, 5.20 and 2.47 in LD 14:10 and 11.00, 7.93, 7.53 and 3.42 in LD 16:08. (Table 1and fig.1).

In the double hybrid (FC2×FC1)

In this race protein maintained a more or less stable concentration with a marginal difference of 1% from 1st to 10th day (1.42, 1.03, 3.98, 2.93, 3.22, 3.85, 2.70, 2.88, 3.66 and 6.09 in LD 14:10 and 2.43, 2.47, 3.83, 4.84, 6.52, 7.09, 7.19, 7.53, 5.90 and 8.12 in LD 16:08) as the influence of 16:8 compared to 14:10. A reversible change in the active synthesis of protein level on 3rd day (3.90) in the 14:10 ratio was favoured as an effective stimulus that affects the level of protein. (Table 2 and fig.2).

Carbohydrates

In single hybrid (SK6×SK7):

The pattern of change in the expression of carbohydrate level in the embryonic stage of single hybrid racemaintain a more or less stable concentrations with a marginal difference of 1% from 1st day to 8th day (2.56, 1.86, 0.60, 1.78, 1.71, 1.12, 0.59 and 3.11respectively in LD 14:10 and 0.64, 0.62, 1.20, 1.18, 2.27, 3.37, 2.35 and 1.86 respectively in LD 16:08) but on the 9th and 10thday(3.29 and 2.06 in LD 14:10, 5.92 and 6.16 in LD 16:08) a proportionate level of carbohydrate arose almost 2 folds as influenced by LD 16:08 compared to LD 14:10. A reversible changes in the active synthesis of carbohydrate level in the LD 14:10 and 16:08 are observed in day 1st, 2nd, 4th and 8th(2.56, 1.86, 1.78 and 3.11 in LD 14:10 and 0.64, 0.62, 1.18 and 1.86 in LD 16:8). The LD 14:10 rate is most favoured as an effective stimuli that effects the level of carbohydrate where as 3rd,5th and 7thday (0.60, 1.71 and 0.59) the LD 16:08 facilitates the active cellular carbohydrate level over a period of development and it a reverse phenomena switch over due to the impinging of photoperiodic stimuli.(Table 3and fig.3).

In the double hybrid (FC2×FC1)

In this race carbohydrate maintain a more or less stable concentrations with a marginal differences of 1% from 1st day to 6th day (3.75, 0.64, 1.83, 2.39, 0.59 and 3.51 in LD 14:10 and 1.88, 3.21, 2.44, 2.99, 1.18 and 4.09 in LD 16:08) but on the 7th,8th and 9th day (6.81, 9.38 and 8.16 in LD 14:10 and 8.97, 7.79 and 4.76) a proportionate level of carbohydrate arose almost 2 folds as influenced by LD 16:08 compared to 14:08. A reversible changes in the active synthesis of carbohydrate level in the 14:10 and 16:08 are observed. On day 7st, 8th and 9thday (6.81, 9.38 and 8.16) the LD 14:10 ratio is most favoured as an effective stimuli that effects the level of carbohydrate, whereas on 7th day and8th day (8.97 and 7.79) the LD 16:08 facilitates the active cellular carbohydrate level over a period of development and in a reverse phenomena switch over due to the impinging of photoperiodic stimuli.(Table 4 and fig.4).

DISCUSSION

The result on "The Impact of photoperiodic regimes on rhythmic changes of selected bio-molecules during embryonic developmental stages of *Bombyx mori* L"is presented in the following paragraphs:

Impact of Photoperiod on Selected Bio-Molecules

Photoperiodic regimes augmented during the sensitive indices of the light influenced a maximum extent over a period of a progressive consistency on selected bio-molecules (protein and carbohydrate).These results are in conformity with those of Kobayashi *et al*., (1986) who reported that the environment is dynamic and hence brings about propounded changes in the physical and biotic factors dominating the expression of commercial characters in silkworm. Similar trend was noticed by Muller (1960) that metabolic pathways are the key events in the maintenance of metabolic energy for the active functioning of cell is largely based on the photoperiod and temperature.Tsuchida and Yashitake(1979),Yamashita and Hasegawa (1974).

Protein

In single hybrid (SK6×SK7):

The pattern changes in the expression of protein level in the embryonic stage of single hybrid race maintain more or less stable concentrations with a marginal difference of 1% from 1st day to 4th day but on 5th and 6th day a proportional level of protein arose almost 2 folds as influenced by 16:8 compared to 14:10. A steady increase in the biochemical activity is observed in diapausing eggs to meet the increasing energy demand during the process of embryogenesis, Chino(1961). A reversible change of decrease in the synthesis of protein level was observed in 16:8 and 14:10 from 7th to 10th day.

In the double hybrid (FC2×FC1):

In this race protein maintained a more or less stable concentration with a marginal difference of 1% from 1st to 10th day as the influence of 16:8 compared to 14:10. A reversible change in the active synthesis of protein level on 3rd day in the 14:10 ratio was favoured as an effective stimulus that affects the level of protein. The chemical composition of hemolymph is highly variable within same breeds and diversified among the distant breeds at different development stages, Florkin and Jeuniaux(1974).

Carbohydrates

In single hybrid (SK6×SK7)

The pattern of change in the expression of carbohydrate level in the embryonic stage of single hybrid race maintain a more or less stable concentrations with a marginal difference of 1% from 1st day to 8th day but on the 9th and 10th day a proportionate level of carbohydrate arose almost 2 folds as influenced by LD 16:08 compared to LD 14:10. A study increase in the bio-chemical activity is observed in diapausing eggs to meet the increasing energy demand during the process of embryogenesis, Chino (1961).

A reversible changes in the active synthesis of carbohydrate level in the LD 14:10 and 16:08 are observed in day 1st, 2nd, 4th and 8th. The LD 14:10 rate is most favoured as an effective stimuli that effects the level of carbohydrate whereas 3rd,5th, 7th ,6th,9th and 10th day the LD 16:08 facilitates the active cellular carbohydrate level over a period of development and it a reverse phenomena switch over due to the impinging of photoperiodic stimuli. Significant changes in carbohydrate level are noticed in diapauseing eggs, Yamashita and Hasegawa (1974). Same changes was also reported in many insects, Candy and Kilby(1961).

In the double hybrid (FC2×FC1)

In this race carbohydrate maintain more or less stable concentrations with marginal differences of 1% from 1st day to 6th day but on the 7th, 8th and 9th day a proportionate level of carbohydrate arose almost 2 folds as influenced by LD 16:08 compared to 14:08. A reversible changes in the active synthesis of carbohydrate level in the 14:10 and 16:08 are observed. On day 1st,8th and 9th the LD 14:10 ratio is most favoured as an effective stimuli that effects the level of carbohydrate, where as 2nd-7th day and on 10th day the LD 16:08 facilitates the active cellular carbohydrate level over a period of development and in a reverse phenomena switch over due to the impinging of photoperiodic stimuli. Significant changes in carbohydrate level are noticed in diapausing eggs, Yamashita and Hasegawa (1974). Same changes were also reported in many insects, Candy and Kilby (1961).

The result from the study data demonstrated that the photoperiodism is a sensitive indices stimulating the active synthesis of the metabolic reserves to facilitate the developmental progression of the embryonic stage and also observed the successive changes under imposed photoperiod regimes, where LD 16:08 revealed a greater impact and proportionately more on bio-molecules content compared to LD 14:10 in both carbohydrates and protein level of single and double hybrids.

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Table-1: Changes in the protein content of single hybrid (SK6×SK7) during embryonic development exposed to photoperiodic schedules (mg/gm) (each value is mean of three separate replications)

Days	Control	LD 14:10 (In hrs)		LD 16:08 (In hrs)	
	Mean ±SD	Mean ±SD	%Change	Mean ±SD	%Change
1.	34.75±0.10	35.38±1.05	1.82	35.11±0.06	2.07
2.	33.67±0.10	33.75±0.15	1.25	34.21±0.10	1.60
3.	30.62±1.32	30.99±0.14	1.20	31.20±0.11	1.91
4.	27.66±0.06	27.95±0.10	1.05	27.99±0.15	1.22
5.	25.22±0.13	26.68±0.43	5.81	26.98±0.14	7.01*
6.	20.17±0.12	22.29±0.12	1.05	22.68±0.11	12.46**
7.	19.26±0.06	20.42±0.07	6.06*	21.37±0.13	11.00**
8.	18.50±0.11	19.58±0.11	5.80*	19.97±0.35	7.93*
9.	17.36±0.16	18.27±0.07	5.20*	18.67±0.11	7.53*
10.	16.75±0.10	17.17±0.12	2.47	17.33±0.14	3.42

** = highly significant at 0.05% probability * = significant at 0.05% probability

Table-2: Changes in the protein content of double hybrid (FC2×FC1) during embryonic development exposed to photoperiodic schedules (mg/gm) (each value is mean of three separate replications)

Days	Control	LD 14:10(In hrs)		LD16:08(In hrs)	
	Mean ± SD	Mean ± SD	% Change	Mean ± SD	% Change
1	34.52±0.090	35.01±0.12	1.42	35.36±0.19	2.43
2	33.96±0.06	34.31±0.16	1.03	34.80±0.06	2.47
3	31.69±0.06	32.95±0.06	3.98	32.90±0.07	3.83
4	26.68±0.11	27.46±0.10	2.93	27.97±0.11	4.84
5	23.11±0.16	23.85±1.73	3.22	24.61±0.12	6.52*
6	21.79±0.11	22.63±0.12	3.85	23.33±0.10	7.09*
7	20.57±0.07	21.13±0.11	2.70	22.05±0.10	7.19*
8	19.63±0.09	20.20±0.36	2.88	21.11±0.14	7.53*
9	18.50±0.09	19.18±0.09	3.66	19.60±0.07	5.90*
10	17.16±0.10	18.20±0.09	6.09*	18.55±0.06	8.12*

** = highly significant at 0.05% probability * = significant at 0.05% probability

Table-3: Changes in the carbohydrate content of single hybrid (SK6×SK7) during embryonic development exposed to photoperiodic schedules (mg/gm) (each value is mean of three separate replication)

Days	Control	LD:14:10 (In hrs)		LD 16:08 (In hrs)	
	Mean ±SD	Mean ±SD	% Change	Mean ±SD	% Change
1.	13.00±0.25	13.33±0.68	2.56	13.08±0.38	0.64
2.	13.42±0.38	13.67±0.38	1.86	13.50±0.68	0.62
3.	13.92±0.50	14.00±0.52	0.60	14.08±0.63	1.20
4.	14.08±0.25	14.33±0.50	1.78	14.25±0.63	1.18
5.	14.67±0.50	14.92±0.76	1.71	15.00±0.25	2.27
6.	14.83±0.38	15.00±0.80	1.12	15.33±0.43	3.37
7.	14.17±0.52	14.25±0.52	0.59	14.50±0.28	2.35
8.	13.42±0.50	13.83±0.29	3.11	13.67±0.29	1.86
9.	12.67±0.52	13.08±0.52	3.29	13.42±0.50	5.92
10	12.17±1.32	12.42±0.76	2.06	12.92±2.27	6.16

Table-4: Changes in the carbohydrate content of double hybrid (FC2×FC1) during embryonic development exposed to photoperiodic schedules (mg/gm) (each value is mean of three separate replication)

DAYS	Control	LD 14:10 (In hrs)		LD 16:08(In hrs)	
	MEAN±SD	MEAN±SD	% CHANGE	MEAN±SD	% CHANGE
1.	13.33±0.25	13.83±0.14	3.75	13.58±0.63	1.88
2.	13.00±0.63	13.08±0.38	0.64	13.42±0.66	3.21
3.	13.67±0.63	13.92±0.50	1.83	14.00±0.14	2.44
4.	13.92±0.38	14.25±0.29	2.39	14.33±0.25	2.99
5.	14.08±0.38	14.17±0.25	0.59	14.25±0.43	1.18
6.	14.25±0.38	14.75±0.43	3.51	14.83±0.52	4.09
7.	13.42±0.38	14.33±0.38	6.81*	14.17±0.25	8.97*
8.	13.33±0.29	14.58±0.52	9.38*	13.83±0.88	7.79*
9.	12.25±0.38	13.25±0.38	8.16*	12.83±0.52	4.76
10.	11.92±0.38	12.12±0.58	1.82	12.25±0.52	2.80

** = highly significant at 0.05% probability * = significant at 0.05% probability

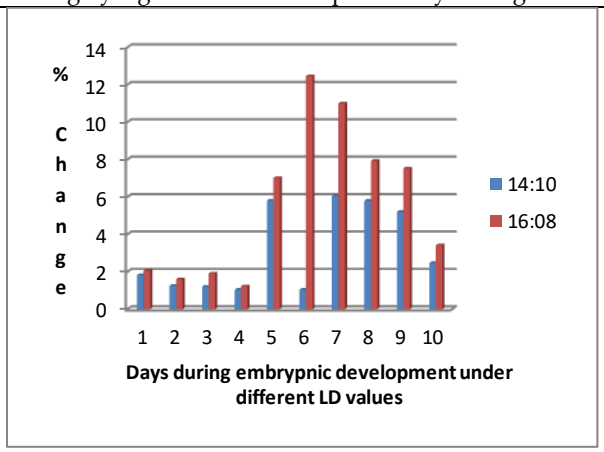

Fig-1: Percentage changes in the protein content of single hybrid (SK6×SK7) during embryonic development exposed to photoperiodic schedules.

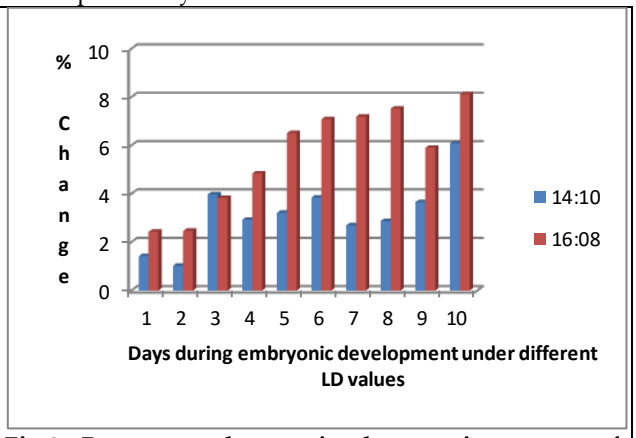

Fig-2: Percentage changes in the protein content of double hybrid (FC2×FC1) during embryonic development exposed to photoperiodic schedules.

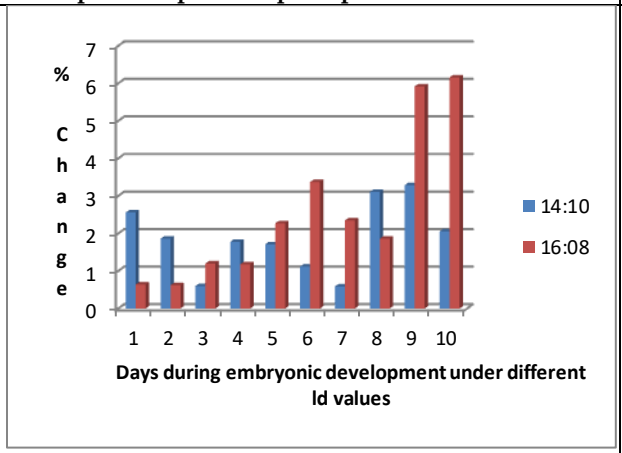

Fig-3: Percentage changes in the carbohydrate content of single hybrid (SK6×SK7) during embryonic development exposed to photoperiodic schedules.

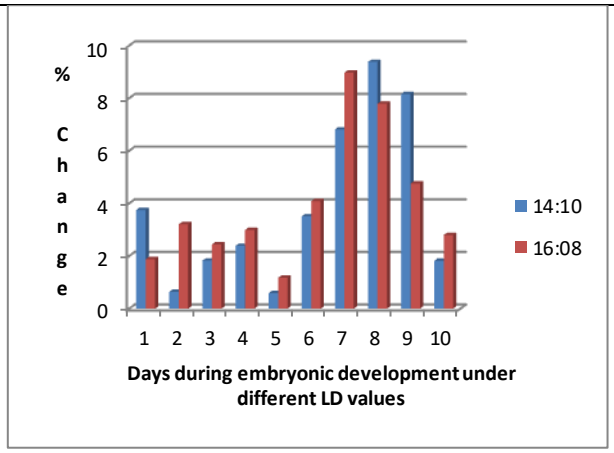

Fig-4: Percentage changes in the carbohydrate content of double hybrid (FC2×FC1) during embryonic development exposed to photoperiodic schedules.

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RESEARCH ARTICLE

Metamemory Functioning in Young Adults: A Mixed-Methods Approach

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ABSTRACT

Insight about one's own memory and the process involved in monitoring and controlling the memory is called metamemory. Knowledge about one's own memory process helps the individual in selection, allocation of cognitive resources, planning, strategy selection, comprehensive monitoring and evaluation. An exploratory sequential mixed methods design was used to understand the basic metamemory functioning in young adults. Data were collected from 20 young adults using a structured interview and from 50 young adults using the Memory Functioning Questionnaire which focuses on Retrospective functioning, frequency of forgetting, remembering past events, the seriousness of memory failure, and Mnemonic usage. The importance of understanding metamemory functioning among young adults will be discussed in this study.

Keywords: Forgetting, Memory, Metamemory, Mnemonics, Young Adults

INTRODUCTION

Metamemory can be broadly defined as cognitions about memory (Wellman, 1983). Metamemory is actually multiple specific concepts which include knowledge, beliefs and behaviours related to memory (Cavanaugh, Kramer, Sinnott, Camp, & Markley, 1985; Dixon, 1989; Gilewski & Zelinski, 1986; Hultsch, Hertzog, Dixon, & Davidson, 1988). There are four broad aspects of metamemory according to Hultsch *et al.* (1988) memory task and memory process knowledge, memory monitoring, memory self – efficacy and memory-related affect. Memory task and memory process knowledge focus on knowledge about memory functioning and the memory strategies used based on the tasks, and memory monitoring is the awareness of the current state of one's memory and how an individual uses it.

Similarly, memory self-efficacy is one's capability to use their memory effectively during memory – demanding situations; and memory-related affect talks about different emotional states which are related to memory demanding situations. Nelson and Narens (1990) proposed that two cognitive levels exchange information, the meta-level and the object level. The object level is the actual memory and the meta-level is the model of object-level or the metamemory. In other words, the information from the object level is received by the meta-level through monitoring. The information obtained from the monitoring process, the meta-level tries to control the object level by providing and modifying the information which exists in the object – level. This process of metamemory provides information that is used to regulate memory performance and behaviour. Nelson and Narens (1990) proposed another elaborative metamemory model, which focuses on metamemory components in various stages of memory such as memory monitoring judgement and control processes. In other words, it talks about different types of monitoring judgements and control processes that take place in the acquisition and retrieval process of memory. These processes often do not happen consciously.

Young adulthood is considered a problem age because the individuals have to make a lot of adjustments in this distinctive period of life span and they are expected to make adjustments by themselves unlike previous stages of life where they had parents, teachers, friends or others to help them make adjustments they are faced with. Young adults play new roles and develop new interests, attitudes, and values in keeping these new roles. In such a situation, effective learning and good memory skills are required as young adults learn and experience their life. According to Chen *et al.* (2014), 14.4% of young adults report subjective memory impairment. When compared with old aged adults, younger and middle-aged adults report high frequencies of subjective memory impairment (Cutler & Grams 1988). Also, young adults require a higher level of memory performance as they have more tasks and responsibilities that require memory performance (Rendell & Thomsom,1999). Similarly, memory performance can be improved by metamemory knowledge and simple memory strategies (Henry& Norman, 1996). Crystallized intelligence refers to the better accumulation of knowledge, skills and facts increases through adulthood and it helps when encountered in a situation that requires recalling previously acquired knowledge. Also, understanding metamemory functioning in young adults can indirectly help to improve crystallized intelligence. In other words, metamemory can help in seeking new knowledge which helps to build crystallized intelligence.

METHOD OF INVESTIGATION

Aim: To qualitatively and quantitatively study the Metamemory functioning among young adults.

Study Design: Exploratory sequential mixed methods design was used in the study.

Sample Description: Sample consists of 20 young adults for qualitative study and 50 young adults for quantitative study.

Sampling Technique: Purposive sampling technique was used in the study.

Inclusion Criteria

- Participants between the ages 18 to 35
- Participants who can read and write in English

Exclusion Criteria

- Participants below the age of 18 and above the age 35
- Participants who cannot read and write in English
- Participants diagnosed with severe cognitive impairment and other psychiatric disorders.

Study Method: The participants in the study were briefed about anonymity and confidentiality of the information provided by them. They were also briefed about voluntary participation and right to withdraw from the study. The study was divided into two phases, where phase one includes structured interview and, phase two includes a survey that participants were asked to fill the Memory Functioning Questionnaire (Gilewski, Zelinski, & Schaie,1990), which assess selective aspects of metamemory.

RESULTS AND DISCUSSION

A mixed-methods approach was adopted in the study, where both qualitative and quantitative methods were used. In a qualitative method, a structured interview was done to understand the following components among 20 young adults. When interviewed about the individuals' perception of their general memory, about 65% of the individuals replied that they were unsatisfied with their memory and few replied that they feel neutral and satisfied with their memory, that is 30% and 20% respectively. Similarly, to understand the most commonly used memory strategies by the young adults a question was posed accordingly, and about 55% of the young adults used association strategy, out of which 25% used Organisation Strategy, and 10% of the individuals used Rehearsal and Mental imagery respectively. When asked about individuals' perception about their memory issues in stages of memory about 65% of the young adults replied that they felt they had issues in the retrieval stage, 25% felt they had issues in the acquisition stage and 10% in the retention stage. Young adults reported that few areas of their lives are often affected due to memory issues. About 45% reported that memory issues affected their career. Similarly, individuals also reported that personal and social lives were also affected, that is about 40% to 15% respectively. Similarly, a quantitative method was used in this study. Memory Functioning Questionnaire (Gilewski, Zelinski, & Schaie,1990) was administered on the young adults to understand few aspects of metamemory components among 50 young adults.

Table.1. shows the metamemory functioning in young adults which includes general memory, retrospective functioning, frequency of forgetting, remembering past events, the seriousness of memory failure and mnemonic usage. The general memory functioning mean score was 4.65 and the standard deviation was 1.46. The mean score of retrospective functioning is 23.35 and the standard deviation score was 5.98. Most of the young adults reported that 21% of the individuals remember one year old information, 19% reported that they remember twenty years ago information and 20% reported that they remember information when they were eighteen. Similarly, individuals reported that about 20% of them remember information that was five and ten years old. The most frequently forgotten information are appointments, phone numbers, faces and words, which were reported by about 12% of the individuals. The mean score of forgetting frequency is 88.90 and the standard deviation is 18.45. Similarly, about 28% remember last month events, 26% remember six months to one-year events, and about 23% remember events of one to five years and six to ten years respectively. In remembering past events the mean score of the individuals is 17.85 and the standard deviation is 5.06. Memory failure is considered common but when the individual fails to retain certain information they consider that as a serious problem. Young adults reported that when they fail to remember names, faces, phone numbers and important dates of the events. Such memory failures are considered serious problems. The mean score of Seriousness of memory failure in young adults is 77.30 and the standard deviation is 17.28. Commonly used mnemonics in young adults are to fill the appointment books, to make a note in the to-do lists, to make reminder notes, to do mental repetition, and to plan a daily schedule in advance. The mean score of Mnemonic Usage in young adults is 36.35 and the standard deviation is 10.41.

CONCLUSION

Metamemory is a broad concept which talks about memory knowledge, beliefs and behaviours related to it. Many young adults reported that they are unsatisfied with their memory and most of them felt that they had memory failure issues in the retrieval stage compared to the acquisition stage. Due to memory failure issues, they feel that their personal, social and career lives are affected to some extent.

Limitations and Directions for Future Research

This study tries to understand the metamemory functioning in young adults but does not suggest ways to improve memory performance and to reduce memory lapses. Further study can be carried to develop a tool which covers the important concepts of metamemory for young adults. Which will help to understand the metamemory control and

monitoring skills in young adults, and also focus on improving memory performance and reduce memory lapse which is one of the major causes for human error.

CONFLICTING INTERESTS

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Table.1. Metamemory functioning in young adults (N-50)

Metamemory functioning	Minimum score	Maximum score	Mean	Std. Deviation
General Memory	1	7	4.65	1.46
Retrospective Functioning	13	32	23.35	5.98
Frequency of Forgetting	51	122	88.90	18.45
Remembering Past Events	9	28	17.85	5.06
Seriousness of memory failure	53	113	77.30	17.28
Mnemonic Usage	14	52	36.35	10.41

RESEARCH ARTICLE

Utilization of Plastic Bottles with Sand and Rice Husk Ash as Eco Friendly Bricks

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ABSTRACT

Bricks play the important roles in the construction of any engineering structure. Maximum of the residential and industrial construction uses bricks and mortar which consists of cement, aggregates and water as the materials to construct the structure. But cement and bricks production method will make contributions to an excessive emission of carbon dioxide (CO_2) which may also result in global warming. Consequently, it is necessary to search an alternative option to reduce these environmental problems. The alternative way that can solve the problem is by replacing the use of bricks in building construction by an eco-friendly plastic bottle bricks. Reuse of these non-biodegradable plastic bottles not only can resolve the environmental trouble, but it may also lesser the pollution. Laterite quarry waste is commonly available and disposal of waste plastics (PET, PP, etc.) is the biggest challenge. The per capita consumption in India still low in comparison to developed countries. In accordance FICCI, Indians consume 11 kg of plastic per year in comparison to 109 kg by an average American. The solution to India's issues with plastic waste can be addressed via centered investments in recycling and making sure sustained effort to reduce down consumption. Only one in six plastic bottles is properly recycled. On other hand excessive cost of primary requirement for constructing the homes in places on in which people are below poverty line is forming certainly one of most great issues of human beings. In this research we have replaced the normal standard bricks by using the plastic bottle bricks. The main concern of this study is strength of the plastic bottle brick for the construction. Therefore, experiments had been done to evaluate the properties of bricks and plastic bottle packed with sand and rice husk ash which was compression test in indoors and outdoors of wall structure.

Keywords: PET Plastic Bottle Bricks, Eco Friendly material, Rice Husk Ash.

INTRODUCTION

Disposal of the non-biodegradable materials has grown to be most important hassle now days. Lots of plastic wastes get accumulated every day in the world. Plastic is such thing that's shaped through the oil that is considered as non-renewable resource due to the fact plastic has insolubility. And plastic is non-decomposable material additionally i. e. It considered as the sustainable waste. Most of the residential and industrial development uses bricks and mortar which is the mixer of cement, aggregates and water as the substances to construct the structure. However, cement and bricks production system will make contributions to a high production of carbon dioxide (CO_2) which may also result in global warming. Additionally with populace growth in day today world, the need to the construction has vary and to respond to this demand, the world generally tend to use the industrial constructing materials and refuses the usage of local and ordinary substances. These factors regardless of growing the power intake in the industry phase; they can also increase the value of construction and are taken into consideration due to this acts as the barrier for users to attain the fundamental desires of the lives. So we need to consider an innovative concept through which those troubles can sort out. In this research we've got changed bricks by the plastic bottle bricks. Plastic bottle bricks are in the manner by means of which we can reuse the non-biodegradable substance like plastic bottles and can reduce not simplest environmental trouble but additionally value of construction. The main difficulty of this study is the strength of the plastic bottle brick on which we have focused in this research. Consequently, experiments have been done to evaluate the properties of bricks and plastic bottle filled with the sand and rice husk ash that are compression test of modified bricks.

At the existing time, the possibility of using the renewable resources consisting of solar, wind, geothermal has been provided for us greater than before, and development of this science is making growth. However those energies may be selected as one of the renewable and substitute energies in preference to fossil fuels that are low cost as feasible and have less environmental effects. Various varieties of houses have been constructed from plastic bottles including ecological house constructed the use of 6000 bottles in New Delhi, may 2011. Samarpan foundation school built using the pet bottle; a residence of waste plastic bottles constructed in India by Priyankajain in Kanpur plastic bottle building; ecological bottle residence constructed using 600 pet plastic bottles for the modal close to the IIT Kanpur. In this study, lots of plastic bottles were filled with soil and rice husk ash and the bottles have been planned laid and packed down with a mixer of mud and cement, developing a constructing material which is stronger than normal bricks. As a consequence on the subject of the different experiments conducted until now by various researchers, in this research paper we have tried to discover the relative strength and valuation or cost of the bottle brick in comparison to the conventional brick.

Necessity and Scope of Plastic Bottle Brick

Plastic bottle brick made by the PET bottles that are present in large amount and easy to locate. We've got used soil and rice husk ash as the filler substances within the bottle and packed it tightly within the bottles. A few scopes could be plastic waste reduction, resource conservation, environmental safety, social fairness and construction improvement etc.

Advantages

The technical characteristic of PET plastic bottle brick has most of the merits that contribute in reducing the adverse impacts on environment. Some of the main advantages are reported by Dr. Pratima A. Patel (2016), MojtabaValinejad Shoubi (2013) and Shilpi Saxena (2013) are:

- It contributes to decreasing the pollution particularly in urban communities, towns, streams, lake and oceans.

- Recycling of plastic without CO_2 outflow and best arrangement is reusing as bricks which no extra vitality is required and doesn't increase contamination.
- Plastic bottle brick's building structure are lighter than the other building structure worked by brick and concrete. That makes these structures to show a decent reaction against seismic tremor. Flexibility of plastic is a characteristic which makes the building's performance higher against the unexpected load.
- The plastic bottle is free from dampness due to the impervious material.

Practical Experience to the Related Work

Aditya Singh Rawat and Kansal R. (2014) investigated the mechanical behavior of the plastic bottle by using collate the compressive strength of plastic bottle with brick. PET bottles were gathered from viable sources and were filled of domestically available soil by means of tamping it. The bottles had been tightly capped and sealed. Compressive strength test was performed on UTM for PET bottles and brick. The effects have been compared and analyzed. It changed into determined that the PET bottle has compressive strength almost same to that of a normal standard brick. Also the value of construction in case of PET bottle is greater least expensive than well-known normal bricks and the weight of one bottle brick was found to be much less than that of a standard brick.

MardihaMokhtar *et.al.* (2015) recommended the significance of the usage of bottle bricks in the wall structure instead of using clay bricks. Their fundamental challenge became to examine the strength of bottle bricks. Compression test and temperature test was done for 1.5 L bottle brick, 250 ml bottle brick and ordinary clay brick. Effects showed that the energy of 1.5 L bottle bricks and 250 ml bottle bricks are three and four times stronger than that of normal clay brick. Temperatures of outer structure were recorded as 36ºc. From this result, it has concluded that plastic bottle have a capacity to be used as a building material on wall.

MojtabaValinejad Shoubi *et al.* (2013) investigated the use of plastic bottles as one of the city wastage in any construction and its sustainable development. It has proposed to fill the bottles with sand and mortar. Hence bottle blocks had been casted. Various types of structure varying in length and orientation of the bottles had been constructed. The compression strength and fracture bearing of every wall was measured and compared. It was found that PET bottle structure can undergo as much as 4. 3 N/mm² while the bottles are full of sand which is the weakest filling material. The bottles bear 1/3rd of the load while the plaster bears two thirds.

ShilpiSaxena, Monika Singh has located that by using utilizing PET bottles in construction reusable substances, thermal comfort may be attain in very low cost housing, benefits residents that cannot invest in functional heating and cooling structures. The outcomes of this research need to be spread to citizens, in order that the tenants can enforce the changes themselves without having to lease developers or professionals in order to have a home that gives extra thermal consolation and is more sustainable. This gives alleviation for lower family of India to provide reasonably-priced and satisfactory houses for residing. And this type of construction does not require any high-priced machinery so construction get more effortlessly and in very low price and this idea provide eco-friendly to the environment.

EXPERIMENTAL WORK

Materials and Methods

In this novel idea of construction we have used some materials. These are such materials which are local and are very cheap. And by this idea we had attempted that we are able to reduce the plastic waste from the nature which has end up greater dangerous hassle of world and for nature additionally. There are given below used materials in this research-

Plastic PETE Bottle

Polyethylene Terephthalate Ethylene (PETE) bottles is thermoplastic substances. This type of plastic are polymers and with or without cross linking and branching, and they melt at the use of warmth, without or with pressure and require cooling to be set to a form.

Following are properties of plastic bottle:

Full name: Polyethylene Terephthalate

Molecular Formula: $C_{10}H_8O_4$

Composition: Polyester of Terephthalic Acid and Ethyleneglycol.2, 3

Cement

Cement is the most important construction material. In this work it is use to bind the plastic bottles to make the masonry structure more durable.

Soil

Soil is the basic material of this research. We have used soil as a filler material. We fills the soil in bottles to give strength. In this research we have took virgin soil. This soil has dig out directly from the ground. For giving better strength purpose we have done sieve analysis of this soil. We have sieved this soil by the 0.600mm sieve and then we have filled this purify soil in the bottles. We have used soil also for binding the bottles to each other.

Rice Husk Ash

Rice husk ash (RHA) is a second filler material which we have used with the soil. The rice paddy milling industries supply the by-product rice husk. Because of the increasing rate of environmental pollutants and the consideration of sustainability element have made the idea of making use of rice husk. The usage of RHA will make contributions not only the manufacturing of concrete of a higher quality and decrease value, but additionally the reduction of carbon dioxide (CO_2) emissions from the manufacturing of cement. The partial alternative of cement by means of RHA will result in lower energy consumption related to the manufacturing of cement. India is a second largest country in the world which producing rice husk.

METHODOLOGY

Collecting Bottles

First step is collecting the bottles from dumping area. Bottles should be used and fresh and should in equal size. Bottles should have also caps. We know that bottles are provided in major amount in nature so these can be available easily. We have used 1 lit. Drinking water bottles in our project, Bottles should use without its label.

Collecting Soil

Second step is to collect the soil which should be virgin in nature. And also should be moisture less and dry. Collected soil does not contain so much unwanted vegetation's and stone pieces. If soil contains large pieces so we should press with the hammering and convert it in to fine grade.

For more precise grain of soil we can sieved it. Soil is such as that it should contain compaction property. We cannot use the sand because of it contains less compaction property. Soil is also easily available material and can be provided in less cost. Soil is the basic filler material which we have used in filling of bottle.

Collecting Rice Husk Ash

Next step is to collect the rice husk ash. We all know that India has second place in the world which produces more rice. And rice husk produces from the synthesis of rice. So this can be also easily available material. After that this process we go to step of converting the rice husk in to the rice husk ash (RHA). For converting in to ash, make a rectangular boundary of brick and put that material in it. Then now we burn this with the help of papers. We cannot

used any inflammable liquids such as petrol, diesel etc. We should keep in mind that temperature and fire should not be more. After this process we get the rice husk ash. This mixed with the soil and after that we can use this as the filler material for bottles.

Sieving of Soil

After that we go to next process of sieving of soil. We need the sieving because of this process compaction of soil proceed in better way. We used the sieve size 600 micron. By the sieving process we removed the unwanted vegetation and stone pieces and many more impurities. Sieving process provide a fine and equal grain of soil.

Mixing of the Soil and Rice Husk

After that these processes we go to further process of prepare the filler material. We prepare material by mixing of soil and rice husk. We take ratio of mixing of these two filler material as 50-50 means 50% we take the sieved soil and 50% take rice husk. We will be used for the bottles. We have used this combination of filler material because it's providing more compressive strength to the bottle brick when we have tested different combination of material such as soil

Filling the Bottles with Material

After prepare the filler material next step is the filling process. This is the more important process because of strength of brick majorly depend upon it. If voids will remain during the compaction, it can affect the strength of bottle brick. Here we take some steps which are given below-

- Firstly we take fresh used bottles with the caps.
- Then we started to fill the material in bottles.
- Then with the help of iron bar we compact the material properly. Approx. 40 times we
- compacted after filling the ¼ bottle with the material
- Now after compacting the bottles properly close the caps of bottles.

RESULT AND DISCUSSION

Bottle Compressive Strength Test Result

Bottle compressive strength test is done to know about compressive strength and failure limit when it is filled with different filler materials. Here we have tested 5 samples bottle on ultimate testing machine which calculation and interpretation is given below:

Calculation

PETE Bottle Standard Size

Length of Bottle = 220 mm.
Width of Bottle = 250/4
= 60 mm
Total area of bottle = 220*60
=13200 mm^2

Calculation of Compressive Strength

For 5 numbers of Samples:
Compressive Strength = Load of PETE Bottle/Area of PETE Bottle
= 400×1000/13200
= 30.30 N/mm^2.
≈ 30 N/mm^2
.

So Soil and Rice husk bottle sample has net compressive strength is30 N/mm².

CONCLUSION

The present work provides an alternative solution of recycling the waste plastic bottles. This can be an alternative way that can solve the problem is by replacing the use of bricks in building construction by eco-friendly plastic bottle bricks. Reuse of these non-biodegradable plastic bottles not only can solve the environmental problem, but it can also reduce the pollution. After all using of this innovative idea of use of eco-friendly agricultural waste materials like sand and rice husk ash in the plastic brick form can be a better eco-friendly bricks in future applications. Use of this eco-friendly material with the sustainable application reduces environment degradation and reduces plastic waste from the nature. This method reduces consumption of raw material and energy which are using to manufactures building materials. And also reduces CO_2emission in manufacturing the cement. As per analysis and testing results plastic bottle brick has 30 N/mm²compressive strength which is three times more than normal brick's compressive strength. Cost estimation of plastic bottle brick construction is half of the conventional brick construction. Hence this analysis will be very innovative and beneficial for the future applications in green building construction.

Declarations

Author Contribution Statement

Kirtika Gupta: Performed the experiments, materials, analysis tools or data.
Islamuddin: Analyzed and interpreted the data; wrote the paper.

Competing Interest Statement: The authors declare no conflict of interest.

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Table No.-1: Bottle Compressive Strength Test Result

S.no.	Material	Weight	Load	Compressive Strength
1	Sand + Mauram	1.800 kg	69.6 kN	5.27 N/mm^2
2	Sand + Mauram	1.900 kg	121.6 kN.	10 N/mm^2
3	Soil	1.506 kg.	176 kN.	13.22 N/mm^2
4	Husk	0.584 kg.	184 kN	14 N/mm^2
5	Soil + Rice husk	1.131 kg.	400 kN	30 N/mm^2

Fig.-1- PET Bottles

Fig.-2- PETE Bottles

Fig.-3 Rice Husk

Fig.-4 Rice Husk Ash

Fig.5- Bottles filled with materials

Fig.6- Tested Bottles from UTM

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RESEARCH ARTICLE

Redefined Third Zagreb Energy of Graph

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ABSTRACT

Redefined third Zagreb index is a topological [4] which is defined as
$RTZ_3(G) = \sum_{if uv \in E} d_u d_v (d_u + d_v)$.

Motivated by this index, in this paper we are introducing and investigating the new energy i.e., Redefined third Zagreb energy of graph $RTZ_3E(G)$.

Keywords: Redefined third Zagreb connectivity Matrix, Redefined third Zagreb energy.
2010 AMS Subject Classification: 05C50.

INTRODUCTION

In this paper E represents the edge set and V mentions the vertex set. We use ~ to represent the connectedness. We can represent a chemical structure in the form of graph which is known as molecular graph. 20th century witnessed the evolution of new concept which is related to both Chemistry and Discrete Mathematics. Ivan Gutman introduced the concept of energy of graph, he defined it as the sum of the absolute values of eigenvalues of adjacency matrix with respect that graph [1]. More information on energy of graph can be found in [1] and [2]. Topological indices are the molecular descriptors which will give the details of the topology of the molecular graph. To represent the degree of any i^{th} vertex V_i, we use the notation d_i. Many topological indices of graphs exist in the literature.

Redefined third Zagreb index is also one of it and defined as [4]
$RTZ_3(G) = \sum_{if uv \in E} d_u d_v (d_u + d_v)$

We introduce the Redefined third Zagreb matrix $RTZ_3(G)$ *as* $RTZ_3(G) = (RTZ_3)_{n\times n}$

$$RTZ_3 = \begin{cases} d_u d_v (d_u + d_v) \text{ if } v_i \sim v_j, \\ 0 \qquad\qquad \text{otherwise} \end{cases}$$

The Redefined third Zagreb characteristic polynomial of the matrix $RTZ_3(G)$ is denoted by $\phi_{SL}(G,\lambda) = \det(\lambda I - RTZ_3(G))$. The Redefined third Zagreb energy is given by

(1) $$RTZ_3E(G) = \sum_{i=1}^{n} |\lambda_i|$$

Here λ_i represent the Redefined third Zagreb eigenvalues.

Redefined third Zagreb energy of some standard graph structures

Theorem 2.1. The Redefined third Zagreb energy of a complete graph K_n is $RTZ_3E(K_n) = 4(n-1)^4$.

Proof. Let K_n be the complete graph with vertex set $V = \{v_1, v_2, ..., v_n\}$. The Redefined third Zagreb matrix is

$RTZ_3(K_n) = (2(n-1)^3 (J-I))$.

Characteristic equation is

$(\lambda + 2(n-1)^3)^{n-1}(\lambda - 2(n-1)^4) = 0$

and the spectrum is $SpecRTZ_3(K_n) = \begin{pmatrix} 2(n-1)^3 & 2(n-1)^4 \\ n-1 & 1 \end{pmatrix}$.

Therefore, $RTZ_3E(K_n) = 4(n-1)^4$.

Theorem 2.2. The Redefined third Zagreb energy of Crown graph S_n^0 *is*

$RTZ_3\ E(S_n^0) = 8(n-1)^4$.

Proof. Let S_n^0 be a crown graph of order $2n$ with vertex set $\{u_1, u_2, ..., u_n, v_1, v_2, ..., v_n\}$. The Redefined third Zagreb matrix is

$$RTZ_3E(S_n^0) = 2(n-1)^3 \begin{pmatrix} O_{n\times n} & (J-I)_{n\times n} \\ (J-I)_{n\times n} & O_{n\times n} \end{pmatrix}.$$

Characteristic equation is

$(\lambda - 2(n-1)^3)^{n-1}\ (\lambda + 2(n-1)^3)^{n-1} + (\lambda + 2(n-1)^4)(\lambda + 2(n-1)^4) = 0$

Spectrum is $Spec\ RTZ_3(S_n^0)$

$$= \begin{pmatrix} 2(n-1)^4 & -2(n-1)^4 & 2(n-1)^3 & -2(n-1)^3 \\ 1 & 1 & n-1 & n-1 \end{pmatrix}$$

Therefore,

$$RTZ_3E(S_n^0) = 8(n-1)^4.$$

Theorem 2.3. For complete bipartite graph $K_{m,n}$. The Redefined third Zagreb energy of $K_{m,n}$ *is*

$RTZ_3E(K_{m,n}) = 2(mn)^{\frac{3}{2}}(m+n)$.

Proof. $RTZ_3(K_{m,n}) = RTZ_3(K_{m,n}) = (mn)(m+n)\begin{pmatrix} O_{m\times m} & J_{m\times n} \\ J_{n\times m} & O_{n\times n} \end{pmatrix}$.

Characteristic equation is

$\lambda^{m+n-2}\left(\lambda^2 - (mn)^{\frac{3}{2}}(m+n)\right) = 0$.

Hence, spectrum is

$$Spec\ RTZ_3(K_{m,n}) = \begin{pmatrix} 0 & (mn)^{\frac{3}{2}}(m+n) & -(mn)^{\frac{3}{2}}(m+n) \\ m+n-2 & 1 & 1 \end{pmatrix}.$$

Therefore, $RTZ_3E(K_{m,n}) = 2(mn)^{\frac{3}{2}}(m+n)$.

Theorem 2.4. The energy of the cocktail party graph $K_{n\times 2}$ is

$RTZ_3E(K_{n\times 2}) = 16(n-1)^3$.

Proof. Let $K_{n\times 2}$ be the cocktail party graph of order $2n$ having vertex set $\{u_1, u_2, ..., u_n, v_1, v_2, ..., v_n\}$. The degree sum square matrix is

$$\begin{bmatrix} 0 & 0 & 16(n-1)^3 & 16(n-1)^3 & \cdots & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 \\ 0 & 0 & 16(n-1)^3 & 16(n-1)^3 & \cdots & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 \\ 16(n-1)^3 & 16(n-1)^3 & 0 & 0 & \cdots & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 \\ 16(n-1)^3 & 16(n-1)^3 & 0 & 0 & \cdots & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots \\ 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & \cdots & 0 & 0 & 16(n-1)^3 & 16(n-1)^3 \\ 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & \cdots & 0 & 0 & 16(n-1)^3 & 16(n-1)^3 \\ 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & \cdots & 16(n-1)^3 & 16(n-1)^3 & 0 & 0 \\ 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & 16(n-1)^3 & \cdots & 16(n-1)^3 & 16(n-1)^3 & 0 & 0 \end{bmatrix}$$

In that case, the characteristic equation is

$\lambda^n\left(\lambda + 16(n-1)^3\right)^{n-1}\left(\lambda - 16(n-1)^4\right) = 0$

And hence the spectrum becomes

$$Spec\ RTZ_3(K_{n\times 2}) = \begin{pmatrix} -16(n-1)^4 & 0 & -16(n-1)^3 \\ 1 & n & n-1 \end{pmatrix}.$$

Therefore we arrive at the required result:

$RTZ_3E(K_{n\times 2}) = 32(n-1)^4$.

Definition 2.5.[7] Let *G* be a graph and $P_k = \{V_1, V_2, ..., V_k\}$ be a partition of its vertex set *V*. Then the – complement of *G* is obtained as follows: For all V_i and V_j *in* P_k, $i \neq j$ remove the edges between V_i and V_j and add the edges between the vertices of V_i and V_j which are not in *G* and is denoted by $\overline{(G)}_k$.

Lemma 2.6. The Redefined third Zagreb energy of the complement $\overline{K_n}$ of the complete graph K_n is $RTZ_3E\left(\overline{K_n}\right) = 0$.

Proof. Here according to the definition of complement of graph, the complement of K_n is edge less disconnected graph. Thus the matrix will be having all the entries as zero. Thus the energy is also zero.

Theorem 2.7. The Redefined third Zagreb energy of the complement $\overline{K_{n\times 2}}$ of the cocktail party graph $K_{n\times 2}$ of order $2n$ is

$RTZ_3E\left(\overline{K_{n\times 2}}\right) = 4n$.

Proof. Let $\left(\overline{K_{n\times 2}}\right)$ be the cocktail party graph of order $2n$ with vertex set $\{u_1, u_2, ..., u_n, v_1, v_2, ..., v_n\}$. The Redefined third Zagreb matrix is

$$RTZ_3\left(\overline{K_{n\times 2}}\right) = \begin{bmatrix} 0 & 0 & 0 & \cdots & 2 & 0 & 0 \\ 0 & 0 & 0 & \cdots & 0 & 2 & 0 \\ 0 & 0 & 0 & \cdots & 0 & 0 & 2 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \\ 2 & 0 & 0 & \cdots & 0 & 0 & 0 \\ 0 & 2 & 0 & \cdots & 0 & 0 & 0 \\ 0 & 0 & 2 & \cdots & 0 & 0 & 0 \end{bmatrix}$$

Characteristic equation is

$(\lambda + 2)^n (\lambda - 2)^n = 0$.

Hence, spectrum is $SpecRTZ_3\left(K_{n\times 2}\right)$

$$= \begin{pmatrix} 2 & -2 \\ n & n \end{pmatrix}.$$

Therefore, $RTZ_3E\left(\overline{K_{n\times 2}}\right) = 4n$.

Some properties of the redefined third Zagreb energy of a graph

The following results will give the initial coefficients of the Redefined third Zagreb characteristic polynomial and can be easily proven using the definition of characteristic polynomial.

(2) $$RTZ_3E(G) = \sum_{i=1}^{n} \left[d_u d_v (d_u + d_v)\right]^2$$

Proposition 3.1. In the Redefined third Zagreb characteristic polynomial $\phi RTZ_3(G, \lambda)$, the first three coefficients are 1,0 and $-\sum_{i=1}^{n} \left[d_u d_v (d_u + d_v)\right]^2$ respectively.

Proposition 3.2. *If* $\lambda_1, \lambda_2, ..., \lambda_n$ are the Redefined third Zagreb eigenvalues of $RTZ_3(G)$, then

$$\sum_{i=1}^{n}\lambda_i^2 = 2\sum_{i=1}^{n}\left[d_u d_v\left(d_u + d_v\right)\right]^2 .$$

The upper bound and lower bound for the Redefined third Zagreb energy are in the next results.

Theorem 3.3. Let *G* be a graph with *n* vertices. Then

$$RTZ_3E(G) \le \sqrt{2n\sum_{i=1}^{n}\left[d_u d_v\left(d_u + d_v\right)\right]^2} .$$

Theorem 3.4. Let *G* be a graph with *n* vertices.

$$RTZ_3E(G) \ge \sqrt{2n\sum_{i=1}^{n}\left[d_u d_v\left(d_u + d_v\right)\right]^2 + n(n-1)\left[Det\left(RTZ_3(G)\right)\right]^{\frac{2}{n}}} .$$

CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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RESEARCH ARTICLE

Pedestrian Gap Acceptance and Crossing Behavior at Signalized Intersections

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ABSTRACT

A large number of pedestrian are getting killed in traffic Road crash each year. It is known, pedestrian crash are more severe than other types of crashes. A review of pedestrian crash data shows that most of the crashes occur while the pedestrian was crossing the road. The pattern of pedestrian behavior when crossing the road is dependent on various factors such as traffic condition, pedestrian characteristics and vehicular characteristic. All these factors are pedestrian exposure to risk in relation to pedestrian crossing behavior. In this research, the main focus is leveraged on the study of gap acceptance and crossing behavior of pedestrians at signalized intersections. Because of the common and widely observed illegal crossing decisions of pedestrians at signalized intersections, it is interesting to investigate gap acceptance of pedestrians on their decision to cross at intersections. As a result, this paper has tried to cover crossing behavior of pedestrians such as: gap acceptance, compliance with signal, pedestrian-vehicle interaction in mixed traffic condition and identifying influencing factors. For the study, a field survey was carried out at signalized intersection in Bhubaneswar, India. The collected data, from the signalized intersection AG Square, Damana, KIIT, Nalco and Jayadev Vihar, consists of gap data point which include both accepted and rejected vehicular gaps and probable factors that may influence crossing . Pedestrian road crossing behavior at the intersection selected has been modeled by the size of vehicular gap accepted by using multiple linear regression (MLR) technique. Choice model has been developed to capture the decision making process of pedestrian. The result from the survey showed that pedestrian noncompliance arises with signalized rules because allocated green time is small, there is no facility assigned where they can avoid conflict and or being in a hurry. The MLR model shows pedestrian speed, vehicular speed, rolling gap, pedestrian speed change, driver yielding behavior, type of vehicle, gap type, age and lag or gap are important factor on size of gap acceptance. For the size of gap model the independent variable explain

the dependent variable 72.7 % (R^2) and the critical gap was found to be 4 sec. The choice model represents the data 94.2%. And from model Pedestrian make the decision to cross or not based on four major factors size of traffic gap, the vehicle speed, waiting time, and the frequency of attempts before crossing. These inferences are helpful for pedestrian facility design, policy toughening and create awareness for different stakeholders.

Keywords: Pedestrian, road crossing behavior, gap acceptance, signalized intersection

INTRODUCTION

Walking is one of the most important modes of transport. People tend to choose walking for multiple purpose such as: to visit a nearby neighbor's house, for errands, to go to school, markets and formal meetings (e.g. business meetings). In addition, people also consider walking for recreational activities, health benefits or for the pleasure of enjoying nature and its wonders. (Lindelöw, D.2016). Moreover, every journey starts and ends with walking. The decision of people to choose walking as a mode of transport or not depends majorly on the pedestrian demographics as well as socioeconomic characteristics of the locale. It is because the net benefit of walking has to be quantified and be found to be larger than any other competing alternative modes, as far as mobility is concerned with choosing the low cost and convenient mode of transportation. For convenience of walking, the pedestrian level of service on walkways and the suitability of pedestrian crossing locations are given due attention. Moreover, if we may think in larger scale, pedestrian crossings are critical elements in the traffic system from both pedestrian (primarily safety) as well as traffic flow (primarily interruption to flow) point of view. Pedestrian crossings are usually built around road intersections. The road safety crashes at these locations has been a major concern in urban traffic operations for long time now. Crashes involving pedestrianize major traffic safety problem, as pedestrian fatality is very highly likely to occur at the places of such crashes. In developing countries, many factors have indirect and direct causes for such crashes, such as: high population density, rapid modernization and urbanization, and lack of compliance to traffic regulation by both driver and pedestrians. Traffic crashes involving pedestrians usually occur at locations where pedestrians cross the road, and precisely at places where certain pedestrians do illegal crossings (Chih-Wei, 2016).

But nonetheless, these crashes may also occurat designated pedestrian crossing facilities as well. Asa result, pedestrian crossing behavior is essential to investigate as it has high correlation with the vulnerability of pedestrians to traffic crashes. It is primarily better characterized by the gap acceptance theory/model which reasonably assumes that each pedestrian has respective critical gap to cross a road. It is known that the distance between a vehicle and a pedestrian appear to influence the minimum gap often accepted by pedestrians. In India, even though the mobility of people has increased due to the economic growth achieved in recent years; the adverse consequences of pedestrian crashes have become a more apparent problem. Since most people commute by walking, road crashes have always been severe (sometimes fatal) because road crashes usually involve pedestrian crashes. Classifying countries according to the share of their traffic fatalities in their total deaths, India ranks number 22 among 193 countries with a share of 4.27 percent According to the World Health Organization (WHO) statistics for traffic fatalities, pedestrians, cyclists and motorcyclists have a share of 50 percent in all traffic fatalities in the world (Chan, 2013). In July 2018, The Bhubaneswar police commission report data showed that yearly on average, 2950 pedestrians are victims of traffic crash in Bhubaneswar city alone. For most of the time, traffic researches and studies focus on vehicles and drivers, thus the concerns for safety, comfort and convenience for pedestrians always comes next while designing roadways. The development of sound models that represent the behavior of pedestrians while crossing road intersections can contribute in improving the efficiency and safety of pedestrian at crossing facilities. While crossing, pedestrians select an appropriate gap in vehicular stream depending on their demographic, vehicular and pedestrian behavioral characteristics which will be represented by the model. In this research, the main focus is leveraged on the study of gap acceptance and crossing behavior of pedestrians at signalized intersections. Under ideal conditions, studying gap acceptance of pedestrians does not make sense to do at signalized intersections, since pedestrians are usually given

green times to cross safely. But for common and widely observed illegal crossing decisions of pedestrians at signalized intersections, it is interesting to investigate gap acceptance of pedestrians on their decision to cross at intersections. As a result, this paper has tried to cover crossing behavior of pedestrians such as: gap acceptance, compliance with signal, pedestrian- vehicle interaction in mixed traffic condition and identifying influencing factors.

The specific objectives are:

- To identify factors that affect gap acceptance and crossing behavior at selected signalized intersections in Bhubaneswar,
- To model pedestrian gap acceptance or selection behaviors,
- To determine the critical gap acceptance of pedestrians at selected signalized intersection in Bhubaneswar
- To assess pedestrian compliance behaviors at selected signalized intersections in Bhubaneswar.

LITERATURE REVIEW

The population growth of pedestrians in major urban and suburban areas of India is increasing at an alarming rate. This growth can be seen to be parallel with the rapid increment of pedestrian in India. In relation to this, we can deduce that "The increment in number of walk commuters have a huge effect in road crash" (Tulu, 2015). On the other hand, pedestrians are the most vulnerable to traffic crash involving pedestrian rashes, whenever they are at roadway intersections and pedestrian crossing facilities (Li, 2013). With the existence of high traffic congestion in India, particularly in the capital Bhubaneswar, this situation can lead to conflicts between the movement of vehicles and pedestrians. These conflicts sometimes can make crashes involving pedestrian crashes. In this chapter, a comprehensive literature review is presented. The formal definition of pedestrians along with the discussions of their different walking and behavioral characteristics are presented. Moreover, measurement metrics and characteristics of pedestrians with respect to accepting gaps at intersections and pedestrian crossing facilities is given due attention – which has motivated the main theme of this thesis. Moreover, in other perspective, walking can be categorized as one of the main modes of transport (when we look at its popularity in heavily congested cities) and it is healthier for human society (which makes it highly beneficial) (Kadali & Perumal, 2012).

As a result, we can claim that walking pedestrians are one of the key elements in the transportation system traffic and arrangement, especially in urban traffic. To mention some of the pedestrian parameters that are essential to be considered in the design and planning of pedestrian facilities include (but not limited to): the pedestrian walking speed, pedestrian flow, density, and pedestrian space. In addition, pedestrian perceptions need to be taken into consideration in the planning of pedestrian facilities such as: the current (actual in situ) operating speed, density, and pedestrian space, that are used for theoretical planning. Another important parameter in characterizing pedestrian movements is decision making. The decision making of pedestrians to cross the road is influenced by two factors namely: internal factors (age, gender, physical condition, psychological condition, etc.) and external factors such as traffic conditions. Pedestrians' street-crossing behavior is the outcome of interaction between pedestrians and vehicles. We first introduce the notation that describes traffic flow, pedestrians and traffic signal setting respectively. (Li, 2013) argues that, when vehicular speed is capped by a relatively low speed limit in urban areas (especially in the city/town centers), the most important traffic variable that affects pedestrians' street-crossing behavior is vehicle time headway because it characterizes the gap between two consecutive vehicles and hence provides a measure of opportunity for a pedestrian to cross the street during the red-man phase. (Oxley et al., 2005) have done experimental studies on the effect of age of pedestrian in gap selection. The study reported that, for all age groups, gap selection is primarily based on vehicle distance and speed. (Hamed, 2001) presented that approaching traffic volume and vehicle speeds are instrumental in determining the pedestrian's waiting time (delay) and the number of crossing attempts. Pedestrians, who accept higher risk, have to cease their waiting time, whereas pedestrians, who are likely to lower the risk, have to extend their waiting time at pedestrian crossings. (Guffey, 2009) differently reported that pedestrian's belief, motives and situational factors can affect their crossing behavior at signal-controlled crossings. Situational factors like the presence of other pedestrians and their behavior towards 'Walk' and 'Don't Walk' signs

affect the behavior of female pedestrians and traffic volume affect the behavior of male pedestrians at signalized crossings.

Site Investigations Survey

The three signalized intersections selected for this study are:

1. Bole Michael,
2. Shola and
3. Saris Abo signalized intersections.

Jayadev Vihar Signalized Intersection

This intersection situated in a commercial district is well observed to have high pedestrian movement and vehicular traffic from different approaches presented in Table 1.The high volume in pedestrians is because the intersection is surrounded by retail shops, stores and services such as: pharmacies, mobile shops, bus and taxi transport terminals, hotel, school, small local market, church, mosque, bank, tele center, beauty spa and other different kinds of shops.

Damana Signalized Intersection

Similar to the Bole Michael intersection, this intersection is also situated in a commercial district well observed to have high pedestrian movement and vehicular traffic from different approaches presented in Table 2. The high volume in pedestrians is because the intersection is surrounded by: a school, printing houses, police station, court, cafe, huge local market, bus and taxi transport terminals, hotel, church, mosque, bank, tele center, beauty spa and other different kinds of shops. This intersection is located near to the second largest market (Damana Local Hata) in the city

Study Design

This research aims to investigate and model pedestrian road crossing behaviors at the selected three signalized intersections. Two aspects of pedestrian crossing behaviors are examined. They are: the size of traffic gaps accepted by pedestrians and the decision of pedestrians to either cross the road or not, illegally.

Research Data

The basic data that are required for the research are listed in the table below, with a specific description of the variables that are presumed to affect the pedestrian gap acceptance and illegal crossing behaviors, in general. Table 3 gives detailed descriptions. The main emphasis of this study is on gap acceptance and crossing behavior. That is determining the gap between vehicles that a pedestrian accepts or rejects at signalized intersection. The data were collected during 2018-2019 at three signalized intersection located in Bhubaneswar. The weather was fine (clear sky) on the day of data collection. All road users who entered the observed sites were recorded on video, but only the pedestrians who approached the intersection during red light phases and traveled through the intersection were coded. The pedestrians who approached the intersection during the green light were not valid samples and were excluded in this study.

The video camera was installed at the selected signalized intersection in such a way that it captures the pedestrian crossing characteristic starting from the curb to the finished crossing as well as the approaching vehicle. The crossing movement of pedestrian and approaching vehicles at each location were captured for three hours. Later these data were played using KM player to extract data by play back technique. The way of recording the independent variables have been defined well in advance. The main independent variables and their definitions are listed in Table 3. The approaching vehicle movement towards the pedestrian location and pedestrian crossing maneuver were observed and the following data were extracted. Firstly, the variables of personal characteristics were gender and estimated age group. As to the age concern, pedestrians were classified into three groups: the young (less than 30 years), the

middle-aged (in the 30–50 years), and the elderly (over 50 years).Secondly, the variables describing pedestrian movement information included the movement of pedestrian(whether they start to cross from the curb or median), waiting time, frequency of attempt, pedestrian platoon(whether they are alone ,couple or more than two),pedestrian speed while crossing, if there was speed change or not and pedestrian rolling gap. When we come to vehicular characteristic vehicle speed, driver behavior (weather he yields or change direction), type of vehicle (based on the classification, small car, mini bus, or heavy (bus and truck)). In addition, the situational factors included the gap accepted type; the gap accepted size and gap rejected size.

A statistical analysis was performed on the data to establish the crossing and gap acceptance behavior of pedestrian and correlation between the variables. The effect of selected variables on the pedestrian road crossing behavior at intersection is modeled with the help of multiple linear regression technique. In the model the accepted vehicular time gap size by pedestrian will be estimated with pedestrian behavioral characteristics. The probability of accepting vehicular time gap was modeled with the choice model technique. The purpose of modelling pedestrian crossing decision is to develop a linear function of the selected independent variable. The binary logit model would provide either accept (which is coded one "1") and reject (which is coded zero's"). The critical gap was estimated using raff graphical method for estimating by graphing the Frequency of rejected data and gaps accepted. Crossing these two curves gave a value of t sec for a critical gap.

RESULTS AND DISCUSSION

Multiple Linear Regression Analysis

Preliminary Analyses

Dependent Variable: Gap accepted size

Independent Variables: Movement of pedestrian(MOP),Frequency of attempt (FOA),Pedestrian gender (PG), Pedestrian platoon(PP), pedestrian speed (PS), vehicle speed (VS), Age (Age), Accepted lag or gap (AGOL), Gap type (GAT), pedestrian speed change (PSC), waiting time (WT), pedestrian rolling gap (PRG), Driver behavior (DB), Type of vehicle (TOV). The pedestrians anticipated that the lane would clear by the time they reached it and they used a partial gap (known as "rolling gap") to cross the street (Brewer et al.,2005). In other words, there was a separate gap for each lane of traffic as the pedestrian proceeded across the street. These kinds of behaviors are considered as high risk. This descriptive statistic cannot reflect the exact gap accepting behavior because it doesn't take the censored data into account. The box plots show the distribution of the data about the median and appears to be found approximately with slight skewness to the lower side. The whiskers also show no significance difference in length which again emphasizes no significant skewness.

The normal probability plot graph in shows the pattern of the data proximately following the straight line strengthening the conclusion that the data is from normal distribution As the dependent variable (gap accepted size) was normally distributed, an ANOVA test was carried out for the categorical predictor shaving more than two out comes to identify the influential factors; an independent t-test was carried out for the predictors having two outcomes. Levence'stestwascarriedouttoexaminetheequalityofvariancesbetweentwoormoregroups.Iftheresult of this test was not significant (p-value>0.05) then the variances were equal. In this case, statistics found for one-way ANOVA test were used to evaluate the relationship between size of gap accepted and predictors, The results indicate a, moderate positive correlation between gap accepted size which is the dependent variable and the independent variables vehicle speed and waiting time. Negative correlation between dependent variable and pedestrian speed and frequency of attempt. But all the independent variables are significant except frequency of attempt.

Critical Gap

One method for analyzing critical gaps is to use graphical methods applied by Raff and Hart as outlined in Traffic and Highway Engineering. Frequency of rejected data and gaps accepted. In the graphical method, there are two cumulative curves, one of which is connecting the length of gap time with the number of gaps accepted less than t seconds and the other connecting t with the number of rejected gaps larger than t. Crossing these two curves gives a value of t for a critical gap as shown in Figure 6 below. The calculation procedure is to find the probability value of each interval gap that exists, then poured into the form of graphs. The purpose of the probability here is the magnitude of the possibility of crossing at a time when the flow of traffic provides a certain gap value. In this study, the gap interval is set at 1 seconds from 0 to 20 seconds for the time gap. In the graph above there are two lines, where the blue curve represents the acceptable gap probability, and the red curve represents the gap probability of being rejected. The critical gap value can be found from the point of inter section of the gap accepted and gap rejected. So the critical gap value is 4 sec.

Above data shows that factors that raise noncompliance in which majority of the respondent don't comply because of being in a hurry(34.6%),24.3%doesn't comply because the distance to proper facility is long, 30% of the respondent don't comply by analyzing the traffic situation weather the amount of traffic is small or the speed is slow and the rest are influenced by people that don't comply User Perceptions with Respect to Traffic Conflict and safety A number of questions were asked in order to assess the perceived level of safety (based on the speed of traffic) and user's opinions about personal crossing habit. It was found that a more than 80% of pedestrians cross or accepts gap if the driver yields or stops despite the right of way is for vehicle (on green phase time) and only 6.3% of pedestrians disagreed with crossing the street without compiling with the signal despite vehicle has yielded. With respect to speed of vehicular traffic, more than half of the respondents agree that they will cross the street if the traffic is moving slow and disregarded there crossing if the traffic is moving fast. Making their decision based on the traffic speed in the intersection.

CONCLUSION

This paper has reported pedestrian behavioral study that was carried out in India, Bhubaneswar, in order to investigate pedestrian traffic gap acceptance for signalized Intersection Street crossing in an urban setting where the road and traffic environment is less adapted for pedestrians' needs, and the pedestrians themselves are less compliant with traffic signals rules. A multi linear regression and binary logit model were considered to be the most appropriate methods to analyses the size of the accepted traffic gaps and the probability to cross the street, respectively. an attitude survey was also conducted to asses' perception of the pedestrian. A regression model was developed in order to examine the effect of various parameters on the size of traffic gaps accepted by pedestrians. It was found that the accepted gaps depend on the pedestrian speed, waiting time, speed of incoming vehicle, the pedestrian rolling gap, the pedestrian speed change in crossing, type of vehicle, driver behavior, type of gap, and age. The gap size compared with Pedestrians walking speed was found to have inverse relationship which showed pedestrian speed choice is dependent on the gap size and pedestrian choose gaps that they can take over depending on their speed or wait. But pedestrian are accepting vehicular gap size without much waiting after arriving at the curb or median. They often timed their crossing maneuvers to take advantage of an adequate gap in each individual lane, and thus complete their crossings even though the approach as a whole did not have a critical gap during their crossings.

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Table 1: Jayadev Vihar signalized intersection site description

Name of Intersection		Bole Michael		
Item No.	Approach	No. of lanes	Approach width(m)	Parking/loading unloading
1	Nandankanan	3	11	no
2	Forest Park	3	11	no
3	Baramunda	2	7.5	Yes
4	Cuttack	2	7.5	Yes

Table 2: Damana signalized intersection site description

Name of Intersection		Shola		
Item No.	Approach	No. of lanes	Approach width (m)	Parking/loading unloading
1	Nandanakanan	3	11	no
2	JayadevVihar	3	11	no
3	DAV-CSPur	2	9.6	no
4	Kelucharan Park	3	11	Yes

Table 3: Description of variables

Data	Variable with type	Unit or code	Description
Pedestrian behavioral characteristic	Movement of pedestrian (discrete)	0 (curb) or 1 (median)	The place where the pedestrian started movement
	Waiting time (continuous)	Time in second	Time spent at the curb or median
	Frequency of attempt (continuous)	Number	Number of attempts made by the pedestrian
	Pedestrian platoon (discrete)	0 (single), 1 (two) or 2 (more than two)	Makes to accept the vehicular gap
	Gender (discrete)	0 (female) or 1 (male)	Male or female
	Age (discrete)	0 (elder), (middle aged) or 2 (young)	Visual appearance chosen by discretion of researcher. 3 groups:- Estimated age group: young (<30): 2, middle (30–50):1, elderly (>50): 0

	Pedestrian speed (continuous)	m/sec	The speed of the pedestrian while crossing the road
	Pedestrianspeed change(discrete)	Yes or no	Whether a pedestrian changes speed while crossing the road or not
	Pedestrian rolling gap (discrete)	Yes or no	Whether pedestrian rolls over the available small gaps
Vehicular characteristic	Vehicle speed (continuous)	Km/hr	Speed of the vehicle at the crosswalk area
	Driver behavior (discrete)	Yes or no	Whether the driver reduces speed or changes their vehicular path, when pedestrian is already on the carriageway
	Type of vehicle (discrete)	0 (motor cycle), 1 (car), 2 (taxi) or 3 (heavy)	Motor cycle (0):- any two wheel motorized vehicles, Cars (1):- any passenger car capable of holding <= 5 passengers, Taxis (2):- minibuses and ambulances up to 12 passenger seats, heavy(3):-trucks and buses
Traffic characteristic	Gap type (discrete)	0 (near) or 1 (far)	Whether the gap is close to the curb or median.
	Accepted lag or Gap (discrete)	0 (lag) or 1 (gap)	Whether the pedestrian accepts the lag (first vehicular gap) or successive gaps
	Accepted gap size (continuous)	Time, in seconds	The time headway between vehicles that pedestrian accepts the gap of
	Gap rejected size (continuous)	Time, in seconds	The time headway between vehicles that pedestrian rejects the gap of
	Gap acceptance (discrete)	0 (rejected) or 1 (accepted)	Whether a pedestrian is accepting or rejecting a gap

Table 4: Descriptive Statistics of Extracted Variables

Minimum		**Maximum**	**Mean**	**Skewness**	**Kurtosis**		
Statistic		**Statistic**	**Statistic**	**Statistic**	**Std. Error**	**Statistic**	**Std. Error**
Movement of pedestrian	0	1	0.51	-0.038	0.05	-2.001	0.10
Waiting time	0	124	23.26	1.119	0.05	0.093	0.10
Frequency of attempt	0	5	0.96	1.313	0.05	1.079	0.10
Pedestrian platoon	0	3	1.68	-1.748	0.05	1.809	0.10
Gender	0	1	0.6	-0.408	0.05	-1.836	0.10
Pedestrian speed	0.85	3.81	1.9032	0.27	0.05	-0.84	0.10
Pedestrian speed change	0	1	0.59	-0.351	0.05	-1.879	0.10
Pedestrian roller gap	0	1	0.28	0.967	0.05	-1.066	0.10
Vehicle speed	2.14	10.67	5.1398	0.371	0.05	-0.684	0.10

Driver behavior	0	1	0.67	-0.727	0.05	-1.472	0.10
Type of vehicle	0	3	1.45	1.071	0.05	0.021	0.10
Gap type	0	1	0.41	0.357	0.05	-1.874	0.10
Accepted lag or gap	0	1	0.57	-0.283	0.05	-1.922	0.10
Age	0	2	1.48	-0.664	0.05	-0.515	0.10
Gap accepted size	1	9	3.81	0.125	0.05	-0.758	0.10

Table 5: The Result of One-Way ANOVA Test for Age Group Difference

ANOVA					
	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between Groups	389.147	2	194.574	50.692	0
Within Groups	7718.873	2011	3.838		
Total	8108.02	2013			

Table 6: The Result of One-Way ANOVA Test For pedestrian platoon size Difference

ANOVA					
	Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
Between Groups	91.021	3	30.34	7.607	0
Within Groups	8016.999	2010	3.989		
Total	8108.02	2013			

Table 7: Pearson Correlation Table between Independent and Dependent Variable

Correlations					
	GAS	WT	FOT	PS	VS
Gap accepted size	1				
Waiting time	.067**	1			
Frequency of Attempt	-0.031	.506**	1		
Pedestrian speed	-.523**	-.083**	0.024	1	
Vehicle speed	.317**	.224**	.088**	-0.023	1

Table 8 Compliance rate

Compliance ate			
	Frequency	**Percent**	**Valid Percent**
Almost never	105	25.2	25.2
Rarely	108	26.0	26.0
Sometimes	131	31.5	31.5
Frequently	40	9.6	9.6
Almost always	20	4.8	4.8
Don't know	12	2.9	2.9
Total	416	100	100

Table 9 Factors that raise non compliance

Factors that raise non compliance			
Frequency		**Percent**	**Valid Percent**
Distance to proper facility	101	24.3	24.3
Amount of traffic on the road	82	19.7	19.7
Weather other pedestrian are doing the same thing	46	11.1	11.1
Speed of traffic on the road	43	10.3	10.3
Being in a hurry	144	34.6	34.6
Total	416	100	100

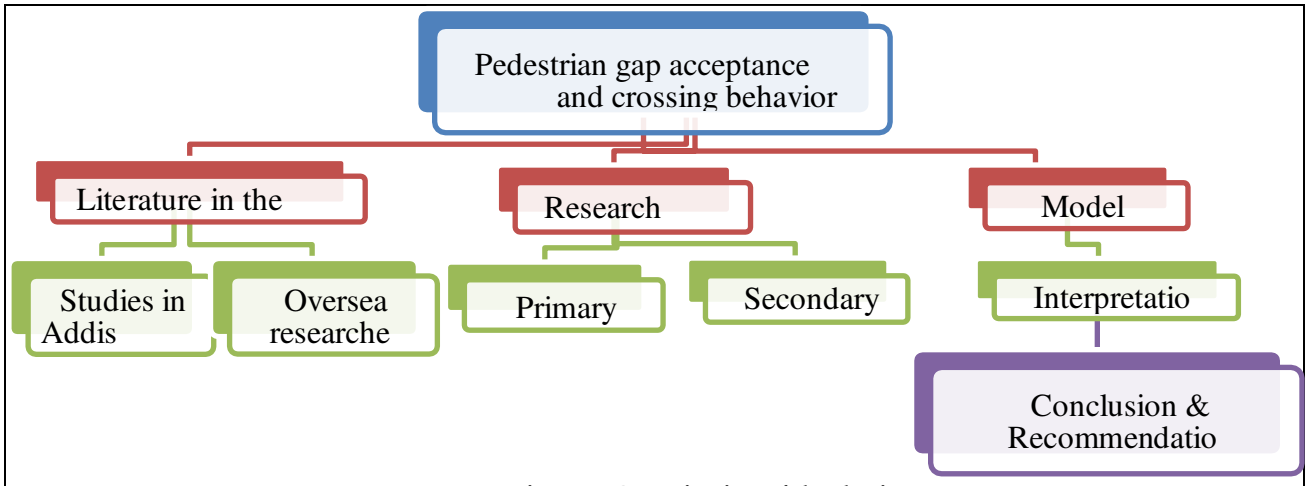

Figure 1: Organization of the thesis

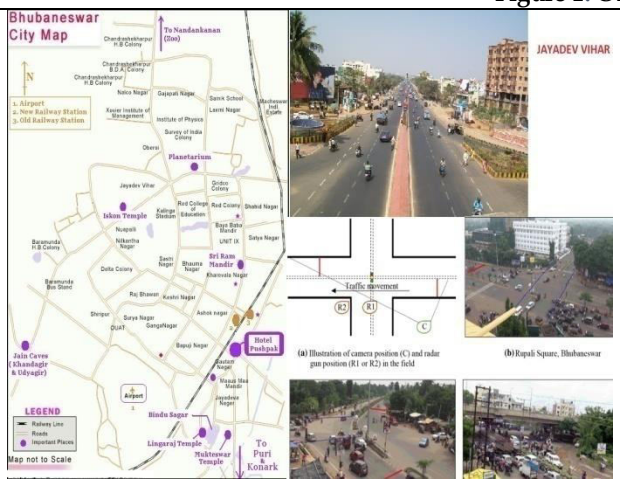

Figure 2: Illustration of study locations (Source: Google Maps, 2021)

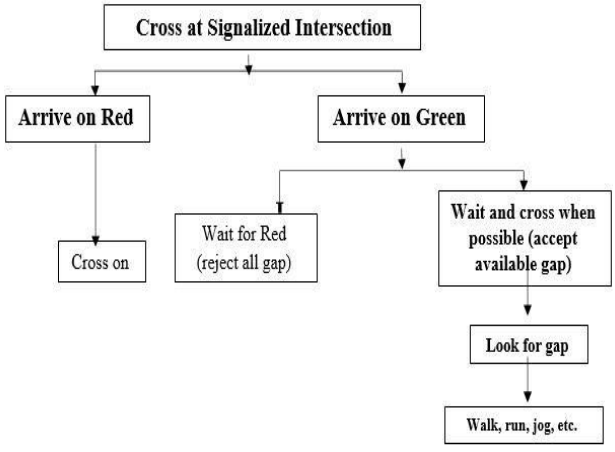

Figure 3.2: Frame work for the choice of study groups

	N	Minimum	Maximum	Mean	Std. Deviation
Movement of Pedestrian	2014	0	1	.51	.500
Waiting Time	2014	0	124	23.26	29.973
Frequency of Attempt	2014	0	5	.96	1.196
Pedestrian Platoon	2014	0	3	1.68	.618
Gender	2014	0	1	.60	.490
Pedestrian Speed	2014	.85	3.13	1.9026	.51163
Pedestrian Speed Change	2014	0	1	.59	.493
Pedestrian Rolling Gap	2014	0	1	.28	.450
Vehicle speed	2014	2.14	8.30	5.1305	1.69964
Driver behavior	2014	0	1	.67	.470
Type of vehicle	2014	0	3	1.45	.729
Gap type	2014	0	1	.41	.492
Accepted lag or gap	2014	0	1	.57	.495
Age	2014	0	2	1.48	.597
Gap accepted size	2014	1	9	3.81	2.007
Valid N (listwise)	2014				

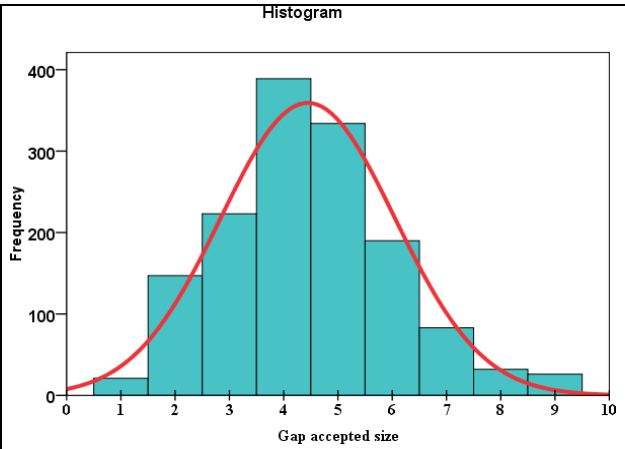

Figure 4 Normal Distribution Curve of Gap Accepted Size

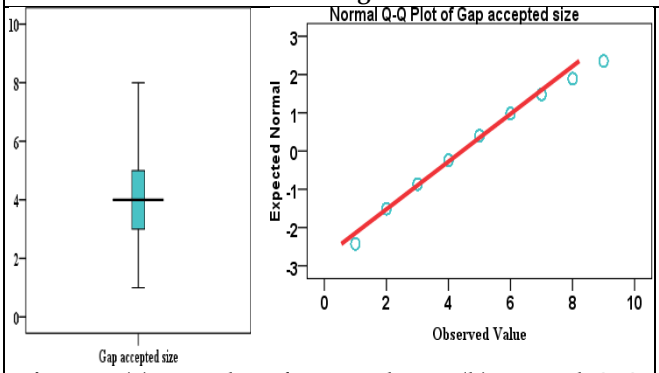

Figure 5 (a) Box plot of accepted gap; (b) Normal Q-Q plot of gap accepted size

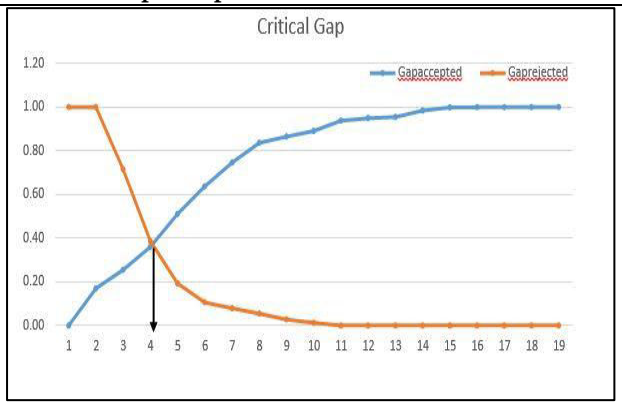

Figure 6: Critical gap

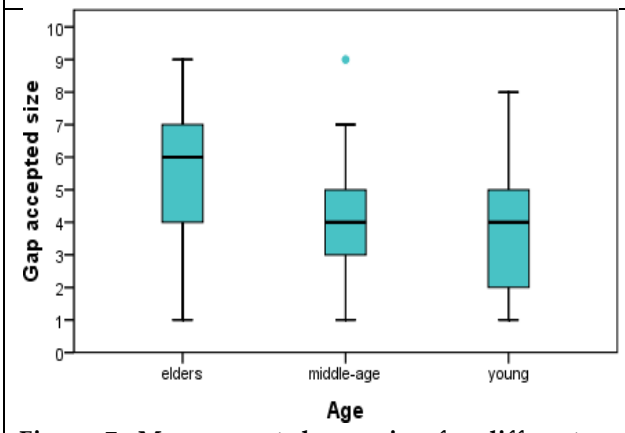

Figure 7: Mean accepted gap size for different age group of pedestrians

Figure 8 : Site Photos

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RESEARCH ARTICLE

Uber Data Analysis using Neural Networks

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ABSTRACT

Sentiments are the human's essential feelings, and deciphering them for multiple problems is similar to characteristic extracting, in which particular sentiments are taken into account for identifying problems and comprehending the use case. There are different procedures for interpreting sentiments; into that case, sentiment analysis is performed using twitter and Uber and Ola, all of which are part of the Taxi Service. Comprehension the concerns and complaints of cab services will support in the enhancement and resolution of different issues linked to users who tweet. When it comes to utilize tweets and remove formations, deep learning is crucial. Google word2Vec is often used to create lexicon in the middle of the terms and help them grasp their parallels, resulting in better tweet outputs. The tweets are split into categories : positive and negative. Deep Feed forward Neural Network convolutional neural network are two deep learning algorithm used for sentimental processing of which are art of multi layered perceptrons. The algorithms are trained using trained dataset and precision is measured to assess whether or they were properly trained. The training data is used to see whether the algorithm correctly forecasts the results indicating whether or not the algorithms is suitable for the data. Python is the Programming language of choice for nostalgic study.

Keywords: Sentimental Analysis, Feed Forward Neural Networks, Multi Layer Perceptrons, Convolutional Neural Network, Python, Twitter.

INTRODUCTION

Twitter's a social media site that makes Sentiment analysis is a technique for determining the thoughts or feelings of the individuals who posted the tweet. A person's/review consumer's is evaluated by a tweet, which lets businesses till understand what is kind of feedback a customer has on object or aid they've used.[1] After the advent of twitter sentiment analysis, it has been immensely useful for corporations to derive, measure, and appreciate the importance of their product from the viewpoint of their consumers. While sentiment analysis on

Twitter can be conducted on any domain. The Domain is chosen in cab-riding service companies . Uber and Ola. The massive data that can be obtained from cab users is one of the reasons why Uber and Ola are preferred. That can then extract the tweets to see if the users are pleased or unhappy with the programmes, as well as what problems they are having. The emotion analysis[6] of 3000 tweets was completed, and the tweets had to be cleaned for stop term, hyper-links, and white spaces after they were extracted [2]. It is possible to perform Twitter sentiment analysis using a variety of principles, methods, and algorithms. The tweets were divided into optimistic and negative emotions by Paper. Deep learning was regarded as a way to better understand how it could affect Uber and Ola's Twitter sentiment analysis.

The algorithms that we have used in this paper for our data sets are Deep Feed Forward Neural Network and Convolution Neural Network. They are seem to be Deep Neural Network (DNN) algorithms (DNN)[3]. An artificial neuron is what a perceptron is. The first procedure, Google Word2Vec, is used after the tweets have been cleaned. Google Word2Vec is a more sophisticated method of text vocabulary training. It improves vocabulary by teaching the world's closest context. The numerous parameters include perceptron weight multiplication, various activation functions, output optimizers, and loss functions [4]. The loss function is used to Measure the accuracies. This feature calculates the loss between the training and examine results allowing us to see how deep the learning algorithm affects Uber and Ola's Twitter sentiment analysis.

LITERATURE SURVEY

Deep Learning [1] has spawned plethora of work [1] in the sentimental analysis field. Deep learning algorithm has significantly assisted researchers in understanding the consistency of the data sets [2]. Deep Learning employs Artificial Neural Networks for teaching computers how to learn from the algorithms and improvise on their own. The data sets used were Uber and Ola, and we chose this domain because of the large number of users [3] [4]. Uber has about 111 million subscribers and completes about 19 million journeys a day. India has approximately 8 million users and Ola has approximately 151 million users, with approximately 2.1 million trips a day. [5]India has approximately 24.1 million users. These two businesses are on the heights of data regarding consumers, thanks to the abundance of data available [6]. With such big numbers, it piqued our interest to learn more about people's reviews of cab services on Twitter and [7] [8] how sentiment analysis can aid in deeper understanding for future deep learning improvements.

The RoD service is still relatively recent, and there are some limitations. As opposed to conventional taxi service, there are fewer studies. Very few compare price, wait time, and other factors, Incentives, as well as the level of service provided by taxi and RoD services, from the standpoint of data statistics. [9], [10], and [11] investigate the usefulness of competitive pricing of regulating & redistributing the supply & the demand across countries, increasing driver's sales, and decreasing passengers wait times, among other things. [12] attempts to assess Uber's surge pricing system using a calculation that treats Uber as a black-box, but their analysis is insufficiently robust due to a lack of evidence.

METHODOLOGY

The methods used to produce the desired outcomes are described in this part of the article, which will be briefly explained in the experimental findings. The technique is broken down into three parts:

Google Word2Vec

A smarter path to train the text to learn the language of related words is to use Google Word2vec [9]. The LP is advanced by using various vocabulary since the Word2vec a double layer structure that includes dissimilar and their similarities, which helps the document in further interpreting the context. The use of deep learning algorithms [7] [8] [9] is the main subject of this study. The easiest way to understand Word2vec is to use Deep Learning [9]. A Feed forward Neural network and CNN are the two Deep Learning algorithm used. These two part system of MLP as a subclass Deep Neural Networks because deep learning algorithm has loops MLP is always a Feed forward Neural Network [7]. Because the Google Word2Vec[9] is not really a deep learning neural network, the algorithms were required to understand the emotions of the tweets and the similarity in the middle of the terms.

Feed Forward Neural Network

This research paper's feed-forward neural network can be classified as:

Non Deep Feed Neural Network

A simple feed forward neural network having only 1-hidden layer is known as a non deep feed forward neural network[8] [9]. Its a simple neural network in which the nodes are joined together by Weights .The weights also known as biased are what allow the model to match correctly. Since the feed forward neural network[7] only has one layer, the bias is auto assigned for it. As a result, bias would have 1 value which is in between the inputs & the hidden layers. The number of neurons which were in the secret layer will vary depending on the usage case. The neurons have an activation mechanism[9] that is caused by unique values.

Deep Feed Neural Network

The deep feed-forward neural network[8] is a more sophisticated variant of the traditional neural networks In comparison to a standard neural network[4] a deep neural-network has more hidden layers . The number of secret layers varies between 2 and 8, and the network learns better as the number grows. The original and final layers are unchanged; however, the connectivity between the hidden layers grows..

Convolutional Neural Network

The Convolutional Neural Network (CNN) is a Feed forward neural network that is part of multilayer perceptron (MLP)[8].The CNN biological activity is focused on the cerebral mantle, specifically the visual cortices which assist the brain in interpreting am! processing visual information. It's usually used for image processing, but in this study, it's being used for nostalgic analysis of tweets for uber and ola. A CNN is a feed-forward neural network multilayer perceptron (MLP)[10] . The CNN biological activity is focused on the cerebral mantle specifically visual cortices which assist the brain in interpreting am! processing visual information. It's usually used for image processing, but in this study, it's being used for nostalgic analysis of tweets for uber.

The CNN has three dimensions or layers of CNN neurons[2] organised in three dimension The three dimensions are classified into three categories: 1-Dimensional CNN, 2-Dimensional CNN, 3-Dimensional CNN[6]. The forward-passing nodes in the convolutional neural network are tightly connected, which ensures that the inputs will be moved to the other layers, which have a greater number of neurons. It is the primary explanation for its ability to distinguish multiple features. The 1-0 C had to be dealt with in the study for nostalgic text analysis. . The height is the most important element in the 1-D CNN[4] when it comes to the words used in the text.

EXPERIMENTAL RESULTS

This study paper's experimental section includes a variety of experiments and findings collected by iterations. The measures in sentimental research are as follows:

- Gathering Twitter Data Analysis using Twitter API .

- For both datasets, comma-separated values files include 3000 tweets.
- Obtaining a sentimental rating for each tweet.
- Sorting the tweets into positive and negative categories .
- For negative= 0 & Positive= 1
- Creating vocabularies with specific terms.
- Partitioning the data into 2400 & 600 for Training & Testing respectively.
- Using a variety of deep learning techniques.

Table II displays the numerical similarity gap for specific terms from the data; these words are the most commonly used words in both datasets.

The dataset yielded a variety of feature aids tracking the algorithm in generating The vocabularies produced from the millions of words were trained with the help of Google Word2Vec[9] is referred to as vocabulary scale. Figure 2 shows a reflection of the vocab scale for datasets with a 500 span varying from 500 to 3000. The max vocab size for Uber datasets is restricted to 392 characters, while it was restricted to 537 characters for Ola datasets. In comparison to both databases, Ola's vocab size was significantly higher than Uber's. For the 500 tweets, Uber's minimum vocab size was 151 characters, while Ola's was 86. When the number of tweets grew, so did the scale of the vocabulary.

A series of Deep Learning algorithms known as Multi-Layer Perceptron [7] is used in data processing for sentimental analysis. Feed-forward neural networks are referred to as MultiLayer Perceptrons[7]. Deep Neural Networks have a variety of parameters. Each version of the algorithm had the same formulas, which are discussed beneath.

Multiplication of Perceptron

The input in the perceptron has some values, which is then passed over to a node having few allocated weights, is then combined to bias and over passed to function. Every perceptron's formula follows: (1).

$$y=\sum_{i=1}^{n} w_i * x_i + b \quad .(1)$$

Activation Functions of Various Types

The activation function is made up of the values derived by multiplying the weights and adding the bias. Many functions are available, although the ones in the paper are Re Lu function (2) and Sigmoid function(3).

1.) ReLu Activation Function

$$\text{Max}(y,0) \quad (2)$$

2.) Sigmoid Activation Function

$$z=\frac{1}{1+e^{-y}} \quad (3)$$

The Optimizers used

Optimizer is used to increase performance over time through different cycles; the number of the optimizers that is used can vary. Adadelta is the one optimizer utilised by Deep Neural Network algorithm (4).

Since the Adagrad[9] is the optimizer missing because of an improvement of magnitude in the divisor, which resulted in the rise of the rate of learning, Adadelta was used for

counteracting the impact [13].

$$\theta_{t+1} = \theta_t + \Delta\theta_t$$

$$\Delta\theta = \frac{RMS[\Delta\theta]_{t-1}}{RMS[g_t]} g_t \quad .(4)$$

Loss Function

Binary-Cross Entropy(BCE) loss function is that function which is utilised to treat the performance loss here (5). Outputs are 0 and 1 respectively, so binary is used [10].

Loss Function= $-(y_i \log(\hat{y}_i)+(1-y_i)\log(1-\hat{y}_i))$ ...(5)

The Non-DFF Neural Networks[4], which is a form of Deep Learning model, is categorised into several categories. The feed-forward neural networks, unlike recurrent neural networks, transfers values towards forward path and contains no loops. Here the word "non thick" refers to the fact that this model only has one hidden layer. In the middle of input output layers is a layer called hidden layer. The back-propagation method is being used here for training the DNN. Back propagation [5] is a technique for changing and adjusting different weights in order to minimise the performance loss. Figure 2 depicts the model network, which includes hidden layers with 300 number of inputs and 128 number of nodes and ReLu, as well as an output layer having one node that can send either zero or one and Sigmoid. To see how a particular interval influenced accuracy of the rest of the datasets, Non-Deep Neural Network [2] was equipped. Both Uber and Ola datasets were used to train the model, and the Training and Testing performance with Validation of both the partitioned datas.

To see how Non-DNN affected the final 3000 datasets, it was checked on a variety of other datasets. The consistency of the model on different datasets is seen in Table III.The accuracies in percentages are seen in the table below, and could be shown that the accuracy produced for five hundred datasets was 87.10 percent for the Uber and was 70.33 percent for the Ola. Here Ola's precision from base dataset was lower, but provided a better score, that is 81.89 percent for the 3000 dataset. Its effect has an average accuracy that is 92.98 percent for the Uber dataset and 75.18 percent for Ola datasets, thats 17.80 percent lesser than The Uber. DFF Neural Networks[5] were used, along with hyper-parameter optimisation, for finding out how many hidden layers were needed for each model. For deep learning model, the number of hidden layers used is two Hidden Layer, keeping all remaining parameters exactly same. In contrast to non-dnn of batch size 50, this model uses 20 epochs.The same method was used to explain what precision was produced on different intervals of datasets for this model. Accuracy developed from several Uber and Ola datasets is shown in Table IV below. It can be found that the Uber datasets had a base accuracy of 88.00 percent and the Ola datasets had a base accuracy of 71.20 percent, and the best accuracy produced for Uber dataset which was 96.30 percent & for Ola it was 82.15 percent, which was not substantial improvement when compared with a 1-Layer model.

The lack of any kind of model is a crucial factor in determining whether or not the model produces a better overall outcome.The loss which occured due to Deep Learning(DL) Neural Networks is also measured and compared with loss of the Non-DL model for finding whether the Deep Learning Neural Network has the lowest loss. CNN[8] which is also known as feed-forward neural network, has been a complicated construct that takes into account a variety of considerations. The single embedding layers having dimensions of three hundred & a total of 2200 words, which has 128 filters having kernel size of about three,four,five and ReLu as an Activation Function. Table V shows the accuracy provided by the CNN model, & its clearly visible that least accuracy developed for Uber dataset is 91.33 percent, and minimum accuracy generated for the Ola dataset was 65.20 percent, which of course was higher in comparison to Accuracy of the Non-DNN & DNN. For Uber and Ola datasets, the maximum accuracy produced is 96.00 percent and 80.37 percent, respectively, which is similar to the other two models. Uber datasets have a mean accuracy of 93.59 percent, while Ola datasets have a mean accuracy of 74.41 percent.

CONCLUSION

DL algorithm is used to train data so that we can better interpret the emotions. To get a proper understanding of related kinds of vocabulary, Google Word2Vec was utilized for creating vocabulary and for rendering terms in a dataset. All three models were used to measure accuracy. The DNN[8] [9] with a two-hidden layer is the model which provided best accuracy in Uber dataset. The hyper parameter optimization allowed for the use of two hidden layers, which were a better fit for tweets which were for Uber.

Likewise, DNN[8] [9] with a two-hidden layer generates best accuracy for Ola dataset is also the same. Accuracy of tweets for Ola were not as high as Uber tweets because extracted tweets had a lot of the texts which weren't in correct order, and even after fixing that, could not produce the accuracy once anticipated. CNN is also considered to be mild in contrast to the DNN, which was questionable. Even if CNN was well known for its image recognition, it was utilized for checking how well it performs for text analyses.

Future Scope

Sentiment analysis can possibly be performed for a variety of dataset using a variety of techniques. It can also be achieved with a number of new Twitter hash tags, except the ones currently in use. Deep learning models need more data than machine learning models, so the count of tweets should be expanded to get decent output. The parameters used in this analysis were adadelta, BCE, and Functions such as ReLu Activation Function[12] and Sigmoid Activation Function.

For the long run, more diverse types of parameters may be used to explain how the data works on them and provide precision. Similarly, Recurrent neural networks may be utilized for calculating the accuracy of different dataset. While its the member of Deep Neural Network, Recurrent neural networks aren't a multilayer Perceptron. Since it isn't feed-forward neural network, RNN outperforms CNN because of the loops that provide feedback to individual nodes, which CNN lacks. The LSTM[11], abbreviates as Long short term memory and the member of DNN, is another algorithm that can be used to obtain sentiments.

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Table I. Google Word2Vec Distance

Sr. No of Words	Words	Distance Similarity
1	via	0.37331557273864746
2	message	0.3613654673099518
3	direct	0.34762924909591675
4	this	0.3421033024787903
5	email	0.32505300641059875

Table II. Non-DNN's Accuracy

Dataset	500	1000	1500	2000	2500	3000
Uber	87.10	91.00	94.33	95.75	93.20	96.17
Ola	70.33	74.00	73.33	72.50	79.40	81.89

Table III. DNN's Accuracy

Dataset	500	1000	1500	2000	2500	3000
Uber	88.00	91.50	93.33	94.75	95.00	96.30
Ola	71.20	73.00	74.67	73.00	80.20	82.15

Table IV. CNN's Accuracy

Dataset	500	1000	1500	2000	2500	3000
Uber	91.33	92.00	92.6	95.50	94.4	96.00
Ola	65.20	75.00	71.33	77.25	77.60	80.37

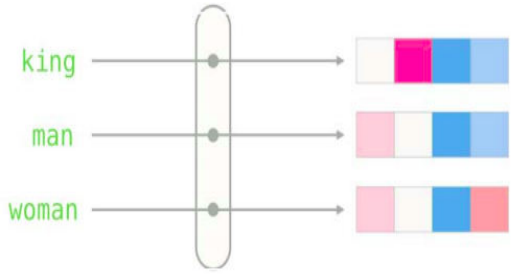

Fig. 1. Representation of Google Word2Vec[9]

Layer (type)	Output Shape	Param #
dense_4 (Dense)	(None, 128)	38528
dropout_3 (Dropout)	(None, 128)	0
dense_5 (Dense)	(None, 1)	129

Fig 2. Non-DNN Layers

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RESEARCH ARTICLE

Flood Resilient Residential Building: An Assessment

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ABSTRACT

The research assessed the enhanced model of flood-resilient two-storey residential building for flood-prone areas in San Juan, Surigao City during the academic year 2016-2017. It determined the technical requirements in terms of architectural, structural design and cost. Effectiveness was also ascertained with respect to the requirements and the difference was also measured. A descriptive developmental research design was used. The assessment was done by 85 respondents through a researcher-made questionnaire. Data were analyzed using mean and standard deviation for the effectiveness of the design, One-Way Analysis of Variance and Scheffe's Test for the difference on the effectiveness of the design. The design adhered to the technical requirements that include structural, architectural and cost. Based on results, it has a very good structural and architectural design as perceived by the architects, engineers, faculty and students. It has a very good structural attachment as evaluated by the engineers, faculty and students but just good for the architects. Its cost is very reasonable as determined by the engineers but only reasonable as perceived by the architects, faculty and students. The three respondent groups did not significantly differ in their evaluations on the effectiveness of the Technology-based Flood Resilient Two-Storey Residential Building except on structural attachment and cost. Based on findings, the study concluded that the design possessed all necessary requirements and most of all safe from danger. However, the structural attachment and cost effectiveness, need enhancement and improvements since the architects found them not so good.

Keywords: Flood Resilient Residential House, Stable and Aesthetically Designed House, Descriptive Research, Assessment, Perceptions

INTRODUCTION

Background and Rationale

The most basic and important in human needs is shelter. It should built a strong foundation to protect from hazards such as flood. It is written in the bible in the book of (Luke 6:48)."It is like a person building a house who digs deep and lays the foundation on solid rock. When the floodwaters rise and break against that house, it stands firm because it is well built". The most common and perennially occurring hazard in the mainland of Surigao City is flooding (Buenaflor & Bataan, 2018)). This study is about the designed model of flood resistance two-storey residential building. It is to be constructed in the flood-prone areas in Surigao City. Thus, Kircher, *et.al.* (2010) discussed the foundation styles in coastal and flood-prone areas. It introduced types of foundation that can withstand the moving floodwater. In order to have a flood-resistance house, the building code must be followed (Bramley & Bowker, 2002,). To reduce flood risk, as emphasized by Xian, Lin & Kunreuther (2017)the designer should know the based flood elevation(BFE). Then, these are the bases of identifying the height of the elevation, flood characteristics and site factors(Kahan, 2015).

Precisely, architectural design is always be considered in any building construction. Aside from having strong foundation structure, aesthetic value or beauty be included. Adaptation of modern architecture is added to enhance the decorative design. The modern man's shelter shall have necessities of warm and dry house. Plumbing/sanitary and electrical plan also a part of the design. To complete the elements and principles of design, spatial and project cost factor must be integrated. This study will provide technical guidance in designing two-storey residential house for the flood-prone areas. It is not only in Surigao City but in the other places who are affected. It use as basis in building safer house to minimize the loss of life and property. It is beneficial to the students in drafting and architecture. Home developers also can be benefited on this study. And it could be used as reference for the future researchers**.**

Objectives of the Study

The general objective of this study is to assess the designed flood resilient residential building.The specific objectives are:

1. To design a footing system that can to prevent flotation, collapse or significant permanent movement resulting from flood action;
2. To evaluate the base flood elevation or the highest flood elevation as the basis of the height of the finished ground floor level;
3. To introduce the compliance of the National Building Codes and building regulations in designing flood resilient building;
4. To evaluate the effectiveness of the present design of the technology-based flood resilient building;
5. To conduct information drive about earthquake, landslide, storm surge and flood threat awareness; and
6. To recommend the adoption of the present design of the technology-based flood resilient building in the flood- prone areas in Surigao City.

RESEARCH METHODOLOGY

This research used the descriptive developmental research method. This descriptive developmental research describes and interprets the present characteristics or development of a subject or phenomenon through stages [(Labouvie, 1975);(Lijnse, 1995)]. This type of research is suitable for this study because it will describe the responses of identified respondents on their perception on the effectiveness on the designed technology-based flood resilient two-residential building for flood-prone areas in Surigao City using a research made evaluation questionnaire.

The study is conducted in Surigao City. The latter is located in Northeastern Mindanao, 9 deg. to 10 deg. North latitude and 125 deg. to 126 deg. East longitude. Towards North is Dinagat Island; Southward is the mainland of

Surigao del Norte; Eastward is the Hinatuan passage and Westward is Surigao strait and Southern Leyte. Surigao city has no regular dry season but it has a rainy season from November to January. Based on a 50-year period, the city has an average annual rainfall of 3,673.8 millimeters. Surigao is dubbed as one of the "wettest" places in the country with an average of 216 rainy days each year. It has an average temperature of 26.9 degrees centigrade and a humidity level of 85%.

With a total land area of 245.34 sq.km. and a jurisdictional area of 690.37 sq.km. Surigao City has 32 mainland and 21 island barangays. Three major barangays compose the city: Brgys. Washington, Taft, and San Juan. Within the city's jurisdictional area, Surigao's 21 island barangays are distributed among the 17 islands and islets. Topographically, the city's physical make up is hilly and irregular, and has an elevation level of 65.5 feet above sea level. Of its land area,75.8 percent is classified as alienable and disposable and only 24 percent are still forest lands. In terms of land use, crop lands comprise 62 percent of the city's land area. Figure 3 shows the map of Surigao City and Figure 4 shows the Vicinity Map indicating the location of Surigao in the Philippines.

RESULT AND DISCUSSION

Significant Difference of Effectiveness of the Design Technology-Based Flood Resilient Two-Storey Residential Building

This section revealed the difference on the effectiveness of the Technology-based Flood Resilient Two-Storey Residential Building as perceived with respect to the type of respondents.

Difference on the Effectiveness of the Design

Table 11 presents the difference on the effectiveness of the Technology-based Flood Resilient Two-Storey Residential Building with respect to the type of respondents. The Table shows that when the structural effectiveness of the design as to footing system, floor height and enclosure below the flood hazard level, material requirements, and utilities were compared among respondent groups, the obtained p-values are 0.427, 0.101, 0.198, and 0.538 respectively. Since the p-value are greater than 0.05, the null hypotheses are accepted. These entail that there is no significant difference on the evaluations of the three groups of respondents concerning the structural effectiveness of the design in terms of the above-mentioned areas. The same results were obtained when the architectural effectiveness of the design as to aesthetic value or beauty, maximization of space and characteristics that defined modern architecture when compared among the three groups of respondents. These are based on p-values which are greater than 0.05. These are 0.551, 0.285, and 0.330 respectively.

However, a p-value of 0.017 and 0.031 were obtained when the structural effectiveness of the design as to structural attachment and when the architectural effectiveness of the design as to cost were compared among the three groups. Since the p-values are less than 0.05, the null hypotheses are rejected. This suggests that there is a significant difference on the evaluations of the three groups of respondents concerning structural attachment and cost of the design. Table 12 compares the evaluations of the three groups on structural attachment and cost pairwise. It can be gleaned from the Table that architects and engineers obtained a p-value of 0.02 when their evaluations in structural attachment were compared. Since the p-value is less than 0.05, the null hypothesis is rejected. The mean difference of -0.85 implies that the mean value of the engineers is greater than that of the architects. Also engineers Faculty and students got a p-value of 0.03 when their evaluations on cost of the design were compared. Since the p-value sis less than 0.05, the null hypothesis is rejected. The mean difference of 0.37 imply that the group of engineers has higher mean value compared to the faculty and students.

The results suggest that the engineers are more convinced that the design has a very good structural attachment and a very reasonable costs than the other groups.

Based on the results, the study concluded that the technology-based flood resilient residential building for flood-prone areas in Surigao City possesses all necessary characteristics of a building that is durable, comfortable, convenient, cost effective and most of all safe from danger. However, in the structural attachment and cost effectiveness of the design need to be checked and developed for improvements since the architects found not so good.

Recommendations

The following are forwarded for recommendations:

1. The designed Technology-Based Flood Resilient Residential House is hereby indorse for implementation. However, in the structural attachment and cost effectiveness of the design need to be checked and developed for further improvements since the architects found not so good.
2. Civil engineers should consider constructing residential buildings in flood prone areas using the developed design.
3. Architects, building and building developers are encouraged to consider creating designs that are flood-resilient which are based on this design.
4. It can be used as references to the students in drafting, civil engineers, architecture and future researcher for enhancement and further improvements.

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Table 1. Difference on effectiveness of the technology-based flood resilient two-storey residential building among respondent groups

Characteristics	F-value	p-value	Decision
Structural			
Footing System	.860	.427	Accepted
Floor Height and Enclosure Below the Flood Hazard Level (Fhl)	2.355	.101	Accepted
Structural Attachment	4.269	.017	Rejected
Material Requirements	1.654	.198	Accepted

Utilities	.625	.538	Accepted
Architectural			
Aesthetic Value or Beauty	.601	.551	Accepted
Maximization of Space	1.275	.285	Accepted
Characteristics that Defined Modern Architecture	1.123	.330	Accepted
Cost	3.621	.031	Rejected

Table 2. Pairwise comparison for difference on effectiveness of the technology-based flood resilient two-storey residential building in terms of structural attachment and cost among respondent groups.

Variable	Group		Difference	Std. Error	p-value	Decision
	I	J	(I-J)			
Structural Attachment	Architects	Engineers	-0.85	0.29	0.02	Rejected
		Faculty and Students	-0.62	0.27	0.09	Accepted
	Engineers	Faculty and Students	0.23	0.15	0.31	Accepted
Cost	Architects	Engineers	-0.35	0.27	0.42	Accepted
		Faculty and Students	0.02	0.25	1.00	Accepted
	Engineers	Faculty and Students	0.37	0.14	0.03	Rejected

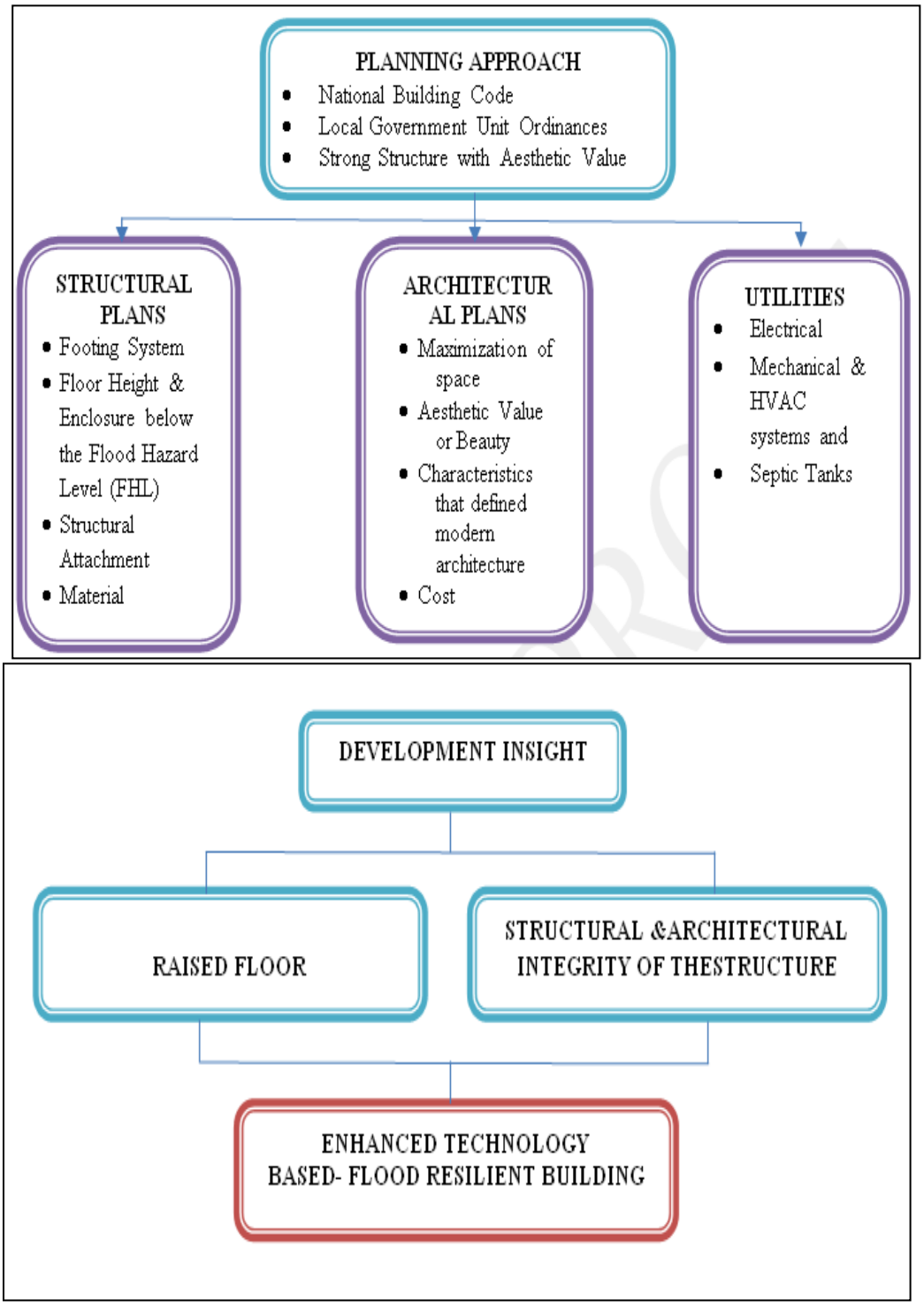

Figure 1. Conceptual Framework

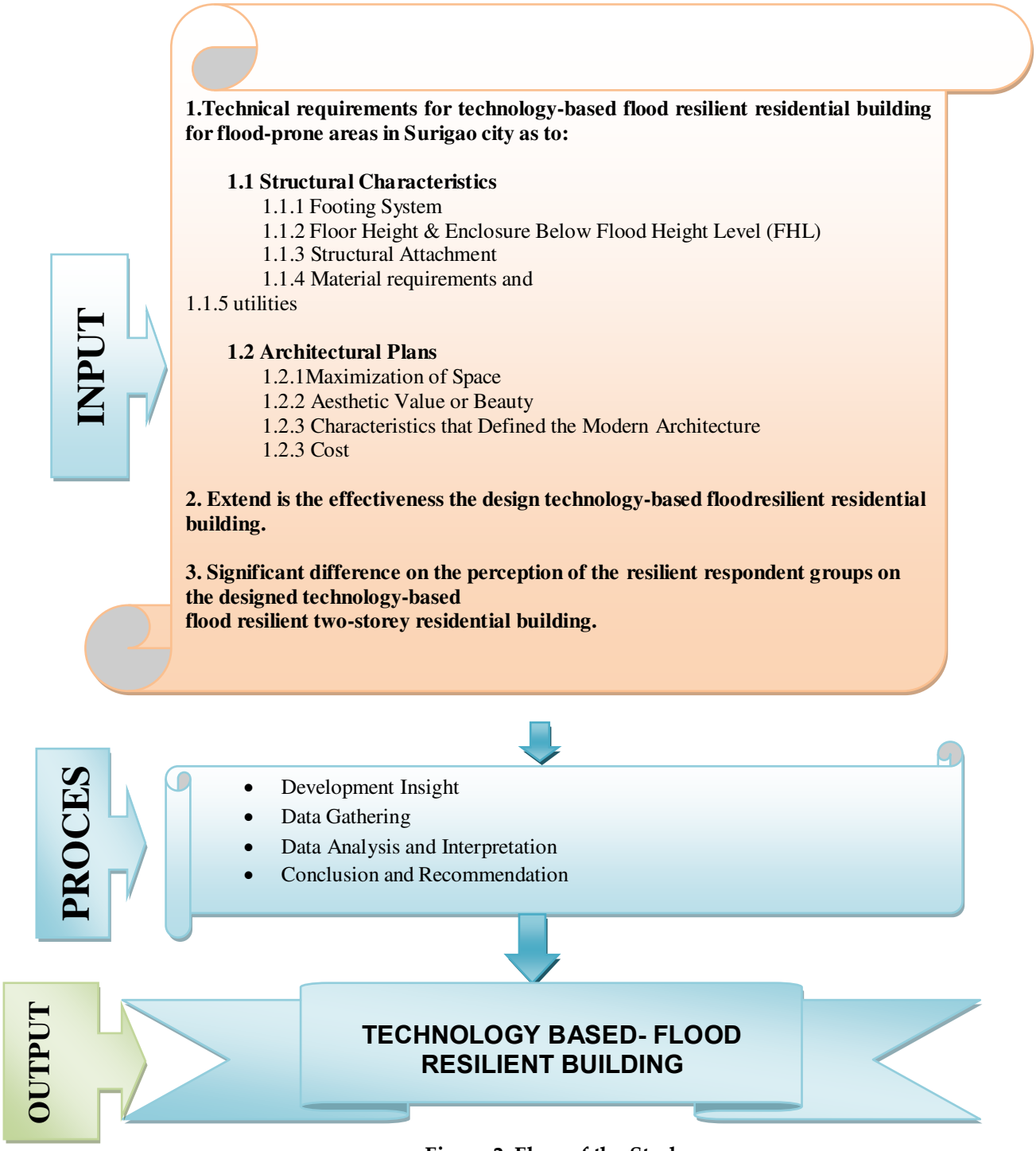

Figure 2. Flow of the Study

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RESEARCH ARTICLE

Formulation and Evaluation of Antiinflammatory Gel from the Leaves Extract of *Acalypha indica*

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ABSTRACT

Gels are the semisolid systems in which a liquid phase is constrained with the three dimensional polymeric matrix consisting of the natural or synthetic gums. *Acalypha indica* is a weed that grows in the South-East Asia. It contains several valuable compound as that can be used for curing various disease such as rheumatism, skin infection. Here, the extraction of *Acalypha indica* using Soxhlet extraction with different solvents methanol and ethanol .In soxhlet extraction, ethanol solvent provided the highest extraction yield. The release of drug is faster to the particular site of action compare to cream and ointments .The gel formulation were prepared by using carboxy methyl cellulose sodium, Hydroxy propyl cellulose, propyl paraben , ethyl acetate, glycerin, triethanolamine and the required amount of the distilled water. The formulation were evaluated for physical parameters appearance, pH , spreadability, extrudability. The extract of *Acalypha indica* shows significant improvement in anti-inflammatory properties.

Keywords: *Acalypha indica* , Carboxy methyl cellulose sodium , Glycerin, Spreadability, Extrudability

INTRODUCTION

Gels are semisolid systems in which a liquid phase is constrained within a three dimensional polymeric matrix consisting of natural or synthetic gums in which a high degree of physical (or sometimes chemical) cross-linking has been introduced. Topical application of gel at sites offer great advantage in a faster release of drug directly to site of action, independent of water solubility of the drug as compared to cream and ointments. Some of these systems are as clear as water in appearance, visually aesthetically pleasing as in gelatin deserts and other are turbid. The clarity

range from clear to a whitish translucent [1]. The polymer are used between 0.5 – 15% and in most of the cases they are usually at the concentration between 05 -2%. Gels are usually clear transparent semisolid containing the solubilized active substances. In a gel the liquid phase does not consist of isolated pockets, but is continuous. Consequently, salts can diffuse into the gel almost as fast as they disperse in a dish of free liquid. Thus, the gel seems to resemble a saturated household sponge, but it is distinguished by its colloidal size scale, the dimensions of the open spaces and of the solid objects constituting the network are smaller (usually much smaller) than a micrometer. This means that the interface joining the solid and liquid phases has an area on the order of 1000 m^2 per gram of solid. As a result, the properties of a gel are controlled by interfacial and short-range forces, such as van der Waals, electrostatic, and hydrogen-bonding. Factors that influence these forces, such as introduction of salts or another solvent, application of an electric field, or changes in pH or temperature, the interaction between the solid and liquid phases. Variations in these parameters can induce huge changes in volume as the gel imbibes or expels liquid, and this phenomenon is exploited to make mechanical actuators or hosts for controlled release of drugs from gels. For example, a polyacrylamide gel (a polymer linked by covalent bonds) shrinks dramatically when it is transferred from a dish of water (a good solvent) to a dish of acetone (a poor solvent), because the polymer chains tend to favor contact with one another rather than with acetone, so the network collapses onto itself [2]. The most striking feature of a gel is its elasticity: if the surface of a gel is displaced slightly, it springs back to its original position. If the displacement is too large, gels, except those with polymers linked by covalent bonds, may suffer some permanent plastic deformation, because the network is weak. The process of gelation, which transforms a liquid into an elastic gel, may begin with a change in pH that removes repulsive forces between the particles in a colloidal suspension, or a decrease in temperature that favors crystallization of a solution of polymers or the initiation of a chemical reaction that creates or links polymer [3].

MATERIALS AND METHODS

Materials

Carboxy methyl cellulose sodium were obtained from Colorcon Asia Pvt .Ltd. Hydroxy propyl methyl cellulose were obtained from Colorcon Asia Pvt .Ltd. Glycerin were obtained from Scientific mercury. Ethyl acetate were obtained from Loba chemicals [4].

Plant materials and extract preparations

Acalypha indica (Family: Euphorbiaceae) The dried leaves of *Acalypha indica* were collected from ABS Botanical conservation, research and training center Kaaripati, Salem. The plant material was taxonomically identified by botanist & horticulture Dr.A.Balasubramanian. The Leaves of *Acalypha indica* were dried under shade and then powdered with a mechanical grinder. The powder was passed through sieve no.40 and stored in an airtight container for further use.100 gm of the coarse exhaustively and successively with various solvents in an increasing order of polarity viz, petroleum ether (60-80) and ethanol in soxhlet apparatus .The ethanolic extract was concentrated in vacuum under reduced pressure using rotary flash evaporator. The aqueous extract by cold maceration process. It was further concentrated and dried in desiccator. The dried powdered leaves of *Acalypha indica* were defatted with petroleum ether (60-80°C) in a soxhlet apparatus. The defatted powder material thus obtained was further extracted with ethanol. The solvent removed by distillation under the low pressure and the resulting semisolid mass was vacuum dried using rotary evaporator. The aqueous extract (distilled water with chloroform) extracted by cold maceration.

Data Showing the Extractive Value of Aqueous extract of the Leaves of *Acalypha indica*

Weight of Leaves before drying	:	389gms
Weight of Leaves after dried	:	359gms
Weight of Leaves after powder	:	345gm
Dry weight / Initial weight x 100	:	88.68%

Evaluation of the gel

Appearance

The *Acalypha indica* Gel formulated was observed for their Visual appearance, Colour; feel upon application such as grittiness, greasiness, stickiness, smoothness, stiffness and tackiness. The results are shown in **Table no: 6**

pH

The pH of the gels, were found immersing pH meter to a depth sufficient in a beaker containing gel. The determinations were carried out in the triplicate and the average of three reading is recorded. The results are shown in **Table no: 8**

Viscosity

The viscosity of formulated gel bases was determined. The viscosity determinations were carried out on Brook-field viscometer using spindle number S -06 and the determinations were carried out in triplicate and the average of three reading is recorded [5].

Spreadability

The parallel plate method is the most widely used method for determining the Spreadability of semisolid preparations. The advantages of the method are simplicity and relatively lack of expense. Also, the assemblies can be designed and fabricated according to individual requirements to type of data required. ON the other hand, method is less precise and sensitive, and the data it generates must be manually interpreted and presented [6]. Vennat et al validate the spreading diameter measurements of hydrogels on the basis of cellulose derivatives and established the linearity of spreading diameter measurements. The spreading capacity of the gel formulations was measured 48 hrs. after preparation by measuring the Spreadability diameter of 1 g of the gel between two 20 x 20 cm glass plates after 1 min. The mass of the upper plate was standardized at 125g is used as a similar apparatus to assess the Spreadability of gels. The following equation was used for the purpose.

$$S = m \times \frac{L}{T}$$

Where:

S, is the Spreadability of gel formulations

M, is the weight (g) tied on the upper plate,

L, is the length (cm) of the glass plates, and

T is the time taken for plates to slide the entire length.

Procedure

Two glass slide of 20 x 20 cm were selected. The gel formulations who's Spreadability had to be determined was placed over one of the slides. The other slide was placed upon the top of the gel such that the gel was sandwiched between the two slides in an area occupied by a distance of 60 cm along 100g weight was placed upon the upper slide so that the gel between the two slides was pressed uniformly to form a thin layer. The weight was removed and the excess of gels adhering to the slide was scrapped off. The two slides in positioned were fixed to a stand without slightest disturbance and in such a way that only the upper slide to slip off freely by the force of weight tied to it. A 20g weight was tied to upper slide carefully. The time taken for the upper slide to travel the distance of 6 cm and separate away from the lower slide under the direction of weight was noted. The determinations were carried out in triplicate and the average of three reading is recorded [7].

Extrudability

I am useful empirical test to the measure the force required to extrude the material from a tube. Since the packing of

gels have gained a considerable importance in delivery of desired quantity of gel from jar extrusion of gel from collapsible tube, therefore measurement of Extrudability becomes an important criteria for gels [8].

Procedure

The gel formulation was filled in standard caped collapsible lami – tube and sealed. The tube was weighed recorded. The tube was placed between two glass slides and was clamped. A 500 g weight was placed over the glass slide and then cap was opened. The amount of gel extruded were collected and weighed. The % of gel extruded was calculated; and grades were allotted (++++ excellent, +++ good, + +fair, + poor) [9].

***Iv vitro* Drug Diffusion Study**

Arrangement of assembly

Six Franz Diffusion Cells are interconnected to each – other in crisscross motion, for maintaining the temperature 32°C. The Franz Diffusion Cells are interconnected by nylon tube and the both ends of these tubes are connected to the chiller. The one end of the chiller provides water of 32°C temperature to outer jacket of cell and another end recycles the water to the chiller [10].

Preparation of Media

In a 500 ml of volumetric flask ethanol: Water is mixed in 80:20. After mixing, flask is shaken, to facilitate the uniform mixing of solvents

Procedure

- Before starting the study the cells are calibrated for their volume capacity.
- Media taken in 50ml beaker, in which diffusion membranes (6) are poured and stand for few minutes.

Membranes are removed out and dried in oven at 30 – 35° C [11].

Characteristics of Gels

Ideally gelling agents for pharmaceutical and cosmetic use should be inert, safe and noncreative with other formulation components. A potential incompatibility is illustrated by the combination of cationic drug, preservative or surfactant with as anionic former. Example: Sodium alginate has been shown to reduce the concentration of cationic preservatives in solution as well as complex with chlorpheiramine, reduce the drug release rate from gelled formulation. Polyether has been shown to interact with phenols and carboxylic acids a gelling agent in a formation should provide a reasonable solid like nature during storage that can be broken when subjected to the shear force generated in shaking a bottle, squeezing a tube, or during topical application. A cost consideration requires a low concentration of gallant to produce the desired characteristics [2].

The gel should exhibit little viscosity change under the temperature variations of normal use and storage. For e.g. platibase exhibits a lesser decrease in consistency than petrolatum over the some temperature range. This minimizes unacceptable changes in the products' characteristics. The gels particularly those of polysaccharide nature are susceptible to microbial degradation. Incorporation of a suitable preservative may prevent contamination and subsequent loss of gel characteristics due to microbial attack. The gel characteristics should match the intended use. A topical gel should not be tacky. Too high a concentration of gel former or the use of an excessive molecular weight may produce a gel difficult to dispense or apply. An ophthalmic gel must be sterile. The aim in to produce a stable elegant, economic gel product adequately suited for its intended use [12].

Swelling

Gels can swell, absorbing liquid with an increase in volume (e.g.Xerogels). This is referred to as swelling and the pressure developed is known as swelling pressure. The swelling can be looked on as the initial phase of dissolution as osmosis occurs. When solvent penetrates the gel matrix, Gel – Gel interaction are replaced by gel –solvent interactions. Limited swelling is usually the result of some degree of cross linking in the gel matrix that prevents

total dissolution. Such gels swell considerably when the solvent mixture possesses a solubility parameter comparable of that of the gallant [13].

Syneresis

Many gels systems undergo a contraction upon standing. The interstitial liquid is expressed, collected at the surface of the gel. This process is referred to as syneresis or bleeding. Syneresis is not limited to organic hydro gels but has been seen in organogels and inorganic hydrogels. Typically syneresis becomes more pronounced as the concentration of polymer decreases. The mechanisms of concentration have been reduced to the relaxation of elastic stress developed during the setting of the gel. As these stress are relieved the interstitial space available for solvent is reduced forced the expression of fluid. Osmotic effects have been implicated, as the both pH and electrolyte concentration influences syneresis from gels composed of the ionic gel former gelatin or psyllium seed gum [14,15].

Structure

Inorganic particles are capable of gelling a vehicle due to formation of a "house of card" structure. Clay's e.g bentonite or kaolin possesses a lamellar structure that can be extensive hydrated. The flat surface of bentonite particles are negatively charged while the edges are positively hydrated. The flat surface of bentonite particles are negatively charged while the edges are positively charged. The attraction of face to edge of these colloidal lamellae creates a three-dimension network of particles throughout the liquid, immobilizing the solvent. The interactions between the particles are fairly weak, being broken by stirring or shaking [13]. The long chain of organic gel formers are extended in good solvent would be the case in aqueous gels as the result of hydrogen bond formation between water and hydroxyl groups of the gelling agent. In a poor solvent, the gel molecule would be more tightly coiled preferring self-interaction to with the solvent [16].

Each segment of the dissolved molecules is in constant random motion, buffered by movement of solvent through the bulk of the liquid. This random motion serves to entangle polymer strands. Molecular entanglement is responsible for the viscosity and structure of organic gels [17]. The organic polymers used in hydrogels tend to be sheathed with an envelope of water of hydration. This enables the polymer molecules to slip past each other at low concentration because of the lubricity of the intervening water molecules. If the degree of hydration is low, then intermolecular attractive forces such as hydrogen bonding and vander walls forces from weak secondary bonds between polymer strands. At sufficient high concentration, a continuous network of weakly interacting chains can be formed. The associated may proceed far enough to produce small local regions of crystalline nature dispersed through a bed of randomly entangled polymer strands [18].

Salts may attract part of the water of hydration of the polymer, allowing the formation of more intermolecular secondary bonds, leading to gelation and precipitation. This is known as salting out. Multivalent cautions have a strong effect on the solutions of anionic polymers. Bridging of polymers by di or trivalent captions, as in the addition of cooper to solutions of sodium carboxymethylcellulose or calcium to sodium alginate, leads to gel formation.[19]

Alcohols have a similar effect. In addition, alcohols alter the solvent's characteristics, changing the solubility parameter. The addition of alcohol often brings about coacervation rather than gelation. Conservation is the production of a viscous, solvated, polymer-rich phase, leaving behind a phase that is mostly solvent and, therefore, poor in polymer [20]. The effect of temperature depends on the chemistry of the polymer and its mechanism of interaction with the medium. Many gel formers are more soluble in hot than cold water. If the temperature is reduced once the gel is in solution, the degree of hydration is reduced and gelation occurs. Some polymers exhibit thermal gelation. These polymers are more soluble in cold water; solutions of these materials gel on heating. Examples include methyl cellulose and poloxamer [21]. Physical observation of the sample was done at every week for any colour change or lumps formation and flow. There is no colour change but slightly lumps observed in sample charged at 40°C/75%RH for 1 month [22].

UV Spectrophotometric Analysis

UV Spectrophotometer is used for analysis of drug by its absorption Peak at the specific wave length (λ max). The aqueous extract was diluted to the concentration of (µg) level by using water as solvent and run through photometric mode in UV Spectrophotometer to find the (λ max). With the (λ max) the extract is serial diluted in conc. of 10(µg), 20(µg)….. And measured the absorbance at spectrum mode [23].

RESULTS AND DISCUSSION

Pre Formultion Study

In the preformulation study of *Acalypha indica* Linn leaves Ethyl Acetate extract was characterized for organoleptic properties. Identification of active ingredients was done by UV-visible spectrometer and IR spectrum does *Acalypha indica* Linn Ethyl Acetate extract. Results are shown in Table No :1

Physical Evaluation

The valves of physical observation, appearance, gelling and ph. were shown in Table no: 2, 3 and Figure no: 2
Viscosity of formulation was determined by the spindle no. S-06, 10 rpm. The selection of spindle and rpm was done on the basis of validation method for all formulations. So on the basis of validation method for all formulations .so on the basis of validation it found that this spindle is an appropriate one for all formulations. Results were shown in Table no: 5

Comparision of Viscocity Extrudabilty and Spreadibility Table no:4

Stability Study

Stability study was carried out for optimized formulation according to ICH guide lines at 40^0 C/75%RH for 1 month. The results showed that there was no significant change in physical chemical parameter of the gel, hence the formulation (F4) as found to be stable. Results were shown in **Table no:5**

SUMMARY AND CONCLUSIONS

The main aim of the present study was to formulate and evaluate a natural anti-inflammatory gel by using different polymers. Preformulation was carried out initially and the results were directed for the further source of formulation with different batches with polymers by using selected excipients. The leaves of *Acalypha indica* were collected from ABS Botanical garden, Karipatty and was dried under shade for one week. The drug was extracted using sox let apparatus using ethanol for 72 hours. The extract was formulated into gel by using different polymers. The *Acalypha indica* gel formulation was optimized on the basic of different physical parameters. Studies mainly carried out for pH, viscosity, Spreadability, Extrudability, *iv vitro* and stability studies. Various formulation of *Acalypha indica* leaves extract gels were formulated by using various polymers such as CMC Na, HPMC K100, HPMC K4M, and Carbomer 940. The F4 shows greater drug release 82.25% which is complied with F3 drug release which is 70.52% in 6hrs, other parameters such as pH of F4 formulation is 8.15 viscosity of F4 formulation is 4,34,060cps, Spreadability of F4 formulation is 20.53. The pH of F4 was 8.15 which were basic in nature and by the future addition of 3-4 drops of HCL the pH was bought to neutral level i.e., 6.95. Also the pH of F3 was 5.06 with acidic nature which might have cause skin irritation. The addition of 4-5 drops of NaoH solution, there by the pH range was brought to7.2. Thus by the addition of suitable neutralizing agents both formulations are made more elegant and applicable for skin pH. Stability study was conducted for optimized batch F4 at 40°C / 75% RH for 1month. Gels were evaluated for appearance; feel on application, pH, Viscosity after 1 month. It concluded F4 was stable. Results of all physical parameters of the formulation concluded that formulation F4 was the most promising formulations. Based on the above parameters, the formulation F4 was concluded as most promising formulation and can be directed for further studies.

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Table No: 1 Composition of Formulation F 1 – F 6

S.No	INGREDIENTS	F 1 %	F 2 %	F 3 %	F 4 %	F 5 %	F 6 %
1	Ethyl Acetate Extract of Acalyphaindica	3	3	3	3	3	3
2	Sodium CMC	2	3	-	-	-	-
3	Carbopol 940	-	-	2	3	-	-
4	HPMC K 4 M	-	-	-	-	2	3
5	Glycerin	12.5	12.5	12.5	12.5	12.5	12.5
6	Ethanol	2.5	2.5	2.5	2.5	2.5	2.5
7	Methyl Paraben	0.3	0.3	0.3	0.3	0.3	0.3
8	Propyl Paraben	0.5	0.5	0.5	0.5	0.5	0.5
9	Triethanolamine	q.s	q.s	q.s	q.s	q.s	q.s
10	Purified Water	77.2	76.2	77.2	76.2	77.2	76.2

Table No: 2 PHYSICAL EVALUATION : APPEARANCE: GELLING

FORMULATION	APPEARANCE	APPLICATION	GELLING
F1	Dark green	Smooth	++
F2	Dark green	Smooth	++
F3	Dark green	Smooth	++
F4	Dark green	Smooth	+++
F5	Dark green	Smooth	+
F6	Dark green	Smooth	++

Table No: 3 COMPARISION OF P^{H}

S.NO	Formulations	pH
1.	F1	8.54
2.	F2	8.24
3.	F3	7.96
4.	F4	8.15
5.	F5	8.15
6.	F6	8.15

Table No: 4 Comparision of Viscocity Extrudabilty and Spreadibility

Formulations	Viscosity (CPS)	Extrudability	Spreadibility
F1	8728	++	17.62
F2	1,58,060	++	18.78
F3	2,18,115	++	19.24
F4	4,34,060	++	20.53
F5	72,015	+	15.42
F6	2999	++	15.49

Table No: 5 Stability Parameters of Formulation F4

S. NO	PARAMETERS	CONTROL	AFTER 1 MONTH 40/75˚(C/RH)
1	Appearance	Dark green	Dark green
2	Feel on application	Smooth	Smooth
3	pH	6.95	6.95
4	Viscosity	4,34,060	4,35,570

Fig. No: 1 *Acalypha indica*

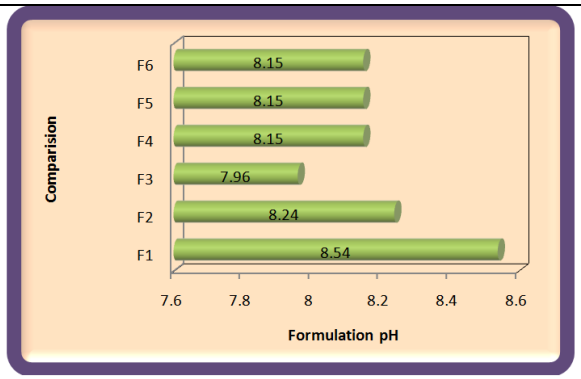

Fig. No: 2 Comparison of pH

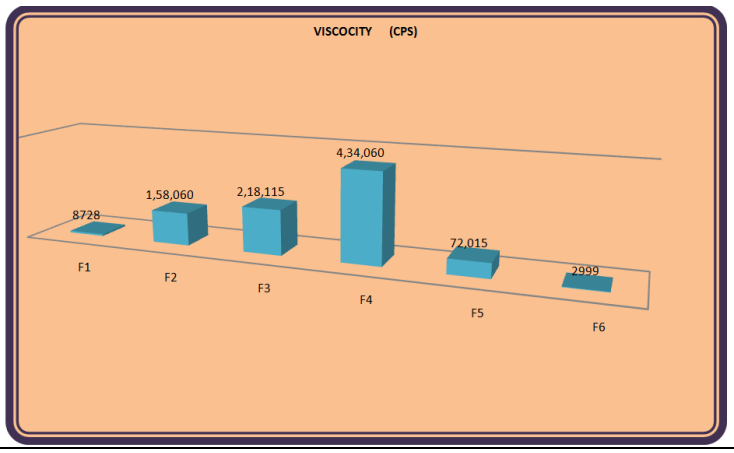

Figure No: 3 Comparison Of Viscosity

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RESEARCH ARTICLE

Design of Air Powered Car

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ABSTRACT

Today there is a need for search of alternative fuels due to many reasons like air pollution andscarcity of fossil fuels. Compressed air shall be an alternative for fossil fuels. It is desired thatan alternative fuel is to be pollution free to environment and should be renewable. Compressed air is an energy source which is used for many purposes and helps to reduce greenhouse gases. Compressed air may therefore be used as the fuel to drive cars. Compressed air car use is cost-effective, which requires very less maintenance. The present study describes the design of components used on a compressed air car.

Keywords: Compressed air engine; Air tank; 2-stroke engine; Compressed air car.

INTRODUCTION

In France, in 1870, Louis Mekarski developed the compressed air-vehicle. It was copyrighted in the years 1872 and 1873, and tested in 1876 in Paris. In the year 2008, in India, TATA came forward and announced to build vehicle that would run on compressed air, named as Airpod [1]. There are other researches going on across the globe in order to come up with new concepts. Global warming has been one such an issue and really it's dangerous for the human being. Earth's temperature is increasing progressively and that in turn triggers climate change. The fossil fuels are now being scares, commonly used as an electricity source in numerous fields such as power stations, internal & external combustion engines, etc. Yet its stock is being reduced and fossil fuels are dwindling at a faster pace because of this enormous use [2]. This is also important to establish green technology for the usage of sustainable energy sources, in order to conserve the fossil fuels. Smoke, which emerges from the cars, is one of the constituent of emissions. Therefore an effective way of making the car working needs to be rendered so that we can avoid any disruption to the atmosphere. Alternative greenenergy options include wind, thermal, chemical, etc. The compressed air engine is the active air driven system. Air is the gaseous mixture which makes it stable and non-polluting. Air has the ability to be packed to a very high density and can be held under heavy pressure. This is inexpensive and is easily

present in the environment. The compressed air engine, uses the compressed air contained in the tank, and via the pressure release valve, reaches the compressed air engine through which the compressed air forces the piston down to operate and generates mechanical power [3]. Generally, air and fuel are combined in I.C engines and

combusted in engines to push pistons with hot expanding gases, compressed air engines use compressed air to accelerate the engine and force the piston to create acceleration through thecrank shaft, which is then transmitted to the wheels. Boyle's law proves that if the volume of air if redued by half through compression then the pressure will be doubled. Charle's law proves that the gas volume is directly proportional to gas temperature. Most work is ongoing in this compressed air system and scientists seek to increase the performance of this device. Experimentally it has been observed that the vehicle's performance varies from 80 to 95 percent [4]. Consequently, such cars do not emit any CO, NOx, hydrocarbons, etc. and thus will not affect the ecosystem. As a result, compressed air car will prove to be environmentally sustainable of the 21st century. So this compressed air can be an option to drive vehicles.

LITERATURE REVIEW

Pramod kumar [5] showed that in an air car engine, as there is no combustion and using lightweight engine parts such as carbon fiber for piston and connecting rod, it would produce better performance. Naveen kumar et al., [6] showed that "unlike electric or hydrogen driven cars, compressed air vehicles are not costly and do not have a restricted drive range. Compressed air vehicles are reliable and have a production rating that is compliant with international requirements". Abhishek Lal [7] studied the new design strength is strong relative to the other reciprocating compressed air engine. With the basic configuration and mechanical sliding valve, a limited size engine may be made.

Key Advances in the Field Of Compressed Air Vehicles

Currently, several new developments for compressed air vehicles have appeared. The Republic of Korea has set up "a pneumatic hybrid electric car system operating on energy and compressed air. The engine, to drive a Plug-in Hybrid Electric Vehicle (PHEV), is operating to build the power supply besides electric motor [8]. The machine reduces the need for diesel, keeping PHEVs free of emissions. The mechanism is powered by an ECU in the vehicle, which regulates both the power packs, i.e. the compressed-air engine and the electric motor. The compressed air helps to drive the pistons, spinning the wheels of the engine. Using a small generator the air is pumped which is powered by a battery driving both the air compressor and the electric motor. The air is then collected in a tank when compressed [9]. The compressed air is used while the car requires a great deal of power, such as starting and accelerating. If the vehicle has reached regular cruise speed, the electric motor revives as there is no need for a ventilation system, fuel tank, fuel lines, spark plugs or silencers, the PHEV solution can minimize" the cost of automobile production.

Working of Compressed Air Engine

The concept behind the air driven engine's action is the capacity of air to retain compressed energy, and afterwards unleash the same on expansion. On compression, the pumping job is retained as the energy "of compressed air. That's the compressed air is then stored for subsequent usage in tanks. When the expansion of this air is allowed, the air pressure energy is transformed to kinetic energy and induces propulsion [10]. This same concept is applied to engines too. A solenoid valve is used to regulate the piston's air supply on a routine basis, because the valve shuts and opens electrically and without interruptions according to the predefined valve time. When the compressed air hits the piston through the inlet valve, it creates impact force on piston during the first half rotation of the crank shaft, it extends, and then passes back through the outlet during the second half rotation of the crank shaft". Due to this impact force the piston reciprocates [11]. The primary aim of holding air at such higher pressure is to assure that adequate amount of air is available in the car to enable it to operate for a longer period until the tank needs to be refilled.

Main Components of Compressed Air Car

The main components of a compressed air car are air tank, solenoid valve, wheels, 2-Stroke engine.

Air Tank

Air receiver tanks, which are necessary for any compressed air device, not only act as temporary storage but also allow the system to operate more effectively. The air receiver tank is a variety of pressure vessel. It retains the compressed air for potential usage under pressure. The tanks come in a variety of types, both for horizontal and vertical arrangements. Carbon fiber tanks can carry 300bars of air under heavy pressure [12]. The specifications of air tank are presented in Table 1 and the schematic of tank is shown in Figure 1.

Solenoid Valve

A solenoid valve is a valve which is operated electrically. The valve contains a solenoid at center and is an electronic coil with a movable ferromagnetic heart. The plunger seals off a tiny orifice in the rest place. The electric current induces a magnetic field across the wire. Themagnetic field exerts an outward pressure on the expanding orifice of the plunger. The solenoid valve used in this study is presented in Figure 2.

Wheels

The key role of a vehicle wheel is to sustain the vehicle load, transfer friction and braking forces to the ground surface, withstand ground shocks, adjust and retain travel direction. The specifications of the wheel is shown in Table 2 and the schematic of wheel is presented in Figure 3.

2- Stroke Engine

The 2- stroke engine is a light weight engine. So it can be used for compressed air engine. Its capacity and torque generated are also good. The specifications of engine are presented in Table 3.

Chassis Design

The fundamental structure for your automobile is chassis. Often "the chassis is just the frame,while at other times it includes the wheels, the transmission, and sometimes the seats [13]. The chassis is amongst the most important elements of the car without which the car would have no structure" [14]. Usually lightweight frames are constructed of aluminium [15]. The schematic of chassis is presented in Figure 4.

Model of Air Powered Car

The schematic of assembled model of compressed air powered car is shown in Figure 5.

CONCLUSION

The advantages of having zero emission technology are evident. The exhaust from thecompressed air car can be used for the air conditioning because of its low temperature after expansion. The air storage tank should be provided with a heat exchanger. At the same time these vehicles need to be improvised to increase the performance. Excessive work is thereforeimportant to fully prove the technology for commercial use.

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Table 1: Specifications of the air tank

Parameter	Specification
Length (mm)	1000
Diameter (mm)	300
Thickness of tank wall (mm)	3
Capacity (Lit)	150 (Max 30 bars)

Table 2: Specifications of wheel

Parameter	Specification
Material	RUBBER, NYLONE
Construction Type	Radial
Section Width	180mm
Rim Diameter	14

Table 3: Specifications of 2 stroke engine

Parameter	Specification
Cubic capacity	145.45 cc
Engine type	2 Stroke
Torque	13.8 Nm at 3500 rpm
Stroke length	56 mm
Bore diameter	57.5 mm

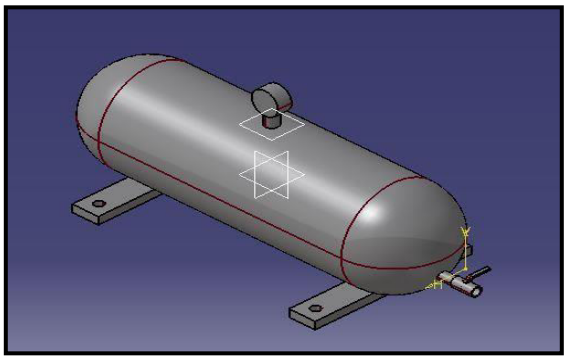

Fig. 1. Schematic of the air tank

Fig. 2. Soleniod valve

Fig. 3. Schematic of wheel

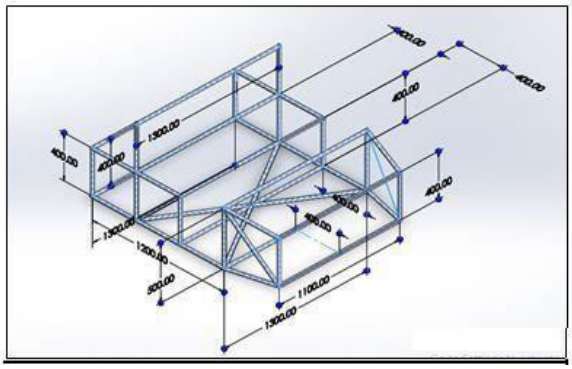

Fig. 4. Chassis

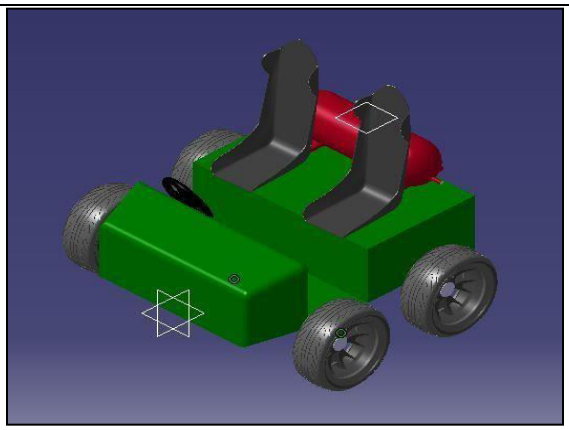

Fig. 5. Compressed air car

RESEARCH ARTICLE

Development of Synthetic Graphite/Polyurethane (SG/PU) – Coated Copper Cathodes for Seawater Batteries

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ABSTRACT

The corrosion of copper in seawater inhibits its sustainable use as cathodic electrode material in seawater batteries. This study aimed to address this present issue by coating the copper electrode with a conductive blend of Synthetic Graphite/Polyurethane (SG/PU). Three different levels of concentration of the SG/PU coating was prepared and compared with the uncoated copper as cathodic electrodes in aluminum-air seawater battery using actual seawater as the electrolyte. The cells' output voltage was observed to determine the stability and polarization curve measurement was used to determine the cells' power and current densities, and the overall internal resistance. Results show that coating the copper with the SG/PU helped increase the stability of the cells by 13% while increasing the power and current density by 15.5-fold and 9.8-fold over uncoated copper cathodes, respectively. This study successfully demonstrated that improved performance in seawater batteries can be achieved by modifying the cathodic electrode material.

Keywords: Synthetic Graphite/Polyurethane, cathodic electrodes, Seawater Batteries

INTRODUCTION

Seawater batteries are an emerging and sustainable clean source of electricity. It uses seawater as its primary electrolyte to facilitate the oxidation-reduction reaction from the cathode (positive terminal) to the anode (negative terminal) inducing a flow of electrons (Chasteen*et al.,* 2008). Due to its simplicity and low-cost design, several studies have been conducted to improve its performance for achieving high power outputs. Commonly used electrode materials for seawater batteries include either zinc or aluminum as anodes, and copper as the

cathodicmaterial, to which the aluminum-air anode and copper cathode seawater batteries are among the most common (Susanto*et al.,* 2017). Despite the considerable amount of achievable power in seawater batteries, practical application is limited in long-term use as its electrodes, mostly the cathode suffers from material deposition and degradation during reduction reaction. This increases the cost and affects the overall operation of seawater batteries as the need to replace the electrodes is frequent.

To address this issue, carbon-based materials were introduced to replace copper as a cathode in aluminum-air seawater batteries. Graphite, as conductive support and cathodic electrode material gained popularity due to its superior chemical resistance, good electrical conductivity, and low cost (Liu *et al.,* 2016). Activated carbon was also explored as a replacement for copper and showed better results. Another different approach introduced was the modification of carbon-based electrodes using polymer materials. Polytetrafluoroethylene (PTFE) modified electrodes was preferred due to its excellent chemical resistance and compatibility with carbon. However, it was later examined that fluorine-based polymers like PTFE is neither sustainable nor environment-friendly (Salar-García*et al.,* 2017). As an alternative to PTFE, polypyrrole modification to carbon felt in zinc-air seawater batteries resulted in an improved overall performance (Al-Eggiely*et al.,* 2016).

On the other hand, another very useful and commonly used polymer material is polyurethane (PU). PU is well-known for its chemical resistance, durability, and low-cost (Rao, 2012). Combining these features of the polyurethane and graphite to modify the existing copper cathode might help to improve the stability and overall performance. Therefore, this study aimed to develop a new cathodic electrode material for seawater batteries using polyurethane and graphite.

Objectives

The main objective of the study was to develop synthetic graphite/polyurethane (SG/PU), -coated copper, as new cathodic electrode material for seawater batteries. Specifically, the study aimed the following objectives: (1) To determine the improved stability of the synthetic graphite/polyurethane (SG/PU)-coated copper cathode-based seawater batteries over the uncoated copper-based seawater battery in terms of the closed-circuit voltage; (2) To determine the improved performance of the synthetic graphite/polyurethane (SG/PU)-coated copper cathode-based seawater battery over the uncoated copper cathode-based seawater battery in terms of power density, current density, and internal resistance.

MATERIALS AND METHODS

This study has three (3) phases: (1) Synthetic Graphite/Polyurethane (SG/PU) cathode preparation, (2) Aluminum-air seawater battery construction, and (3) Electrochemical Tests.

Synthetic Graphite/Polyurethane (SG/PU) Cathode Preparation

A fully synthetic graphite powder with 75 microns mesh size (Ionix-Kemrad, Philippines) and polyurethane gloss finish (PYE, Malasia) were used to synthesize the SG/PU coating. The conductive blend of SG/PU was prepared by dispersing the powers of graphite to the polyurethane solution as shown in Figure 1. A continuous stirring by hand was allowed until a homogenous mixture is achieved. This study prepared and tested three (3) concentration levels of the SG/PU: 50 wt.% SG, 53.33 wt.% SG, and 56.25 wt.% SG. The prepared SG/PU resin was poured onto a prepared cast of stacked layers of copper sheet as the current collector and polyvinyl chloride (PVC) as support. The fabricated SG/PU-coated copper cathode is shown in Figure 2. The 10 samples for each level were made and dried at room temperature. The SG/PU-coated copper cathode has a dimension of 3.5 by 10 cm.

Aluminum-Air Seawater Battery Design and Construction

The study used the existing design of aluminum soda cans to function both as anode and overall cell assembly. The external surface of the can was buffered using 1000 graded sandpaper to remove the manufacturer's protective coating. Removing this outer coating allows the aluminum to react effectively with air. To complete the cell, the cathode electrode is laid in-place inside the can and filled halfway with the seawater electrolyte. An alligator clip is attached at both the aluminum anode and cathode.

Experimental Setup

Triplicates for each factor level of the SG/PU-coated copper cathode and uncoated copper cathode cells were assembled and prepared for tests. The cells were individually connected and monitored simultaneously using a data logger (PicoLog 1000 series).

Stability Test

At first, the stability of the cells was observed when loaded with a high concentration of saline (50 wt.% table salt) and operated at a closed-circuit using a 47-Ohm resistor. Figure 3 shows the schematic diagram of the cells' connection for data acquisition. The voltage of the cells was observed and recorded every 10 minutes. The saline electrolyte of all cells is not replenished throughout the test.

Polarization Curve Measurement

The polarization curve measurement is one of the most common methods in fuel cell and battery analysis. This is done by changing the value of the external load (resistor) stepwise from the highest value to the lowest possible value. The values of voltage obtained for each load is presented in a voltage vs. current graph. The current can be calculated using Ohm's Law. The generated curve shows the characteristic of the cell as well as the cell's overall internal resistance. The power curve can also be derived from the polarization curve to show the maximum power a cell can achieve at a certain value of current. The output power can be calculated using Joule's Law. A new set of seawater batteries and cathodes were used, and actual seawater was fed to the cells after the stability test.

RESULTS AND DISCUSSION

Stability Test

The stability of the cathodes in a high concentration of salt was observed. Figure 4 below shows the actual image of the setup showing the connections of the cells to the data logger.

The stability of the cells was observed for 4500 minutes. It was detected that the output voltage of all the cells did not decline even without electrolyte replenishment. Figure 5 shows the complete data of the closed-circuit voltage of the cells

The data shown is the average of the triplicates. Initially, the cells using the SG/PU-coated copper cathodes exhibited overshoots but steadily normalize as time progresses. During the 3rd day of the test, the copper electrode started showing bluish-green decolorization while the SG/PU coating shows no clear changes. Among the SG/PU coating, a more consistent output was observed in the 53.33 wt. % SG cathode at a standard deviation of 0.00951. The lowest concentration, 50 wt. % SG showed a decreasing trend and inconsistencies with a measured standard deviation of 0.0315 while the highest concentration, 56.25 wt.% SG cathode with a standard deviation of 0.0109 shows a steady increase in the output voltage. The uncoated copper cathode cells showed the lowest output voltage on this test with a standard deviation of 0.011.

Polarization Curves

The polarization curves of the cells are shown in Figure 6. As seen on the shape of their polarization curves, all SG/PU-coated copper cathode-based cells show remarkably higher voltage at a much lower activation energy loss meaning that chemical reaction takes place better using the coated cathodes. On the other hand, uncoated copper has a steep slope indicating a very higher activation energy loss.

Moreover, the slope of the ohmic loss region of 56.25 wt.% SG suggests that it has the lowest overall internal resistance among the three levels. Low internal resistance means less internal energy losses. Using linear curve fitting, the mean internal resistances of the cells using 56.25 wt.% SG, 53.33 wt.% SG, 50 wt.% SG, and Cu is 0.969 Ω, 0.975 Ω, 0.991 Ω, and 0.731 Ω, respectively. Here, the uncoated copper cathode electrode has the lowest internal resistance, and this is because of the high electrical conductivity of copper. It is apparent from these results that the performance of each cell varies.

The power curves of the cells were derived from the polarization to give information about the peak power and current output of the cells. The derived power curve is shown in Figure 7.

The power curve's x-axis is the current of the cells normalized to the geometric area of the cathode while the y-axis is the power of the cells normalized to the volume of the seawater used as the electrolyte. As shown in Figure 7, the seawater battery using the 56.25 wt.% SG coating achieved the highest power density. This is equivalent to 3.41 Watts per cubic meter of seawater at a current density of 0.64 Ampere per square meter of the cathode electrode. There is a huge gap in the power density between 56.25 wt.% SG and 53.33 wt.% SG, but data shows that better performance can be obtained at a higher concentration of graphite. On the other hand, the uncoated copper cathode-based cells achieved the lowest power density. This is already anticipated due to the high activation energy losses observed in the uncoated copper's polarization curve.

RESULTS AND DISCUSSION

The above results show that modifying copper by coating with polymer and carbon can improve the power and current density in seawater batteries. Inarguably, the result of the 4500minute test of the cells in high salt concentration as an electrolyte was not enough to make a solid conclusion about the stability of the cells however, the discoloration of the copper cathode may serve as a good indication that the performance of the copper cathode-based cells will degrade in time. Another remarkable observation in the SG/PU-coated cathode cells is that the cells' output voltage improves. This is more apparent in the behavior of the cells using the 56.25 wt.% SG. Though, a much longer observation time should give more detailed information about the cells.

As for the cell's electrochemical characteristics, the SG/PU coating improved the activation energy losses consequently leading to a much higher output voltage than the uncoated copper cathodes though, a lower internal resistance is still to be desired. More importantly, the overall performance of all the SG/PU cells as well as their stability in tests showed the compatibility of polyurethane and graphite.

CONCLUSION AND RECOMMENDATION

Based on the result of experiments conducted the following conclusions were drawn: (1) The cell with the 53.33 wt. % SG cathode produced the most stable output due to its standard deviation (0.00951) which is 13% lower than uncoated copper cathode (0.011), and (2) the SG/PU-coated copper cathode-based seawater batteries performed better than the uncoated copper cathode-based seawater batteries as shown by an increase of 1547% in the power density and 983% in the current density. These results show that more power can be extracted from seawater

batteries that use actual seawater as the electrolyte by modifying the cathodic electrode material and that practical application like powering autonomous environmental sensors and low-power devices is possible. Longer operation time can also be expected using the SG/PU-coated copper cathodes at a much lesser maintenance requirement.

Lastly, the large differences in the individual cell performance suggest that more research is to be done in the development of the aluminum-air seawater batteries while optimization in the mix and the method of preparation are needed in improving the SG/PU coating.

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Table 1.Summary of the electrical characteristics of the cells.

	SG/PU-coated cathode			Uncoated copper cathode
	50 wt.% SG	53.33 wt.% SG	56.25 wt.% SG	
Maximum Voltage (V)*	0.370	0.349	0.510	0.140
Internal Resistance (Ohmic) (Ω)	0.9834	0.975	0.969	0.731
Power Density (W/m^3)	0.74	1.26	3.41	0.207
Current Density (A/m^2)	0.136	0.266	0.639	0.059

*using 1k-Ω load

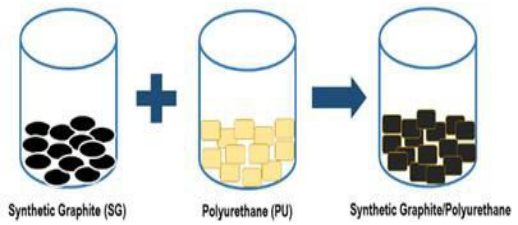

Figure 1. Steps for preparing the SG/PU coating

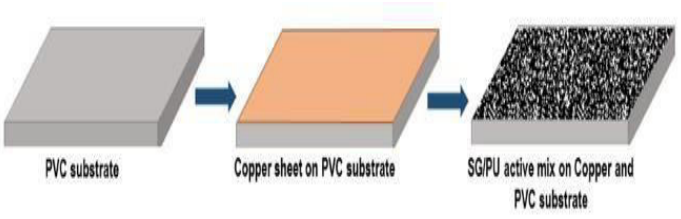

Figure 2. Illustration of preparing the SG/PU-coated copper cathode electrode

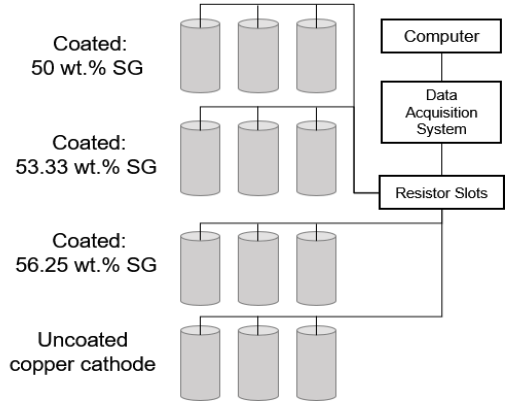

Figure 3. Schematic diagram of the data acquisition and measurement

Figure 4. (left) Actual image of the setup, and (right) actual image of the cells

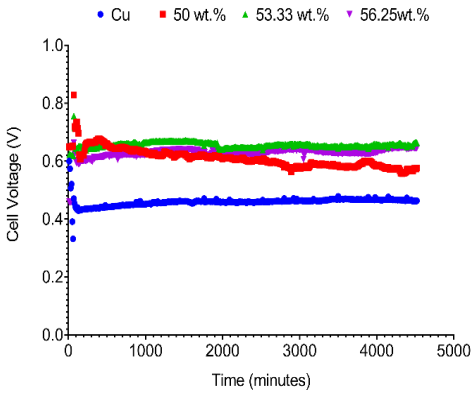

Figure 5. Closed-circuit voltage of the cells.

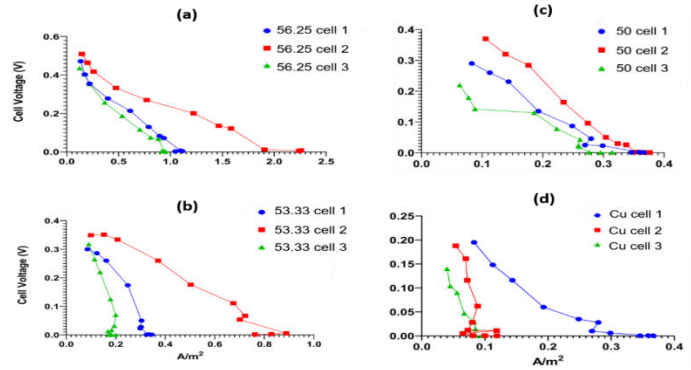

Figure 6. Polarization curves of (a) 56.25 wt.% SG coating, (b) 53.33 wt.% SG coating, (c) 50 wt.% SG coating, and (d) uncoated cathode. Data shows the triplicate cells.

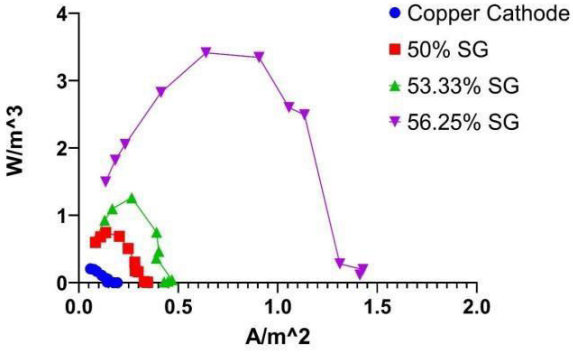

Figure 7. Power curves of the cells. Data show the mean of the triplicates.

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REVIEW ARTICLE

A Review on Li ion Battery Management System

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ABSTRACT

A battery is an energy storage system having multiple cells connected together either in series or in parallel or a combination of the two. The lifecycle of a Li ion battery is reduced dramatically if it is not charged with the charging range. A battery management system has become so important in particular in Li battery technology, as it acts as a gatekeeper between the charger and the battery itself. In the present review, constituents of a battery management system such as longevity, cell balancing, degradation and topologies are discussed.

Keywords: Battery management system; Longevity, Cell balancing; Topology

INTRODUCTION

In electric vehicles, the battery management system (BMS) is a part of the system that stores and converts energy into motion and vice versa. Electrification have a profound impact on the vehicle electrical system going forward. As many systems traditionally based on hydraulics and not driven by electric motors. In the world of battery operated products in specially, electric vehicles, battery management is perhaps the most important aspect of the product. The battery is quoted the battery is the big obstacle on the road to electric vehicles. The battery system is the most expensive component comprising the bill of materials. For this reason the batteries must be able to impact performance in functionality in a big way commensurate with its relative cost so the care and feeding of the battery pack is a big focus to ensure that it delivers the performance and longevity that justifies its cost [1]. Several factors go into the design of a battery pack as well as the battery management unit. Ideally, battery pack should outlast the service life of the vehicle itself and it must do so in a safe and efficient manner. Accomplishing this means monitoring and controlling certain operational parameters.

Longevity

The Cons of battery management in an electric vehicle are that the battery management implemented in electric vehicles is quite different than something like a mobile phone which is optimized for two primary factors that is cost and talk time longevity of the battery is not a concern as mobile phones are typically upgraded every two years. By contrast the electric vehicle battery pack should ideally last for the service life of the vehicle [2]. To do this, the pack is typically sized for a larger capacity than the desired target range based on the efficiency of the vehicle platform. So the BMS and a new vehicle charges and discharges the pack to something significantly less than full capacity as a vehicle battery pack ages, the capacity is diminished and the BMS charges and discharges the pack over a broader range [3]. Thus, overall the perceive vehicle performanceis retained over a longer period of time despite the fact that the capacity of the battery pack is diminished. Intuitively monitoring cell voltage to track charge and discharge and hence the capacity seems like the simplest approach implemented. However, there are potential pitfalls. First, mid charge lithium ion discharge curves are relatively flat as shown in Fig. 1.

In addition, cell voltage is impacted by load current as well as temperature variation further complicating the issue. It is also imperative that the battery be unloaded for a long period of time before cell voltages are sampled. It is to be ensured that the battery charging and discharging is carefully managed. This is not only to manage the vehicle range, the efficiency optimization but also to maximize battery longevity. If an entire battery is charged 50% yet a single is already at 80% the result of charging entire battery to 80% or result in cell damage for that single cell or one or two cells maybe at a lower level of charge than the balance of the battery. If the battery is discharged to 30%, then perhaps these cells are fully discharged in the process as shown in Fig. 2. So the battery field not only takes place over the entire battery but also each individual cell. The charge on brand new cells is not exactly the same either although offering quote and quote matched cells is sometimes marketed by cell manufacturer.

Cell Balancing

Cell balancing or equalization provides a mechanism to level all the cells to nearly identical levels of charge thereby maximizing battery longevity as well as the vehicle efficiency. Without proper cell balancing, the longevity of battery is impossible to maintain over a large number of charge discharge cycles [6]. Cycling a battery pack eventually causes individual cells to become over balanced. Different coulombic efficiencies across the cells is one typical cause for this problem which manifests itself as a difference in state of charge levels at different cells [7]. "This limits the total amount of energy that can enter or exit the battery pack since the weakest cell limits the amount of charge that can be drawn from the entire system. And the strongest cell limits the extent to which the system can be charged [8]. Typically, balancing is done in either of two ways. Using a deceptive method commonly referred to as passive balancing in which the excess charge from the cells at the top is bled through the resistor connected in parallel with each individual cell and using a non-deceptive method, commonly called active balancing in which the excess charge of some cells is redistributed among other cells that require it as shown in Fig. 3.

Degradation

The success of electric vehicles depend largely on the energy storage system. Li ion battery currently features the best properties such as high energy density, long lifetime, good power capabilities and low cost to meet the wide range of requirements specific to automotive applications. However, safety and reliability of Li ion batteries can be problematic if they are not handled appropriately. Exposing Li ion batteries to extremely high or low temperatures reduces voltages or excessive currents results in accelerated battery degradation and in the worst case, battery failure [10]. A BMS monitors critical parameters and ensure safe operation. Moreover, the BMS has to provide information on current internal battery states to high level systems in a vehicle. These states include the state of charge which is equivalent to the fuel gauge in a battery, the total useful capacity and the electric power that can be delivered at any point during vehicle operation. State of charge, Useful capacity and Power capability are not measurable but must be estimated using battery models [11]. The behavior of the battery and its internal state changes overtime and usage as the battery degrades. This is a big issue for electric vehicles developers. Since reliable and accurate estimates of state of charge,

capacity and power capability must be available throughout the entire lifetime of the battery. A large number of physical and chemical processes contribute to battery degradation [12]. These mechanisms depend on many factors such as battery chemistry fabrication operating conditions and usage history etc., [13]. The complexity and interdependence of the processes involved makes it very difficult to model and prediction of future degradation is very much challenging. The Li ion battery degradation model to truly advance the state of the art in BMS development. Multiple objectives must be addressed including estimation of current useful battery capacity and power capabilities prediction of the remaining battery life and possible battery failure. It is therefore necessary to not only quantify the symptoms of battery degradation but also to identify their cause [14]. To establish the links between physical degradation mechanisms and their effects on performance deterioration in Li ion batteries is the need of the hour. This is to ensure the Li ion batteries to be safer and more reliable options for energy storage in electric vehicles. Capacity loss evolution with storage time with model regressed for each aging condition is shown in Fig. 4.

Topologies in BMS

For a battery pack to achieve the desired specifications, various topologies are presented.

Distributed Topology

In this topology, there are small voltage and discharge monitor circuits which communicate with the master control of the BMS as shown in Fig. 5. The advantage of this design is simple to implement and has high reliability. The disadvantage of this system is that it requires a large number of small PCBs and become difficult to mount on every type of cell.

Modular Structure Topology

In this multiple slave BMS controllers are used to phase the data and forward it to master controller.So, no special PCB is needed to connect the individual cell. However, isolated master slave communication is quite difficult. The master module is the one which the whole of battery pack and in turn communicates with other components of the system [17].

Centralized Topology

A centralized master control unit is directly connected to each cell of the battery pack. The controller unit protects and balances all the cells [18]. Using this topology decreases the hardware but excess heat could be generated because the controller is the only source for cell balancing in addition, the cells are distributed in various locations of the vehicle which requires a lot of wiring [19].

CONCLUSION

From the brief review, it can be concluded that,

- "The battery management system for a lithium ion battery pack is both a complex system and a significant contributor to safety, reliability and performance.
- The BMs often requests changes in vehicle operation in response to monitored battery packconditions.
- BMS provide some forecasting of battery pack capability in the near future.
- A more complex BMS includes a charge control function to charge the battery pack, in addition to applying some equalization methods to balance the cell voltage for maximizing battery capacity.
- A more complex BMS monitors many factors affecting the performance and life of the battery as well as ensuring its safe operation.
- As a result, the battery management system requires careful hardware and software design; the development cost and timeline are often underestimated".

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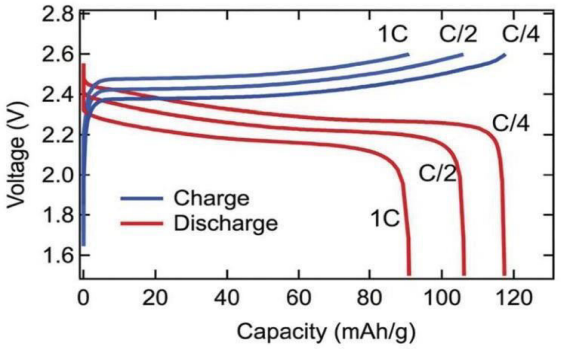

Fig. 1: Discharge curve of lithium ion battery [4]

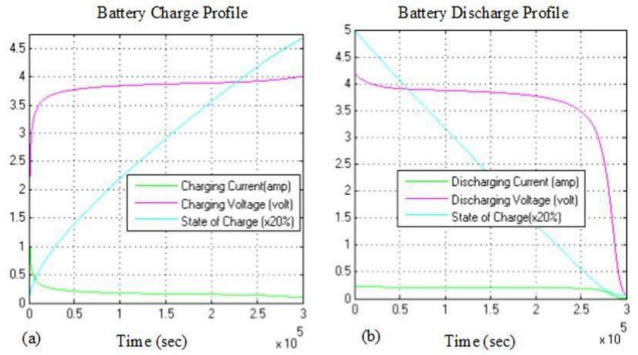

Fig. 2: Li-Ion battery characteristics for charging (a) and for discharging (b) [5]

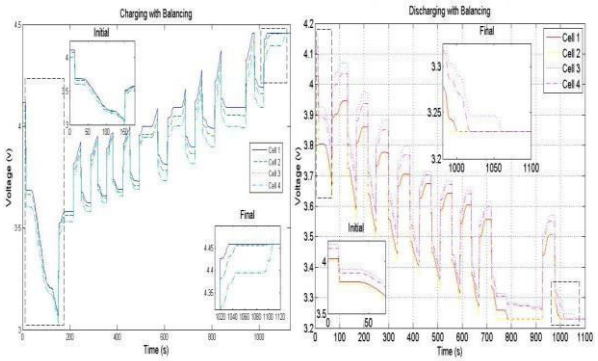

Fig. 3: (a) Charging with balancing (b) Discharging with balancing [9]

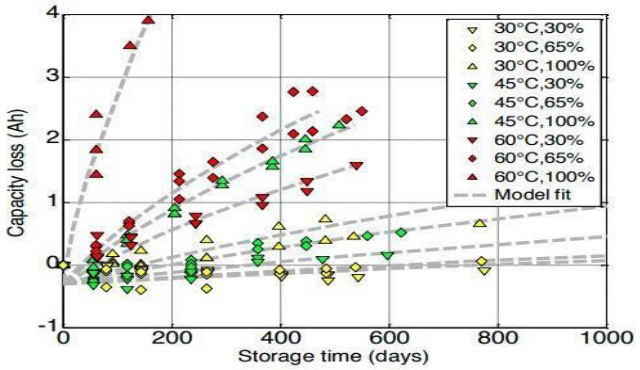

Fig. 4: Capacity loss under storage at various temperatures and SoCs fit with the aging model [15]

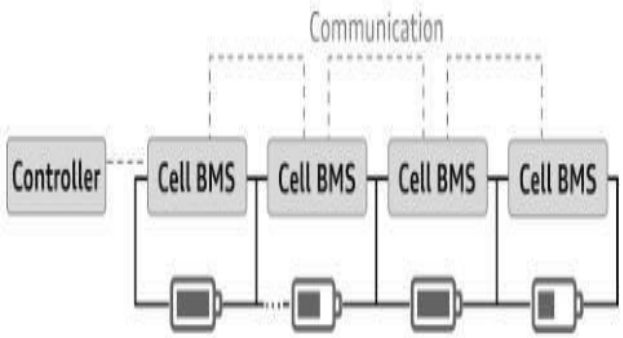

Fig. 5: Block diagram of a BMS based on a distributed topology [16]

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RESEARCH ARTICLE

Formulation and Evaluation of Simvastatin Loaded Nanoparticles

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ABSTRACT

This experimental study deals with the formulation and evaluation of simvastatin loaded nano-particles prepared by double emulsion solvent evaporation technique. This was attempted in order to overcome the problems of poor bioavailability and therapeutic response exhibited by conventional formulations. Eight formulations were formulated varying the concentrations of Drug-excipient compatibility was evaluated using FT-IR spectroscopy (Bruker FT-IR). The finished product was evaluated for mean particle size, drug encapsulation efficiency and % yield. During dissolution studies, F4 RSPO (40mg) formulation consisting of Eudragit showed better release (98.19 %) up to 12 hours, which. So, F4 formulation is converted to optimized formulation. The formulation is also studied for the drug release kinetics in which it is observed to follow Higuchi model. The optimized formulation was also subjected to Scanning Electron Microscopy (SEM) to analyze the particle size and uniformity. Hence the present study was a successful attempt to formulate and extend the drug release of Simvastatin by nano-particulate system.

Keywords: Nano-particles, simvastatin, formulation, kinetics.

INTRODUCTION

Controlled drug release formulation is usually defined as the type of formulation by which the drug concentration released within the body remains constant for longer period of time. This is usually considered as a type of modified release delivery system [1,2]. This is usually considered as the counterpart in comparison with conventional drug therapy [3]. Improved patient compliance reduce the frequency of dosage are considered as some of the advantages of controlled release drug delivery systems (CR DDS) [4-6]. Nanoparticles are considered as a type of CR DDS. Nanoparticles are defined as the small colloidal particles consisting of biodegradable and non biodegradable

polymers with a particle diameter range of 1-1000 nm. the usage of biodegradable polymers in nanoparticle formulation has created a new field called bio nanotechnology. This technology can prevent the ADR formed due to synthetic compounds [7]. There are several preparation techniques for nanoparticles which include techniques like polymer precipitation, amphiphilic macro-molecule crosslinking, etc. It is widely applied in disease-specific localisation, targeting drug delivery systems, etc [8]. This is due to positive effect of nanoparticles on in-vitro release, entrapment efficiency, surface area exposure of drug, etc [9-11].

MATERIALS AND METHODS

Preformulation Studies

FT-IR Studies

This test is performed using Bruker FT-IR spectrometer. The solid powder/Liquid sample directly place on yellow crystal which was made up of ZnSe. The spectrum of the sample was recorded over the 550-4000 cm^{-1}.

Organoleptic Properties

Drug and excipients were checked for the organoleptic properties such as color, odour, taste, and shape were evaluated.

Angle of repose

It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\theta = \tan^{-1}(h/r)$$

Where,

θ is the angle of repose
h is the height in cms
r is the radius in cms.
It is performed by fixed funnel method. Angle of repose helps in determination of flow properties.

Bulk density

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve #20) into a measuring cylinder. The bulk density is calculated using bulk volume according to the formula mentioned below. It is expressed in g/ml and is given by

$$D_b = M/V_b$$

Where,

M is the mass of powder

V_b is the bulk volume of the powder.

Solubility studies

Solubility study was performed by dissolving 10mg of active drug in 10 ml of different solvents, and shaking the test tube. After solvent exists in a clear solution without visible cloudiness or precipitate. This means that, initially 1 mg of drug was dissolved in 1 ml of solvent.

Method of Preparation

Firstly polymeric solution is prepared by dissolving specific amount of Eudragit RSPO in 5 ml of Acetone dissolved. Above obtained solution is emulsified by the drop wise addition of aqueous drug solution under magnetic stirring at 1000-1200 rpm for 15 min to get primary W/O emulsion. Further this is added to 15 ml distilled water containing poloxamer188 under stirring for 10 min to achieve a stable W/O/W double emulsion. The W/O/W emulsion is separated by ultracentrifugation at 11000 rpm for 40 min. Finally, the obtained product is freeze dried or lyophilized

and stored at 2-8^{0}C which leads to the formation of nano-particles. The obtained lyophilized powder is utilized for determination of entrapment efficiency and *in vitro* drug release parameters.

Evaluation of Finished Product

% YIELD

Production yield of Nanoparticles containing a drug was determined by the weight ratio of the dried Nanoparticles to the loading amount of the drug and Polymer. Production yield was calculated using eq. & results are depicted in table %Yield = Total weight of the Nanoparticles/ Total weight of drug and polymer * 100

Drug Encapsulation Efficiency

Lyophilized nanoparticles 3mg were dissolved in 1ml of diluents and the drug amount was determined by UV analysis. The encapsulation efficiency was determinedas the mass ratio of entrapped Simvastatin in nanoparticles to the theoretical amount of the drug used in the preparation. The entrapment of the Simvastatin nanoparticles was expressed as loading capacity.

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Amount entrapped}}{\text{Total drug loaded}} \times 100$$

Mean Particle Size

The particle size was measured using an optical Malvern microscope, and the mean particle size was calculated by measuring 200 particles with the help of a calibrated ocular micrometer. A small amount of dry Nanoparticles was suspended in purified water (10 ml). A small drop of suspension thus obtained was placed on a clean glass slide. The slide containing Nanoparticles was mounted on the stage of the microscope and diameter of at least 100 particles was measured using a calibrated optical micrometer and the mean particle size was calculated.

In-vitro Dissolution Studies

10 mg drug equivalent freeze dried Simvastatin loaded nanoparticles weredispersed in 3 ml pH 7.4 phosphate buffer solution which is transferred in dialysis bag and suspended in 100 ml of isotonic pH 7.4 Phosphate buffer solution (PBS). The bag was placed under magnetic stirring in a water bath maintained at 37 ± 0.5° C. At fixed time intervals 5ml of samples were taken out and fresh buffer was replaced. The obtained solution was analyzed by UV to determine the drug release.

Drug release kinetics

Kinetics of drug release was calculated for determination of type of modified drug release by the formulation. The kinetics are analyzed using the following formulae:

Scanning electron microscopy

The surface morphology of the layered sample was examined by using SEM (JEOL Ltd.,Japan). The small amount of powder was manually dispersed onto a carbon tab (double adhesive carbon coated tape) adhered to an aluminum stubs were coated with a thin layer (300A) of gold by employing POLARON - E 3000 sputter coater. The samples were examined by SEM with direct data capture of the images onto a computer.

RESULTS AND DISSCUSSION

FT-IR Studies

FT-IR studies were performed using Bruker FT-IR spectrophotometer successfully and graphical data of IR spectrum of drug (Simvastatin) was as above. There were no interactions between drug, polymers and excipients.

Organoleptic Properties

Organoleptic properties of the drug (API) were observed as per monograph and was in compliance with Pharmacopeia.

Angle of Repose

The angle of repose was determined using fixed funnel method for 8 different batches. The angle of repose for 8 different batches was as follows:

Based on the above data, it is observed that 3rd batch (F3) has the lowest angle of repose stating the free flow property; while, the 7th batch (F7) has the highest value relating to least inter particulate friction.

Bulk Density

The bulk density was evaluated for 8 different batches and is as follows:

It infers that the 2nd batch (F2) has the highest bulk density, while the 4th batch (F4) has the lowest bulk density.

Solubility Studies

The solubility studies was performed for the drug (Simvastatin) in various solvents to analyze the overall solubility nature of the drug. It is observed that the drug shows poor solubility only with highly acidic buffer (pH 1.2).

Evaluation of Finished Product

Percentage yield

Percentage yield of various batches of finished drug was successfully calculated. The % yield of the 8 batches is as follows:

Drug Encapsulation Efficiency

Drug encapsulation efficiency is a critical factor which describes the efficiency of a drug delivery system. The drug encapsulation efficiency of the various batches are as follows:

It was observed that 4th batch (F4) has the maximum drug encapsulation efficiency of all prepared batches. This states that this batch is a perfect drug delivery system in comparison with other formulation batches. Meanwhile, 5th batch (F5) has the minimum drug encapsulation efficiency of all prepared batches, stating that it is not suitable to be a good drug delivery system.

Mean Particle Size

Mean particle size of various batches are calculated and compared as follows: This infers that 5th batch (F5) has the least mean particle size. This means that it has the highest surface area of all batches, since surface area is inversely proportional to the particle size.

In-vitro Dissolution Studies

In-vitro drug release was performed for 8 different formulation batches (F1-F8) and the cumulative drug release was calculated. The graphical representation of the 4 batches (F1-F8) is as follows: It is observed that even if the cumulative drug release of F3 & F4 after the same period of time is same, the drug release pattern of F4 is better than F3. Hence based on dissolution data of 8 formulations, F4 Eudragit RSPO (40mg) formulation showed better release (98.19 %) up to 12 hours. So F4 formulation is optimized formulation.

Release Rate Kinetics to Dissolution Data

The drug release kinetics of the drug (Simvastatin) was calculated by applying various models like Higuchi model, Korsmeyer-Peppa plot, etc. The Higuchi plot for the drug (Simvastatin) is as illustrated below:

The black line indicates the actual path of the kinetic model. From the above models, it is observed that it follows Higuchi model.

Scanning Electron Microscopy

The optimized formulation (F4) was analyzed for particle size under Scanning Electron Microscopy. The image obtained under SEM is as follows:

CONCLUSION

The method of preparation of nanoparticles of Simvastatin was found to be simple and reproducible. nanoparticles prepared by solvent evaporation technique. The prepared formulations were evaluated for Mean Particle size, %Yield, Drug encapsulation efficiency and *In vitro* drug release. Formulation F4 registered highest entrapment of 93.20 % and practical yield of 96.72 % The incompatibility studies between the drug and polymer was evaluated using FTIR spectrophotometry. There was no significance difference in the IR spectra of pure drug & excipients. The *in- vitro* drug release of formulation F4 is found to be 98.19 % over 12 h in controlled manner hence the present study was a successful attempt to formulate and extend the drug release of Simvastatin by nanoparticulate system.

ACKNOWLEDGEMENTS

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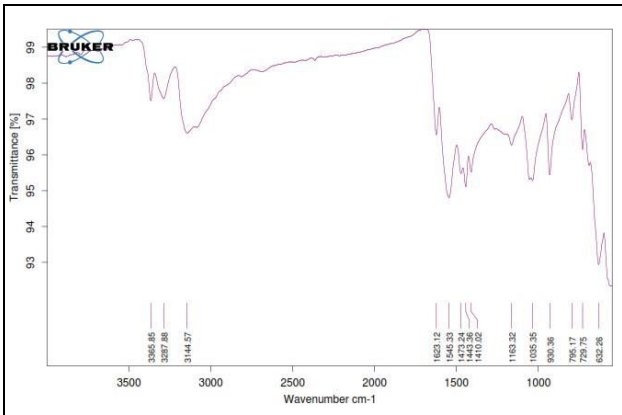

Fig. 1. FT-IR Studies

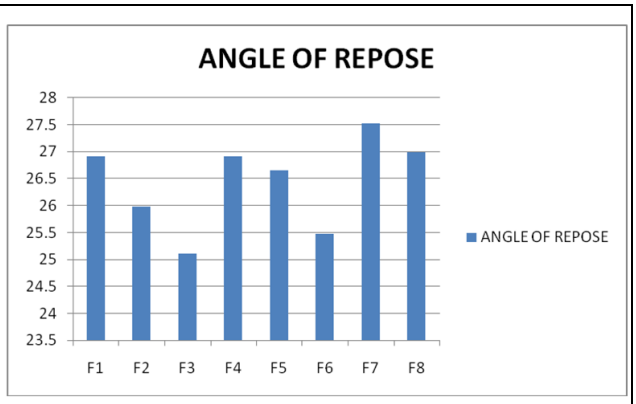

Fig. 2. Angle of Repose

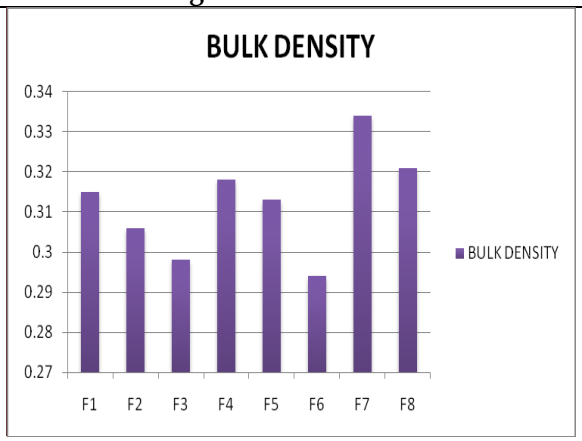

Fig. 3. Bulk Density

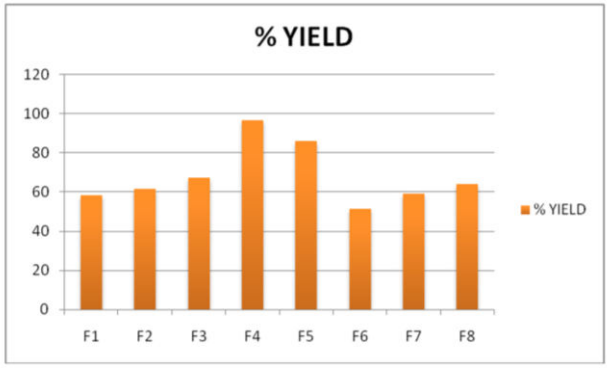

Fig. 4. Percentage Yield

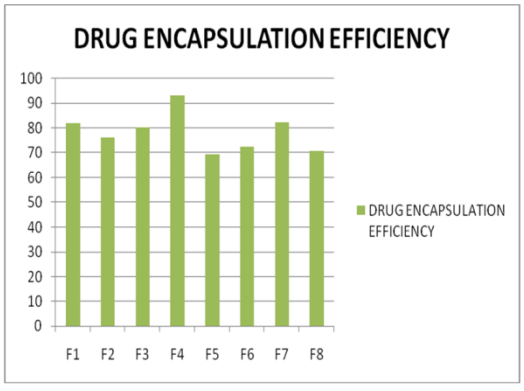

Fig. 5. Drug Encapsulation Efficiency

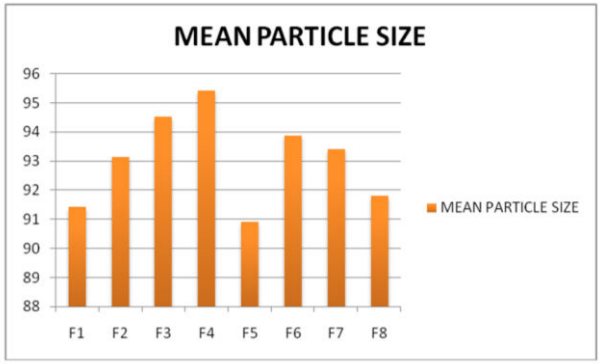

Fig. 6. Mean Particle Size

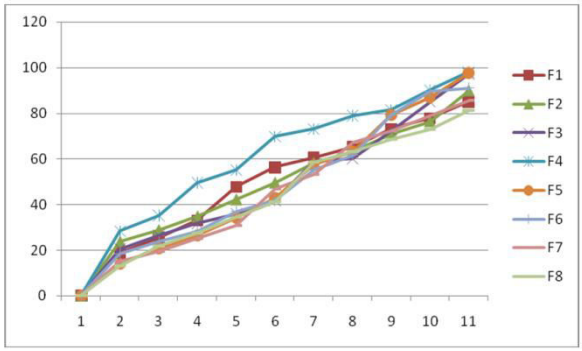

Fig. 7. *In-vitro* dissolution studies

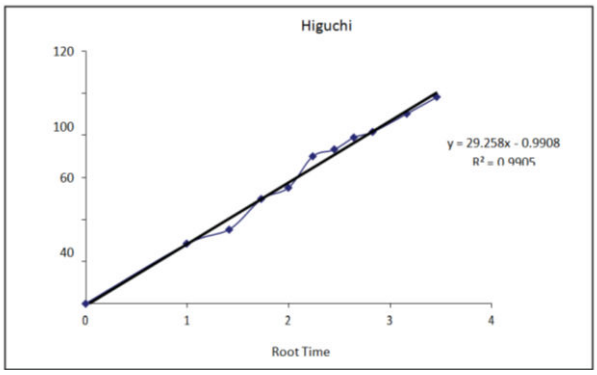

Fig. 8. Release rate kinetics to dissolution data

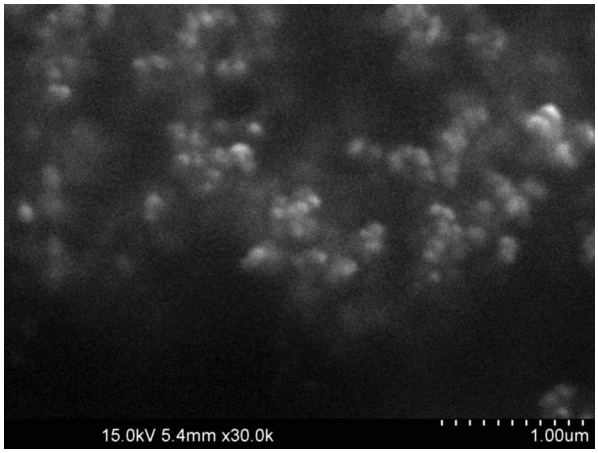

Fig. 9. Scanning Electron Microscopy

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RESEARCH ARTICLE

Minimax Probability based Churn Prediction for Profit Maximization

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ABSTRACT

Churn prediction has become a significant requirement for all customer centric organizations. Accurate prediction of churn can effectively improve customer loyalty and improve profits for the organization. This work presents an effective model that uses a combination of ensemble learning and minimax probability machines to provide a churn prediction system. The model has its major focus towards improving the profitability of the organization. The ensemble learning model has been designed to be computationally efficient, while the weight factors used in the minimax probability machines ensures reduction in losses, hence ensuring profitability. Experiments were performed and comparisons with existing models indicates that the model shows high performance, with 8% improved accuracy levels, indicating improved churn predictions

Keywords: Churn prediction; Ensemble learning; Minimax Probability Machines; Extra Trees Classifier; Profit Maximization

INTRODUCTION

Current technology induced world has brought customers much closer to the organizations. This has also made every customer based industry experience the issue of churn [1]. Customer churn is the process of a customer leaving an organization to opt for another competitor organization for various reasons. Churn has become an unavoidable component in several domains like IT services, social networking services, internet service providers and mobile services [2, 3]. Customer Relationship Management (CRM) has become a vital part of every organization. Effectively utilizing CRM in an organization can result in improving customer loyalty to a large extent, hence better customer

retention. Although this process is necessary for every organization, the main requirement for churn reduction has raised in the telecommunication industry. Rapid changes in the players, many available players, frequent introduction of new technical features and attractive plans has provided ample opportunities for customers to shift between operators [4]. Ease of shift and low cost of shifts has also played major roles in the large number of shifts occurring in the telecom environment [5]. According to management principles, it was observed that it costs higher to gain a customer compared to retaining an existing customer. Several organizations lose customers mainly due to ineffective churn prediction models or the absence of such models in their CRM architecture. Hence, maintaining an effective churn prediction system is of vital importance in any customer centric organization.

Churn prediction has become an interest for research community because of the challenges involved in correctly determining churn. Initial contributions in this domain included machine learning models [6]. These were quickly followed by ensemble models [7], metaheuristic models [8] and neural network models [9]. However, there still exists scope in the domain due to the large number of intrinsic challenges exhibited in the domain, such as data imbalance and noise [10]. Issues due to imbalance occurs due to the unbalanced nature of the occurrence of churners and non-churners. Due to the real-time nature of the domain, the number of non-churners is usually much higher than the number of churners. Further, some probable non-churners also have the possibility of moving out of the organization due to personal constraints. Such records should be identified and eliminated, as they act as noise tend to corrupt the decision rules. This work proposes an effective model that can operate on telecom churn data to handle the above mentioned issues to provide an effective and profit oriented churn prediction model.

Related works

Determining churners accurately has become a major requirement of several customer based industries. In specific, telecom industry exhibits the maximum requirement due to the large number of competitors and the ease at which customers can switch between operators. This section presents recent contributions in the churn prediction domain.
A churn prediction model that uses a combination of logistic regression and logit boost models for the prediction process was proposed by Jain *et al.* [11]. The models have been tested using the WEKA Machine learning tool and analysis of performance has been done using the dataset obtained from the American telecom operator Orange.A Latent Dirichlet Allocation (LDA) based model for predicting customer churn was presented by Slof *et al.* [12]. This work uses a duration based model for predicting the propensity of a customer to churn. The work also employs a risk based model that also determines the reason for the risks. Call logs between the customer and the call center executive are used by the LDA model for analysis. Other similar duration based models include works by Lariviere *et al.* [13] and Jamal *et al.* [14]. A similarity forests based model for churn prediction was proposed by Infante *et al.* [15]. This technique determines the relevance of each existing customer based on social network analysis models and a combination of binary classification techniques. This is a graph based model, that extracts the behavior patterns of churners and non-churners.

Neural networks is one of the most preferred models for the churn prediction process. A model that is based on neural networks for identifying churners was proposed by Omar *et al.* [16]. This work uses the basic multilayer perceptron architecture for the prediction process. V vector embedding based model that uses deep learning models for churn prediction was proposed by Cenggoro *et al.* [17]. This work is solely based on creating a highly interpretable model, as deep learning models by nature exhibits less interpretability. The model generates vector for each customer instance, and the vectors were identified to be highly discriminative in nature, making the model highly interpretable and explainable. The model also deals with providing choices that can be used to convert susceptible churners into non-churners. Behavior based deep learning model for churn prediction was proposed by Alboukaey *et al.* [18]. It is based on the fact that behavior of customers vary from time to time. Hence it is mandatory to watch their behavior continuously to effectively determine their tendency to churn. Time series based modelling has been implemented and CNN based model is used for the prediction. Several similar models have been designed to perform temporal predictions. Such models include hourly based analysis by Zaratiegui *et al.* [19], daily analysis model by Wangperawong *et al.* [20] and weekly analysis model by Óskarsdóttir *et al.* [21].

An evolutionary model used for churn prediction was proposed by Wai-Ho *et al.* [22]. A graph theory based model that utilizes social network analysis was proposed by Kostic *et al.* [23]. This uses graph based modelling for the identification of churners. The model aims to identify significant nodes in the graph model that serves as the major components for the churn identification process. A profit based churn prediction architecture was presented by Hoppner *et al.* [24]. This work mainly concentrates on creating a model that has its major focus on obtaining profitable predictions rather than accurate predictions. The model further concentrates on improving the interpretability of the model for better understanding of the predictions. Other similar profit driven models include works by Maldonado *et al.* [25], and Stripling *et al.* [26].

Minimax Probability based Churn Prediction (MPCP)

Predicting churn accurately is of significant importance, as it involves customers and is highly time constrained. A delay in the predictions or in the secondary actions is bound to result in the loss of customer. Losing a customer results in huge losses for the organization, hence it becomes mandatory to perform strategies that can aid in customer retention. Further, gaining new customers is considered to be much costlier compared to retaining existing customers. Hence it becomes mandatory to consider the loss factors prior to determining possible churners. This work proposes an ensemble based model that is integrated with minimax probability machines for predicting churners from telecom data.The Minimax Probability based Churn Prediction (MPCP) model has been designed in three stages; the initial stage performs data preprocessing, the next stage uses extra trees classifier model to predict the probability levels of the customer being a churner, and the final phase integrates minimax probability to provide profit based final predictions.

Data Analysis and Standardization

This phase has been designed to perform churn prediction on telecom data. Hence this phase exhibits significant importance, as telecom data is usually huge and contains several noise elements and missing information. The training data is explanatorily analyzed to understand the attributes. Attributes that are least significant are eliminated. These includes string data and identifying information. Both these types of data do not provide significant knowledge to the machine learning model. Hence, are eliminated. Further, users with no call logs are also eliminated, as they are considered to be new users. The next type of issue to be handled is categorical attributes. Such attributes are common in real-time data, however, they cannot be handled by machine learning models. Categorical attributes are converted into numerical values using one-hot-encoding techniques. Although this process tends to increase the size of the data to a large extent, it becomes necessary for effective functioning of the model.

Extra Trees (Extremely Randomized Trees) Classifier based Probability Prediction

The data is then segregated into two sections; training and test data. The data division is performed such that training data comprises of 80% of the data and the remaining 20% of the data is used for testing. An ensemble based bagging model is used for the initial phase prediction process. This work is based on Extra Trees classifier model, which is a bagging based model. However, several key differences exists between general bagging models and the extra trees model. Bagging model generally uses bootstrapping for training data creation. In the extra trees model, bootstrapping is not applied. The entire training data is passed to all the base learners. Base learner is a tree based model that is used for decision rule building. Variation in the rule building process is created by selecting the node split points in random, rather than using the entropy values to create attribute splits. The major advantage of extra trees model is that it is much faster than the traditional random forest model.

Input to the model is composed of churn data. The problem domain is considered as a binary classification problem. Data is passed to each base learner to determine the decision rules. The decision rules generated and are modified in this work to provide the probability of the prediction of each class, rather than the final prediction. The output from this phase contains a tuple containing two values; the probability values of a record being a non-churner and

churner. Regular operations consider the class exhibiting the highest probability value as the final prediction. This work passes the probability values to the next phase to perform profit maximization based prediction.

Minimax Probability based Final Prediction for Profit Maximization

This phase uses minimax probability based operations to maximize profits in the final predictions. The proposed model is based on the minimax probability machines by Lanckriet *et al.* [27]. Minimax probability machine is based on creating a hyperplane between the two available classes, and also tends to minimize errors. The model aims to minimize the worst-case probability of misclassification. It considers data from two classes X1 and X2. The mean and co-variance of the classes are calculated and recorded to be μ_i and σ_I respectively, where $i \in \{1, 2\}$. Hence, the separating hyperplane will be of the form $w^t x+b=0$, where w is the weights of classes, x is the actual data, and b is the bias constant. The maximum probability machine is considered as a chance constrained problem. Final predictions are obtained from the minimax probability machine based on the weights for the churners and non-churners. The weights for churners is set to 0.7, and that of non-churners is set to 0.3. This is due to the fact that churners tend to create higher losses than non-churners, hence significance for identifying a churner is considered to be higher than the non-churner. The weights ensure that higher significance is provided to predicting a churner, hence resulting in higher profits in the prediction process. Final predictions are obtained by applying the probability values and weights to the equation. The class with highest value is considered as the final prediction.

RESULTS AND DISCUSSION

The churn prediction model MPCP has been implemented using Python and Scikit libraries. Analysis of the performance of MPCP is performed by applying it on the publicly available churn prediction data [28]. The dataset is composed of records obtained from 3,333 customers. The data is composed of 21 attributes. The class attribute is named as churn, and is a Boolean attribute. The data contains a mixture of categorical and numerical attributes. Details about the attributes are presented in table 1.An analysis of the ROC curve is presented in Figure. ROC curve is constructed with False Positive Rate (FPR) in x-axis and True Positive Rate (TPR) in y-axis. The graph represents the relationship between correct prediction of churners and false alarms. Low false alarms with high prediction levels represent good performance. The figure shows zero FPR levels, which shows that the model exhibits no false alarms. Similarly, the figure also shows high TPR levels indicating that the model exhibits effective identification of churners.

PR plot representing the precision and recall values is shown in figure. PR plot shows recall in the x-axis and precision in y-axis. Precision represents the level of actual churners in the identified list of churners, and recall represents the level of churners identified from the actual list of churners. Both precision and recall values are required to be high for a model to perform effectively. The figure showsexcellent precision and high recall levels. This shows that the proposed model can effectively identify churners, and also that the identified churners are also highly precise with low errors.Performance of the MPCP model is shown based on existing classifier performance metrics. The table could be analyzed to identify that the MPCP model depicts low FPR and FNR levels, and very high TPR and TNR levels. This shows the efficiency of the prediction model in effectively classifying the instances. Further, the aggregated performance metrics Accuracy and F1-score also shows high performance.

A comparison of the performance of the MPCP model is performed with Cenggoro *et al.* Performance comparison is in terms of accuracy and F1-Score. Charts could be perceived to identify that the MPCP model depicts higher values for both accuracy and F1-Score. This indicates that the MPCP model exhibits effective identification of churners from the telecom data. The performance comparison in tabulated form is presented in Table. The best performance is shown in bold. It could be observed that the MPCP model exhibits 8% improved accuracy levels and 6% improved F1-Score levels, indicating that the model is suitable to be used in real-time.

CONCLUSION

Predicting churn effectively not only aids in customer retention, but also provides an effective way to improve the profits in the organization. This work presents a probability based model MPCP, which uses an aggregation of machine learning model and minimax probability machines to provide profit oriented churn predictions. Experiments were performed using the churn prediction data available from Kaggle. Comparisons were performed with existing models in literature. Comparisons based on accuracy indicates that the MPCP model exhibits 8% improvements and F1-Score indicates 6% improvements. The upside of the MPCP model is that it is highly generic in nature. Even though analysis has been performed on telecom data, the model can be used on all types of data. The usage of weight factors in the architecture ensures that the model maximizes profit to a large extent. Although the model provides comparatively better performance, the model still has scope for improvement. Hence future extensions of the model will deal in improving the performance of the model.

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Table 1: Attribute Description

Attribute	Data Type	Attribute	Data Type
State	Object	Total eve calls	Int64
Account length	Int64	Total eve charge	Float64
Area code	Int64	Total night minutes	Float64
Phone number	Object	Total night calls	Int64
International plan	Object	Total night charge	Float64
Voice mail plan	Object	Total intl minutes	Float64
Number vmail messages	Int64	Total intl calls	Int64
Total day minutes	Float64	Total intl charge	Float64
Total day calls	Int64	Customer service calls	Int64
Total day charge	Float64	Churn	Bool
Total eve minutes	Float64		

Table 2 : Performance of MPCP Model

Metric	MPCP
FPR	0
TPR	0.773
TNR	1.000
FNR	0.227
Recall	0.773
Precision	1.000
Accuracy	0.970
F1-Score	0.872

Table 3 : Performance Comparison of MPCP

	MPCP	Cenggoro et al.
Accuracy	**0.97**	0.898
F1-Score	**0.87**	0.811

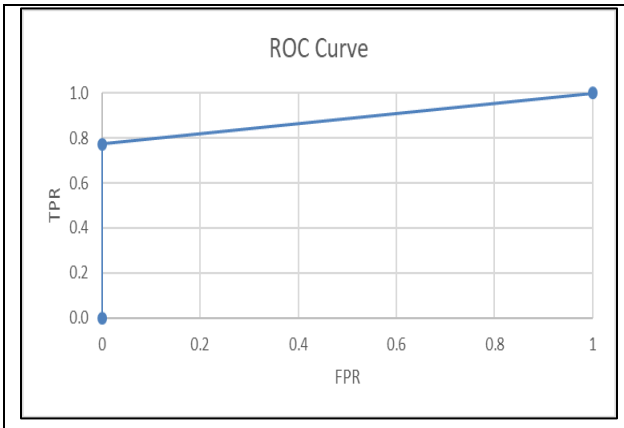

Figure. 1. ROC Plot

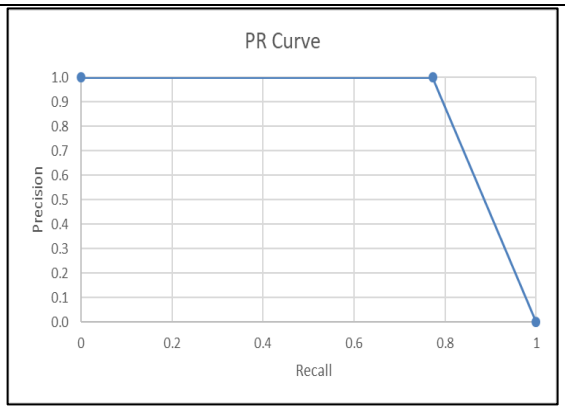

Figure. 2. PR Plot

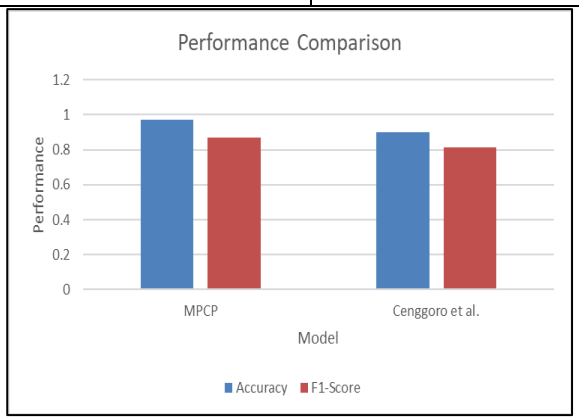

Figure.3. Performance Comparison of MPCP

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RESEARCH ARTICLE

A Noval Approaches of Brain Drug Delivery System

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ABSTRACT

The treatment of CNS related disorder is a challenge as there are various kind of barriers are present in the CNS like blood-brain barrier (BBB), blood-cerebrospinal fluid barrier (BCSFB), the meningeal brain barriers and the blood spinal cord barrier. These barriers prevent the entry of any substance and protect CNS, thus helps in maintaining the homeostasis. The drugs used to treat the disease of brain have a limit to target the brain, so different kind of targeted drug delivery system are required to target the brain. Hence to develop a promising carrier system it is essential to understand the physiology of brain, blood-brain barrier (BBB), blood-cerebrospinal fluid barrier (BCSFB) and all the factors related to the targeted drug delivery. Nanoparticle drug delivery system is the most effectful drug delivery system. This review highlights the role of various physiological barriers that is blood-brain barrier (BBB), blood-cerebrospinal fluid barrier (BCSFB), targeted drug delivery into the brain, transport of drug, the pharmacokinetics of the drug in brain, role of nanoparticles and various colloidal drug delivery techniques (liposomes, niosomes and Solid lipid nanoparticles (SLN)

Keywords: Blood-brain barrier, Liposomes, Solid lipid Nanoparticles, blood-cerebrospinal fluid barrier

INTRODUCTION

The brain is a complex and a delicate organ and has inbuilt mechanism for protection. This protective mechanism also challenges therapeutics interventions and due to this many therapeutic agents are ineffective in many brain diseases [1]. There has been an increasing population worldwide suffering various central nervous system disorders, such as Alzheimer's disease, Parkinson's, cerebral ischemia, and brain tumor. The treatment for these diseases is still confronting a big challenge due to the existence of the blood–brain barrier (BBB), which prevents most drug molecules from entering the brain. The BBB controls substance flow in and out of the brain with precision and strictness, so as to maintain the internal environment of the brain [2]. Systemic delivery of therapeutics to the CNS is not effective for nearly 100% large molecule and 98% of small molecule drugs due to barriers present in the brain, which prevents the entering of therapeutics from the circulating blood to the brain or tightly segregates the brain

from the circulating blood [3]. In the central nervous system, targeted action can be achieved by direct administration of the drugs in to the CNS. Blood brain barrier can considerably impair the effect of the large number of drugs (e.g. antibiotics, antineoplastic agents and Neuropeptides-CNS stimulant drug) because of its obstinate hindrance affect [4].Targeted delivery that would increase the efficacy of pharmaceutical agents, reduce drug doses, and significantly decrease drug toxicity has been an important area of pharmaceutical research. Targeted drug delivery may be achieved by physical, biological, and molecular systems that provide high concentrations of the active agent at the pathophysiologically relevant sites [5].

Advantages [7]

1. Side effect and toxicity reduces.
2. Dose of drug reduces by targeting organ.
3. Avoids degradation of drug (first passmetabolism).
4. Bioavailability increases.
5. Fluctuation in concentration decreases.
6. Permeability of proteins and peptide increases

Disadvantages [7]

1. Enhances clearance from target.
2. Difficult to target tumor cells.
3. Advanced techniques requirements.
4. Skill persons required.
5. Sometimes it may causes toxicity.
6. Difficult to maintain stability of dosage form, e.g.Resealed erythrocytes have to be stored at 40 degree C [7].

The brain barriers established by the endothelial blood-brain barrier (BBB), the epithelial blood-cerebrospinal fluid barrier (BCSFB), the meningeal brain barriers and the blood spinal cord barrier are essential for maintaining central nervous system (CNS) homeostasis [8]. Drug discovery and drug delivery technologies are the two main fields where advancement is required for drug delivery to the brain [6].In advanced technology nanoparticles drugs delivery system can be utilized to delivery drug molecules directly in to the brain [9]. Significant benefits of the Nanoparticles drug delivery system (NDDS) are given in table 1[6].

Blood Brain Barrier

The BBB is a diffusion barrier essential for the normal function of the brain, which impedes the entrance of substances from the blood to the brain to maintain brain homeostasis [10].The blood–brain barrier is composed of brain microvascular endothelial cells, astrocytes, and pericytes. Diffusion between cells is limited by the adhesion of the brain microvascular endothelial cells to each other on the blood side. As a result, substances must pass through the endothelial cells in order to be transferred from the circulating blood to the brain [11]. The blood brain barrier is the highly selective semi permeable membrane. The barrier that separates the circulating blood from the brain and extra cellular fluid in the central nervous system [9].The BBB, therefore, is universally considered as the most important barrier in preventing molecules from reaching the brain parenchyma via extensive branches of blood capillary networks [13]. The BBB performs many functions. It maintains the internal environment of the brain, that is, maintenance of brain ISF and the CSF composition within extremely fine limits for the proper performance of the complex integrative functions of the neurones [14]. The blood–brain barrier (BBB) presents an efficient structural and functional barrier for the delivery of therapeutic agents to the central nervous system (CNS). Due to its unique properties, passage across the BBB often becomes the main limiting factor for the delivery of potential CNS drugs into the brain parenchyma [15].

The BBB is formed by brain endothelial cells and it allows the passage of water, some gases and lipid soluble molecules by passive diffusion [9].Physiologically, in addition to brain capillary endothelial cells, extracellular base

membrane, adjoining pericytes, astrocytes, and microglia are all integral parts of the BBB supporting system. Together with surrounding neurons, these components form a complex and functional "neurovascular unit" [13]. The BBB prevents the brain uptake of most pharmaceuticals, with the exception of small hydrophilic compounds with a mass lower than 150 Da and highly hydrophobic compounds with a mass lower than 400–600 Da that can cross the membrane by passive diffusion [17]. The BBB is a major hurdle for the development of CNS drugs as it prevents over 98% of all small-molecule drugs and close to 100% of large-molecule drugs (biologic drugs) from penetrating the CNS. As a consequence, most drugs have insufficient CNS exposure to be effective, or induce severe secondary effects or toxicity if administered at high doses to increase CNS exposure [18].

The list of BBB-permeant drugs includes opiates (e.g., morphine, methadone, and meperidine), anxiolytics (diazepam, temazepam), SSRIs (paroxetine), and antipsychotics (chlorpromazine, promethazine) but does not include the majority of antibiotics and antitumorals [17]. The BBB drug delivery problem can be solved, but this requires new approaches to this area of pharmaceutics. The old ways of drilling a hole in the head for transcranial brain drug delivery, or medicinal chemistry attempting to lipidize a water-soluble small molecule, must give way to new approaches. The new technology is based on knowledge of endogenous BBB transporters, and aims to reformulate drug structures so that these molecules can cross the BBB via endogenous transport systems. This is a radical departure from existing practices in CNS drug development. However, unless changes are made, the future of CNS drugs will be limited to the small class of drugs that cross the BBB via lipid-mediated free diffusion: lipid soluble small molecules with a molecular weight (MW) <400 Da [19, 20]. All other molecules either do not cross the BBB, or are transported across the BBB via catalyzed transport, owing to the specific interaction between the therapeutic and certain BBB transport systems [21].

Functions of the BBB

1. Controls molecular traffic, keeps out toxins (minimises neuronal cell death, preserves neural connectivity)
2. Contributes to ion homeostasis for optimal neural signalling
3. Maintains low protein environment in CNS, limits proliferation, preserves neural connectivity
4. Separates central and peripheral neurotransmitter pools, reduces cross-talk, allows non-synaptic signalling in CNS
5. Allows immune surveillance and response with minimal inflammation and cell damage [22]

Impact of pathological conditions on the blood-brain barrier and drug transport

The BBB is disrupted under various pathological conditions of diseases such as stroke, diabetes, seizures, hypertensive encephalopathy, acquired immunodeficiency syndrome, traumatic brain injuries, multiple sclerosis, Parkinson's disease (PD) and Alzheimer disease (AD) [10]. It is generally anticipated that BBB interruption that occurs under various pathological conditions may provide an opportunity for enhancement of drug transport into the brain via the paracellular route [13]. In certain pathological conditions, remodeling of the protein complex in interendothelial junctions is an important reason for the BBB breakdown. For example, the BBB becomes hyper-permeable to macromolecules during ischemic stroke [10].

Blood-CSF Barrier (BCSFB)

The surface of the human brain is bathed with about 140 ml of cerebrospinal fluid (CSF) [23]. The entire CSF volume in humans turns over every 4 to 5 h or 5 times every day [24]. The CSF of the brain is produced at the choroid plexi of the ventricles, moves over the surface of the brain, and is absorbed into the general circulation across the arachnoid villi into the superior sagittal sinus of the venous bloodstream [25]. Blood-brain interfaces comprise the cerebral microvessel endothelium forming the blood-brain barrier (BBB) and the epithelium of the choroid plexuses forming the blood-CSF barrier (BCSFB) [26]. It is a barrier between the blood circulation and cerebrospinal fluid (CSF), prevents the entry of drug, toxin, microbes or any material to the CSF. It is composed of arachnoidal and choroid epithelial cells which separate the subarachnoidal CSF and ventricular CSF respectively, from the systemic circulation [27]. The arachnoid membrane is generally impermeable to hydrophilic substances, and its role is forming

the Blood-CSF barrier is largely passive. The choroid plexus forms the CSF and actively regulates the concentration of molecules in the CSF [28]. This barrier is located in the choroid plexus, and it is formed by epithelial cells held together at their apices by tight junctions, which limit paracellular flux. The CSF facing surface of the epithelial cells, which secrete CSF into the ventricles, is increased by the presence of microvilli. The capillaries in the choroid plexus allow free movement of molecules via intracellular gaps and fenestrations [1]. Exchange between blood and CSF at the choroid plexus is affected by local blood flow, fenestrated capillaries, and the substantial surface area created by membrane folding and microvilli [29].

Targeted Drug Delivery into the Brain

Targeted drug delivery, defined as optimization of the therapeutic index by localizing the pharmacological activity of the drug to the site of action, is one of the most important goals of pharmaceutical research and development [30]. Two different mechanisms of transport, i.e. blood-to-brain influx transport and brain-to blood efflux transport, are correlated with the delivery of compounds across plasma membranes of capillary endothelial cells [31]. Drug delivery to the brain through the many endogenous transport systems within the BBB requires reformulation of the drug so that the drug can access the BBB transport system and enter the brain [32]. It is clear from the previous sections that delivery of poorly lipid-soluble compounds to the brain requires some way of getting past the blood–brain barrier [33]. The blood–brain barrier (BBB) is a major obstacle for the effective delivery of therapeutic compounds to the brain, imposing size and biochemical restrictions on the passage of molecules [34]. There are several possible strategies, such as transient osmotic opening of the BBB, exploiting natural chemical transporters, high-dose chemotherapy, or even biodegradable implants. But all of these methods have major limitations: they are invasive procedures, have toxic side effects and low efficiency, and are not sufficiently safe [33].

The various approaches to target drugs to the CNS can be classified as: i) direct delivery, generally bypassing the BBB through direct injection, convection enhanced delivery, biodegradable delivery systems (polymer wafers, nanoparticles, liposomes) or through intra-thecal and intra-arterial injections; ii) enhanced delivery across an intact BBB by non-specific mechanism (e.g., manipulation of lipid solubility) or by specific mechanisms (e.g., receptor-mediated and adsorptive transcytosis, modulation of transport systems, such as P-gp); iii) targeting technologies, that is, methods to increase local concentrations of drugs in the brain after systemic delivery, which include magnetic and immunological targeting, as well as, ultrasound assisted drug release [14]. The biology-based approaches to solving the BBB drug-delivery problem require advance knowledge of the endogenous transporters and could only be accomplished within the pharmaceutical industry if an in-house brain drug-targeting program was supported to the same extent as the in-house brain drug-discovery program [32].

Chemical Drug Delivery Systems

Chemical drug delivery systems (CDDS) represent novel and systematic ways of targeting active biological molecules to specific target sites or organs based on predictable enzymatic activation. They are inactive chemical derivatives of a drug obtained by one or more chemical modifications so that the newly attached moieties are monomolecular units (generally comparable in size to the original molecule) and provide a site-specific or site-enhanced delivery of the drug through multi-step enzymatic and/or chemical transformations [28]. The principle of CDS, in addition to providing access to the brain by increasing the lipophilicity of a drug, exploits specific properties of the BBB to lock drugs in the brain on arrival and prevent them from re-crossing the BBB. The most studied CDS exploits the linking of an active drug molecule to a bioremovable lipophilic targetor moiety, 1,4-dihydro-N-methylnicotinic acid (dihydrotrigonelline), which results in a derivative that readily distributes throughout the body and brain after administration due to its lipophilic character [15].

Transport of Drug in Brain

These BBB transport systems are situated on the luminal and abluminal membranes of the brain capillary endothelium [32].

Passive diffusion

It is well known that only lipid-soluble small molecules with a molecular weight of about 450 daltons can cross the BBB by passive diffusion, which reduces the number of drugs that can enter the central nervous system (CNS) in the drug market to less than 2% of all potential drug candidates [36]. Passive diffusion is the ubiquitous transport mechanism by which most of the essential nutrients including amino acid (AA), neurotransmitters, hormones, etc. and small lipophilic drugs entered into the brain from the systemic circulation. Passive diffusion involves the transfer of drug and endogenous molecules from the blood to the brain under a concentration gradient. It depends on the size and physicochemical properties of the drug. The drug initially dissolved into the lipid bilayer of the brain microcapillary endothelial cell and then releases inside the brain. This mean of transport is suitable only for lipophilic, small size, low molecular weight, neutral compound to cross the BBB [35].

Carrier-mediated transporters (CMT)

Carrier-mediated transport (CMT) is used to shuttle hydrophilic small-molecule nutrients such as glucose and amino acids. CMT tends to be size and stereo selective and has been used to shuttle small-molecule drugs to the brain via linkage of the drug to the natural CMT ligand, but it has not been successfully used for transport of large-molecule biologics. Lipophilic small molecules less than 600 kDa can readily diffuse across the endothelial plasma membrane [37]. Small molecule nutrients and vitamins are water-soluble agents that do not significantly cross the BBB via free diffusion. Instead, these molecules traverse the BBB via transport on specific CMT systems (Pardridge, 2015b) [23]. It is conceivable that some drug/nutrient conjugates could undergo carrier-mediated transport through the BBB, but the most likely event is carrier-mediated transport of a drug that has been modified such that the drug itself has a structure analogous to an endogenous nutrient [1].For example, L-DOPA has the structure of a neutral amino acid. Drugs that undergo carrier-mediated transport through the BBB other than L-DOPA include α-methyl-DOPA, melphalan, α-methyl-para-tyrosine, and gabapentin, which all undergo transport via the BBB neutral amino acid transport system [38].

Active efflux transport (AET)

Active efflux from the CNS via specific transporters may often reduce the measured penetration of drug at the BBB to levels that are lower than might be predicted from the physicochemical properties of the drug, for example, its lipid solubility [28]. The most studied AET system at the BBB is P-glycoprotein, which is a product of the ABCB1 gene. However, BBB AET transport biology extends beyond P-glycoprotein. There are multiple other members of the ABC gene family that represent energy dependent active efflux transporters at the BBB, including members of the ABCC and the ABCG2 gene family. In addition, active efflux transport of drug from brain to blood is a process mediated by two transporters in series, including an energy-dependent transporter and an energy-independent transporter [20]. Active efflux pumps have also been identified, a recognition that has considerably impacted CNS drug development. The existence of probenecid-sensitive, active pumps for organic anions, such as β-lactam drugs or valproic acid (valproate sodium), has been suspected for a while and there is now considerable evidence for their existence [16].

Receptor-mediated transporters (RMT)

Receptor-mediated drug delivery to the brain employs chimeric peptide technology, wherein a non-transportable drug is conjugated to a BBB transport vector. The latter is a modified protein or receptor-specific monoclonal antibody that undergoes receptor-mediated transcytosis through the BBB in-vivo. Conjugation of drug to transport vector is facilitated with chemical linkers, avid in–biotin technology, polyethylene glycol linkers, or liposomes [28]. It is also known as clathrin-dependent endocytosis which is highly specific and involves the internalization of the ligand-receptor complex in the endocytic vesicle. It is a kind of active transport or energy mediated drug transport mechanism. Once a particular ligand entered into the blood circulation, it binds explicitly with the specific receptor. Then the ligand-receptor complex entered into the endothelial cytoplasm through receptor-mediated endocytosis, and finally, the exocytosis releases the ligand bound compound to the abluminal side [35].

The pharmacokinetic of drug delivery

Most therapeutic trials involving drug delivery to the CNS lack basic pharmacology regarding agent delivery. Measurement of brain delivery pharmacokinetics should be a regular component of preclinical, and some clinical studies [1]. The percent of injected dose (ID) of a drug that is delivered per gram brain (%ID/g) is directly proportional to both the BBB permeability–surface area (PS) product and the area under the plasma concentration curve (AUC) [32]: % ID/g = PS × AUC

When the lipid solubility of a drug is increased, the BBB permeability-surface area product may be increased, but the plasma AUC is decreased, generally in proportion to the increase in BBB permeability-surface area product. The decreased plasma AUC occurs because the enhanced lipid solubility of the compound results in an increased distribution of the drug into virtually all peripheral tissues with concomitant rapid removal from the bloodstream. Thus, the increased permeability-surface area product caused by the lipid carrier is offset by the decreased plasma AUC [38].

Nanoparticles (NP)

The application of nanotechnology in drug delivery has gained increasing interest over the past few decades. A myriad of nanoparticles (NPs) have been constructed using various polymers, lipids, inorganic materials or their combinations with the desired physicochemical properties and biological functions for the treatment of various diseases such as cancer, diabetes, and central nervous system (CNS) disorders [39]. In nanotechnology, a particle is defined as a small object that behaves as a whole unit in terms of its transport and properties. It is further classified according to size: in terms of diameter, fineparticles cover a range between 100 and 2500 nanometers, while ultrafine particles, on the otherhand, are sized between 1 and 100 nanometers. Similar to ultrafine particles, nanoparticles are sized between 1 and 100 nanometers. Nanoparticles may or may not exhibit size-relatedproperties that differ significantly from those observed in fine particles or bulk materials [40]. Nanoparticles (NP) are the solid colloidal particles ranges from 1 to 1000nm in size, which are utilized as drug delivery systems [12]. Nanoparticles are defined as solid, submicron-sized drug carriers that may or may not be biodegradable. The term nanoparticle is a collective name for both nanospheres and nanocapsules [41]. Nanoparticles are found to be effective careers in delivery of conventional drugs, recombinant proteins, vaccines as well as Nucleotides. The use of NPs to deliver drugs to the brain across the BBB may provide a significant advantage to current strategies [42].

An ideal nanoparticulate drug delivery system must contain the following characteristics:
(1) Maximum drug bioavailability.
(2) Tissue targeting.
(3) Controlled release kinetics.
(4) Minimal immune response.
(5) Ability to deliver traditionally difficult drugs such as lipophiles, amphiphiles and biomolecules.
(6) Sufficient drug loading capacity.
(7) Good patient compliance [43].

Types of Nanoparticles on the Basis of Morphology Targeting to Brain

There are two different types of NPs based on the morphology of particles: capsules and spheres. Spheres are usually characterized by a porous matrix, in which drugs are contained, while capsule systems consist of a core containing drug compounds surrounded by a shell. NPs can be prepared by using preformed polymers or monomers, which will later be polymerized. The choice of the polymer is directly related to their intrinsic biocompatibility and biodegradability. Many polymers are metabolized by physiological processes and do not induce side effects (i.e. polylactid acid and its derivates), while synthetic polymers may elicit adverse effects, such as incompatibility of the polymers and their degradation products with the physiological environment, adverse metabolic degradation consequences, occlusion phenomena, skin irritation, and allergic responses [31].

Nanocapsules

First of all the nanocapsules can be likened to vesicular systems in which a drug is confined in a cavity consisting of an inner liquid core surrounded by a polymeric membrane (Quintanar et al.,1998a). However, seen from a general level, they can be defined as nano-vesicular systems that exhibit a typical core-shell structure in which the drug is confined to a reservoir or within a cavity surrounded by a polymer membrane or coating (Letchford and Burt,2007; Anton et al., 2008). The cavity can contain the active substance in liquid or solid form or as a molecular dispersion [44].

Nanospheres

From its definition nanospheres are considered as a matrix system in which the matrix in uniformly dispersed. These are spheric vesicular systems [40].Spherical particles having nanometric dimensions and acting as a drug carrier in which drug is enclosed inside the polymer matrix [4]. In the case of nanospheres, where the drug is uniformly distributed, drug release occurs by diffusion or erosion of the matrix. If the diffusion of the drug is faster than matrix erosion, then the mechanism of release is largely controlled by a diffusion process. The rapid, initial release, or 'burst', is mainly attributed to weakly bound or adsorbed drug to the relatively large surface of nanoparticles (Magenheim et al., 1993) [45].

Drug delivery to brain using various colloidal delivery systems

There are two main reasons which account for the failure of drug delivery to the brain, namely,

i) The inability of drug to penetrate or cross the BBB and
ii) The back transport (efflux) of drugs from the brain to the blood.

To overcome these problems, various colloidal delivery systems have been studied by different researchers such as liposomes, microspheres, lipid microspheres, niosomes, polymeric nanoparticles and solid lipid nanoparticles (SLN) [14].

Liposomes

Among nanocarriers, liposomes have been the most studied due to their composition, which makes them biocompatible, biodegradable, and less toxic. Liposomes not only hold potential as vehicles for therapeutic compounds (therapeutics) but also for diagnostic tools (diagnostics) directed to the CNS [46]. Liposomes have been used as potential drug carriers instead of conventional dosage forms because of their unique advantages which include ability to protect drugs from degradation, target the drug to the site of action and reduce the toxicity or side effects but there are some problems that have been faced like liposomes has been limited due to inherent problems such as low encapsulation efficiency, rapid leakage of water-soluble drug in the presence of blood components and poor storage stability. On the other hand, polymeric help to increase the stability of drugs proteins and possess useful Controlled release properties [47].

Niosomes

Niosomes are the bilayer-structured nanoparticles [48]. The two major components utilized for the preparation of niosomes exist: lipid compounds (cholesterol or L-α-soya phosphatidylcholine) and nonionic surfactants. Lipid compounds are utilized to provide unbending nature, appropriate shape, and adaptation to the niosomes. The part surfactants assume the main part in the development of niosomes [49].There size ranges between 10 and 1000 nm [50]. Niosomes are promising candidates for accommodating both hydrophilic and hydrophobic drugs. The surface modification of the niosomes also improves the target specificity for the cancer drug delivery system [48].Niosomes can entrap both hydrophilic and lipophilic drugs in aqueous layer and vesicular membrane respectively. The bilayers of niosomes have both inner and outer surfaces to be hydrophilic with sandwiched lipophilic area in between. Thus a large number of drugs and other materials can be delivered using niosomes (Udupa, 2004) [51].

Solid lipid nanoparticles (SLN): Solid lipid nanoparticles (SLN) are the best-known type of nanospheres [52].SLN introduced in 1991 as an alternative to tradition colloidal carriers such as emulsions, liposomes

and polymeric-micro and nanoparticles [53]. Solid lipid nanoparticles (SLNs) are the first generation of lipid-based nanocarriers that are formulated from lipids, which are solid in the body temperature and stabilized by emulsifiers [54].SLNs are colloidal drug carriers and have been used widely as drug delivery systems in the treatment of a variety of diseases and as alternative carriers to nanoparticles. SLN can improve the targeting and tissue distribution of many drugs and also can improve the tissue distribution of drugs and enhance their bioavailability [55]. SLN are submicron-sized dispersions composed of a solid lipid core and a surfactant (and in some cases a co-surfactant), which surrounds the lipid core and helps the assembly of lipophilic components in an aqueous solution. SLN present many advantages in comparison to other drug delivery systems [56].

Rational for preparation of solid lipid nanoparticles [53]

1. Use of organic solvent may avoided
2. Drug stability may increase
3. Controlled drug release may possible
4. Drug loading capacity is high
5. Hydrophilic and lipophilic drug can be incorporate [53]

Thereby, lipid-based nanocarriers hold strong promise to the delivery of drugs directly to the brain because of their lipid nature (lipophilicity) and small size, which gives the SLNs a natural tendency to cross the BBB; their very low cytotoxicity, shown in vitro; and because they can easily avoid the P-gp efflux activity at brain endothelial cells (especially when coated with polysorbate 80) [36]. SLN production is based mainly, but not solely, on solidified nanoemulsion technologies. High-pressure homogenization (HPH), high shear homogenization, and ultrasonication are used in nanoemulsion preparation [52].

CONCLUSION

Due to blood-brain barrier it is difficult to get the response of a drug, for this targeted drug delivery required which targets the drug directly into the brain. As blood brain barrier is a semipermeable membrane thus target drug delivery is useful for producing the pharmacological effect of drug. Target drug delivery optimize the effect of drug into the brain and produce response. Various techniques have been approached for the drug delivery into the brain like (liposomes, niosomes and Solid lipid nanoparticles (SLN).

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Table 1. Benefits of nano drug delivery system and example of drugs [6]

Benefits	Example of the drugs that can be formulated in NDDS
1. The restraining attributes of the blood brain barrier can be masquerade by NDDS 2. NDDS is an appealing system that offer decreased toxic effects, enhancement of therapeutic efficacy and gradual release of drugs 3. This system have potential to target the desired tissues and attain sustained drug release for longtime(days/weeks)	• Polysorbate 80-coated nanoparticles • Polar hexapeptide dalargin • Tubocurarine • lipid-soluble P-glycoprotein substrates loperamide • doxorubicin

Table 2. Pathological conditions, their impact on the blood–brain barrier, and drug transport opportunities into the brain [13].

Pathological condition	Impact on the BBB	Implication for drug traversing the BBB
Multiple sclerosis	Disruption of TJ; enhanced leukocyte activity; release of Inflammatory cytokines/ chemokines	Potentially it may enhance paracellular transport of drugs.
Alzheimer's disease	BBB disruption and permitted the greater access of peripheral IgG to the CNS Over expression of efflux pumps	Potentially it may enhance paracellular transport of drugs that have affinity for albumin and IgG into the CNS Efflux pump inhibitors may improve drug deliver into the brain.
Parkinson's disease	BBB disruption	It enhanced therapeutic agent concentration in the brain
HIV	Increase in the diameter of cortical vessels, thinning of basal lamina, loss of glycoproteins, apoptosis of endothelial cells and tight junction disruption	Potentially it may increase drug transport into the brain due to the leaky barrier.
Infectious disease	Leukocyte invasion, elevated CSF-to-serum albumin ratio, and BBB impairment	It may enhance paracellular transport of drugs and drugs with affinity for albumin.
Inflammation	Increased BBB permeability	It may facilitate paracellular drug transportation
Stroke	BBB disruption Upregulation of DTR	It enhanced paracellular drug, e.g. Ginkgolide B, passage into the brain. It may provide disease-induced specific drug targeting of the BBB and receptor mediated transcytosis.
Trauma	BBB breakdown	It enhanced therapeutic agent concentration in brain
Pain	Alternation of BBB chemokine receptor due to activated astrocytes Decreased TJ proteins and BBB perturbation	It may lead to astrocyte-targeted therapy. It may facilitate paracellular drug transportation
Brain tumour	Loss of the tight junctions in the tumour	Angiogenic vessels are permeable to nano-

	vascular system, enhanced retention effect Over expression receptors of folate, insulin and transferrin	sized materials. It enhanced folic acid, insulin and transferrin-attached nanoparticles across the BBB
Ischemia/seizures	Upregulation of DTR	Potentially it may increase disease-induced specific drug targeting of BBB and receptor mediated transcytosis.

DTR: diphtheria toxin receptor [13]

Table 3. Strategies for brain drug delivery [10].

Strategies	Advantages	Limitations
Viral vectors	High gene transfection efficiency	Safety concerns; brain direct injection; crossing the BBB; high dose by intravenous administration
Nanoparticles	Actively targeted delivery; brain targeting using specific physiological conditions	Crossing the BBB
Exosomes	Gene delivery to brain; potential ability to cross the BBB	Exosome donor cells; loading procedure; in-vivo toxicity and pharmacokinetics
Delivery through active transporters in the BBB	Potential ability to cross the BBB by intravenous injection	Mainly for small molecules
Brain permeability enhancer	Transiently open the BBB	Mismatch between findings in rodents and humans
Delivery through the permeable BBB under disease conditions	Potential to cross the BBB	Limited knowledge about dynamic changes in the BBB and their mechanisms
Non-invasive techniques to enhance brain drug uptake	Potential to open the BBB and decrease efflux transporters	Toxicity
Alteration of administration routes	Bypass the BBB through nasal administration	Suitable for low dose
Nanoparticles for brain imaging/diagnostics	Enhance imaging; cross the BBB through the hyper-permeable BBB under disease conditions	Cross the BBB; understand dynamic changes in the BBB

Table 4. Advantages of solid lipid nanoparticles delivery systems [55]

Advantages of SLNs
Incorporation of hydrophilic and hydrophobic drugs
High bioavailability
High biocompatibility
High drug payload
Controlled release
Physical stability of SLN
Protection of the labile drug from degradation
Drug targeting and controlled release
Excellent tolerability
Not toxic

Avoidance of using organic solvents
Easy preparation
Easy scaling up
No problems concerning sterilization
Fewer drug leakage and storage problems compared to liposomes
No reported significant acidity and toxicity

Table 5. Disadvantages of solid lipid nanoparticles delivery systems [57]

Disadvantages of SLNs
Drug expulsion after polymeric transition during storage
Relatively high water content of the dispersions (70-99.9%) [57]
because of their perfect crystalline structure they have low drug loading efficiency [54]

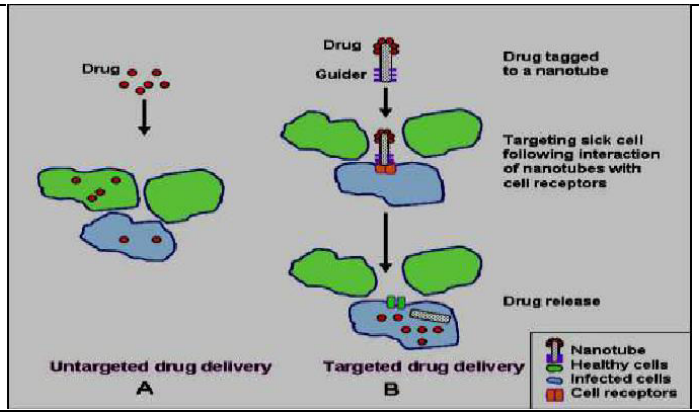

Figure 1. Drug targeting technology [6]

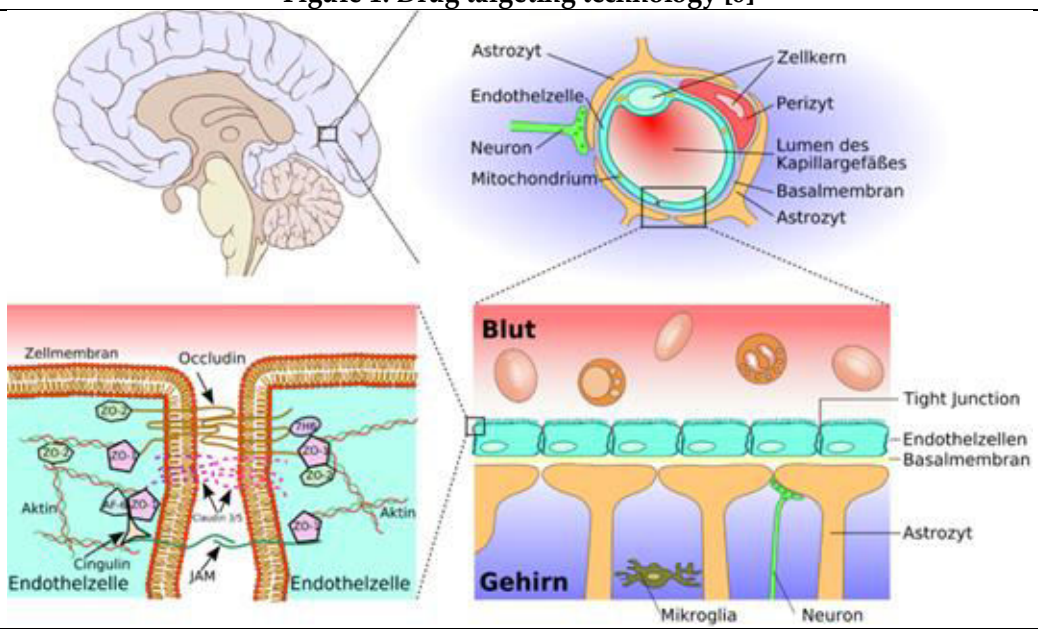

Fig. (2). Schematic representation of blood-brain barrier [12].

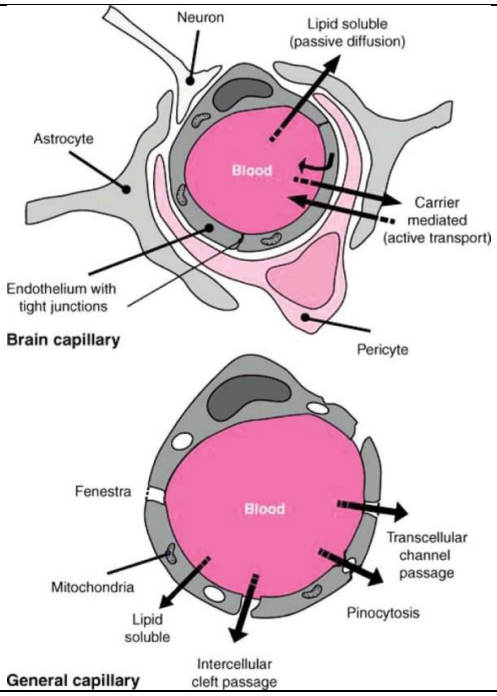

Fig. 3. Schematic comparison of brain and general capillaries. Capillaries in the brain are lined with a layer of special endothelial cells that lack fenestrations and are sealed with tight junctions. These endothelial cells, together with perivascular elements such as astrocytes and pericytes, constitute the blood-brain barrier. In brain capillaries, intercellular cleft, pinocytosis, and fenestrae are virtually nonexistent; exchange occurs only transcellularly. Brain endothelial cells also contain large densities of mitochondria, metabolically highly active organelles. A number of active transporters are also involved in both inward and outward transport of specific substrates [16].

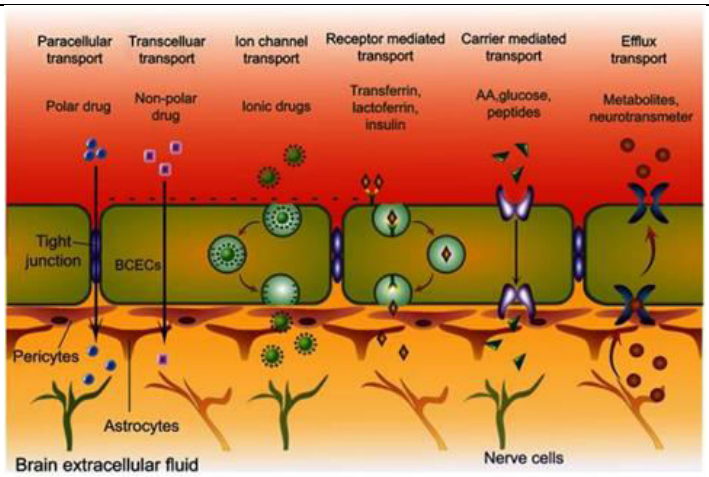

Fig. 4 Schematic representation of drug transport across BBB via different mechanisms including passive diffusion (including paracellular transport of polar or hydrophilic drug and transcellular transport of lipidic or non-polar drug), receptor-mediated transport, ion channel transport of surface charged molecules, carrier-mediated transport of AA, glucose, larger proteins and peptides, and also the efflux transport that regulates the outflow of metabolites, drugs, toxins and neurotransmitters [35].
Abbreviations: AA, amino acid; BBB, blood–brain barrier; BCECs, brain capillary endothelial cells.

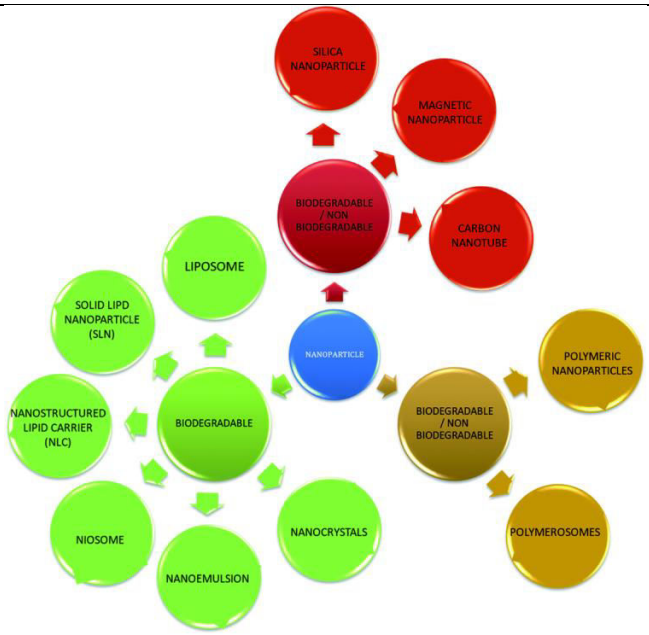

Fig. 5 Schematic diagram of the different types of nanoparticles [43].

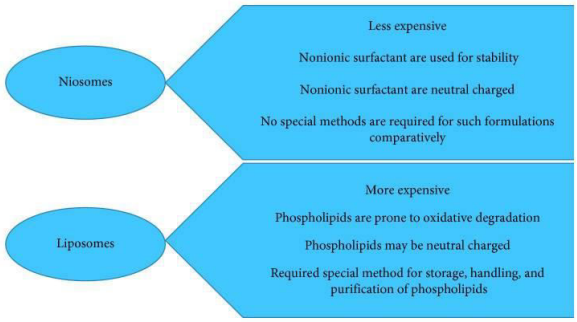

Figure 6 Major differences in characteristics between liposomes and niosomes [49].

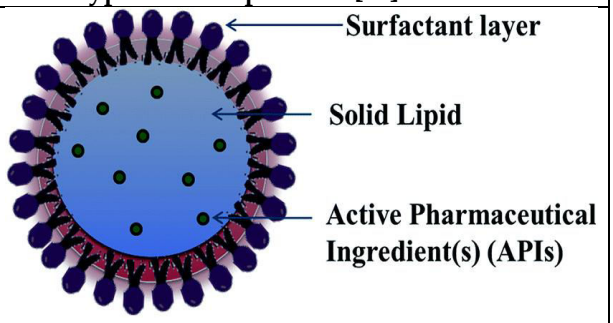

Fig. 7 Schematic presentation of the complete structure of solid lipid nanoparticles [43].

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RESEARCH ARTICLE

Study of Energy Loss for Some Metal Foils (A Possible Source for Secondary Electron)

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ABSTRACT

The secondary electron are very important for many devices like scanning electron microscope, tunneling microscope etc. Not only in material science but also it plays a very important role in the nuclear physics. Especially for the development of many experimental setup or triggering devices. In Present report a study has done for the emission of secondary electron using metal films and identified a possible candidate which can be used as potential source of a secondary electrons.

Keywords: WF, SE, MCP

INTRODUCTION

The study of nuclear instrumentation is very interesting and challenging. Most of the time in market there are ready to use instruments/detectors are available which can be used for any nuclear physics experiment. A detector can detect the outcome of any experiment. Like the HPGE detector which can be used for the measurement of the gamma rays, x-ray. Similarly SSB detectors which can be used for the measurement of the particle spectrum or the nature of the evaporated particles which come out from any nuclear reaction, specially the energy of the emitted particles. Most of the time people uses the existing available instruments or detectors. Some time it needs to devise some detector which are not available. The different raw material are available but not the instrument. In that situation it require to fabricated the device completely from scratch. Sometimes not only device but the associated requirement is there based on the experimental condition which need new to be made, like a triggering device .An online triggering device in an ion beam experiment is very useful. Similarly the ion beam diagnostic instruments need to fabricate where it is not available in market. When the ion beams having very low energy and very low intensity most of the available instruments for the beam diagnostic does not work. In this type of situation one need

to make a device. Out of many possible device configuration, a secondary electron based device is our interest. In the present paper the possible candidates for the secondary electron has been explain and studied.

SIMULATION AND RESULTS

Secondary electron emission, discovered in 1901 by Austin and Starke [1], is the process by which slow electrons escape from the surface of a solid as a result of its bombardment by fast and energetic ions [2]. In the first theories [3], it has been assumed that the process can be described in terms of two mechanisms: the production of secondary electron by incident ions, and the migration and escape of secondary electrons into free space. By combining these two mechanisms, we can write the expression for the yield Y, defined as the number of secondary electrons escaping per incident one, is depends on the stopping energy of the material, energy lose per unit path length, the depth of the material, the excitation energy of the secondary electron and also the flux and energy of the incident ions. It also depends on the work function (WF) of the material. The migration and escape of secondary electrons are influenced by the work function of the material and by the absorption of the secondary electrons inside the solid. The effect of the work function has demonstrated [4], and obtained an increased secondary electron yield by lowering the work function, using negative electron affinity materials. On the other hand, the migration of secondary electrons is part of a more broad subject that deals with the absorption of low energy electrons as they move inside the solid. The absorption is assumed to be exponential, characterized by an attenuation length. Since the material work function play an important role in addition with energy loss. A Monte Carlo simulation has been performed using the code SRIM [5] with various targets to understand the energy loss and shown in Fig.1.It is clear from Fig.1 that the energy lose is more spread in Au foil compared to myler and carbon i.e. the emitted secondary electron energy have also wide range for Au compared to other two. The Simulated recoil energy distribution has also shown in Fig.2. One can see from Fig.2 that the recoil energy has a wide distribution of energy for Au target where as for the myler and carbon foiles the energy distribution of the recoil is not wide that clearly indicated that the emitted energy of the secondary electron will be more monoenergetic and focused in energy for myler and carbon compared to Au foil, whereas the number of secondary electron yield will be more for Au compared to other two.

SUMMARY AND CONCLUSION

A clear picture with a Monte Carlo simulation has been performed and presented for the energy lose in Au, myler and a carbon foils. in all the cases the thickness of the foil has been considered as $30 \mu g/cm^2$ and the incident ion having proton with beam energy 5MeV. It has seen that for higher yield of secondary electron Au foil can be a good candidates where as if the monoenergetic electron are require then the myler or carbon film are the better candidates.

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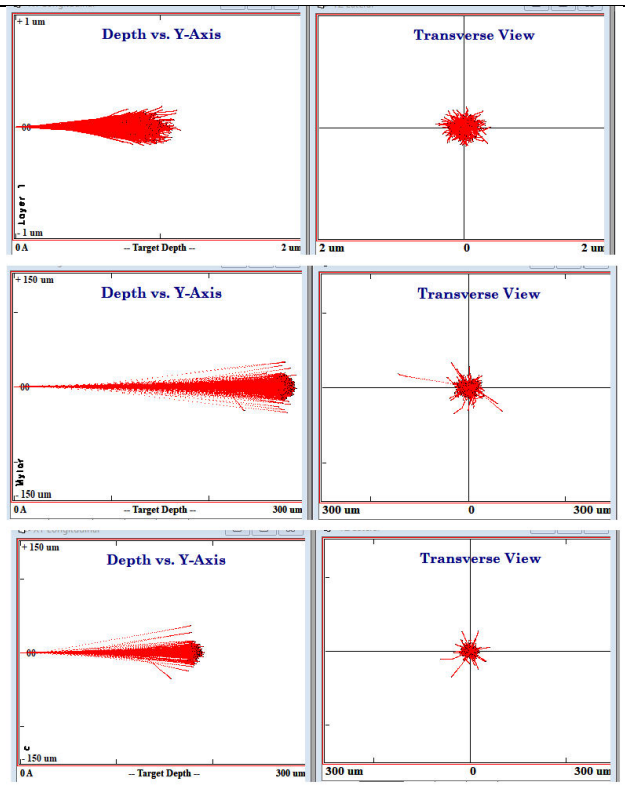

Fig 1 The SRIM calculation for the range prediction and the energy lose pattern for a Au foil (Top) a myler foil (middle) and a carbon foil (bottom).

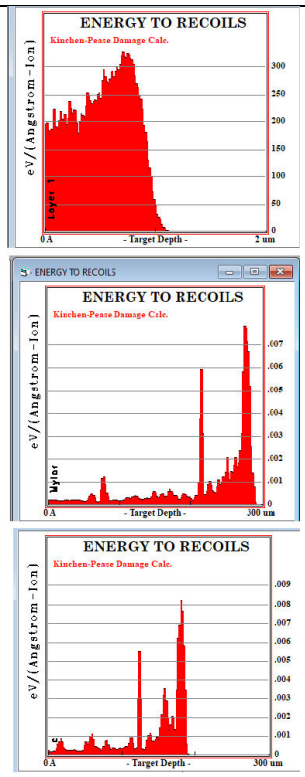

Fig. 2 Then recoil energy distribution from the Au, myler and C foils ,the order of material same as of Fig.1

REVIEW ARTICLE

Hydrogels used for Ophthalmic Preparation –An Overview

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ABSTRACT

Hydrogels are three dimensional cross linked polymeric network system, which have an ability to respond to the fluctuation or changes in the environmental stimuli like pH, temperature and ions. This drug delivery system is hydrophilic in nature which has a capacity to imbibe water content and swell; there by it resembles the normal living tissue .In recent years many research has been done in hydrogel .In this review article, application & common uses etc. has been described by this way we can get have recent knowledge about the hydrogels. Biocompatibility is promoted by the high water content of hydrogels and the physiochemical similarity of hydrogels to the native extracellular matrix, both compositionally (particularly in the case of carbohydrate-based hydrogels) and mechanically. Hydrogels can be classified on basis of method of preparation, ionic charges, structure and mechanism controlling the drug release. It is widely employed in various fields like tissue engineering. High rate of the sol/gel transition of Gelritew in-situ gels results in long pre-corneal contact times. Hence, Hydrogel is a promising drug delivery system for the effective transport of the drugs into the eye for the cure treatment of various kinds of eye diseases.

Keywords: Hydrogels, ophthalmic drug delivery, polymers, applications

INTRODUCTION

Ophthalmic Drug Delivery System

Ophthalmic drug delivery is one of the interesting and challenging endeavours facing the pharmaceutical scientist. The anatomy, physiology, and biochemistry of the attention render this organ highly impervious to foreign substances. Drug deliveries to the attention are often broadly classified into anterior and posterior segments.

Conventional systems like eye drops, suspensions, and ointments can't be considered optimal within the treatment of vision-threatening ocular diseases [1]. However, quite 90% of the marketed ophthalmic formulations are within the sort of eye drops. These formulations mainly target the diseases within the anterior segment of eye [2]. Topical ocular medications don't reach the posterior segment of the attention. Posterior segment [retina, vitreous, choroid] are often treated by high drug dosage regimen given intravenously or by intravitreal administration or implants or by periocular injections. Currently, the posterior segment drug delivery may be a rapidly growing interest area in ophthalmic drug delivery [3].

Various types Ophthalmic preparations are followed by

1. Liquid
2. Solids
3. Intraocular
4. Semisolids

The eye is that the organ liable for vision. Vision is our window to the surface world. This article explores the anatomy of the attention watching the various structures of the human eye and their function. The diagrams below show cross sections of the human eyeball. As we journey through the various structures, ask the diagrams to quickly digest the content on this page. Our eyeballs are fairly round organs cushioned by fatty tissues and that they sit in two bony sockets inside the skull. This helps to guard our eyes from injury [4].

Scelera: The sclera is outermost layer of the eyeball. It's the white [and opaque] a part of the eyeball. Muscles liable for moving the eyeball are attached to the eyeball at the scelera.

Cornea: At the front of the eyeball, the sclera becomes the cornea. The cornea is the transparent dome-shaped part of the eyeball. Light rays from the outside world first pass through the cornea before reaching the lens. Together with the lens, the cornea is responsible focussing light on the retina [5].

Choroid: The choroid is the middle layer of the eyeball located between the sclera and the retina. It provides nutrients and oxygen to the outer surface of the retina [6].

Anterior Chamber: The space between the cornea and the lens is known as the anterior chamber. It is filled with fluid called aqueous humour. The anterior chamber is also known as anterior cavity [7].

Aqueous humour: The Aqueous humour is a transparent watery fluid that circulates in the anterior chamber. It provides oxygen and nutrients to the inner eye and exerts fluid pressure that helps maintain the shape of the eye. The aqueous humour is produced by the ciliary body [8].

Posterior Chamber: The posterior chamber is a larger area than the anterior chamber. It is located opposite to the anterior chamber at the back of the lens. It is filled with a fluid called vitreous humour. The posterior Chamber is also referred to as the Vitreous body as indicated in the diagram below - anatomy of the eye [9].

Vitreous humour: The vitreous humour is a transparent jelly-like fluid that fills the posterior chamber. It exerts fluid pressure that keeps the retina layers pressed together to maintain the shape of the eye and to maintain sharp focus of images on the retina [10].

Iris: The choroid continues at the front of the eyeball to form the Iris. The iris is a flat, thin, ring-shaped structure sticking in to the anterior chamber. This is the part that identifies a person's eye colour. The iris contains circular muscles which go around the pupil and radial muscles that radiate toward the pupil. When the circular muscles contract they make the pupil smaller, when the radial muscles contract, they makes the pupil wider [11].

Ciliary muscles: The cilliary muscles are located inside the ciliary body. These are the muscles that continuously change the shape of the lens for near and distant vision. See diagram anatomy of the eye above.

Ciliary Body: The choroid continues at the front of the eyeball to form the ciliary body. It produces the aqueous humour. The ciliary body also contains the ciliary muscles that contract or relax to change the shape of the lens [12].

Zonules: The zonule also known as suspensory ligaments is a ring of small fibres that hold the lens suspended in place. It connects the lens to the ciliary body and allows the lens to change shape [13].

Lens: The lens is a biconvex transparent disc made of proteins called crystallines. It is located directly behind the iris and focuses light on to the retina. In humans, the lens changes shape for near and for distant vision [14].

Pupil: The pupil is the hole at the center of the iris located in front of the lens. Whenever more light needs to enter the eyeball, the muscles in the iris contract like the diaphragm of a camera to increase or decrease the size of the pupil [15].

Retina: The retina is the innermost layer lining the back of the eyeball. It is the light sensitive part of the eye. The retina contains photo receptors that detect light. These photo receptors are known as cones and rods. Cones enable us to detect colour while rods enable us to see in poor light. The retina contains nerve cells that transmit signals from the retina to the brain [16].

Fovea: The fovea is a small depression in the retina near the optic disc. The fovea has a high concentration of cones. It is the part of the retina where visual acuity is greatest [17].

Optic nerve: The optic nerve is located at the back of the eyeball. It contains the axons of retina ganglion cell [nerve cells of the retina] and it transmits impulses from the retina to the brain [18].

Optic disc: Impulses are transmitted to the brain from the back of the eyeball at the optic disc also called the blind spot. It is called the blind spot because it contains no photoreceptors, hence any light that falls on it will not be detected [19].

Eye muscles: Muscles of the eye are very strong and efficient, they work together to move the eyeball in many different directions. The main muscles of the eye are Lateral rectus, Medial rectus, Superior rectus and inferior rectus [20].

Central Artery and Vein: The central artery and vein runs through the center of the optic nerve. The central artery supplies the retina while the central vein drains the retina. In the diagram above - **anatomy of the eye**, the artery is shown in red while the vein is shown in blue [21].

Tear Duct: This is a small tube that runs from the eye to the nasal cavity. Tear drains from the eyes in to the nose through the tear duct. This is why a teary eye is usually accompanied by a runny nose [22].

Hydrogels

Hydrogels are three-dimensional, cross-linked networks of water-soluble polymers. Hydrogels can be made from virtually any water-soluble polymer, encompassing a wide range of chemical compositions and bulk physical properties. Furthermore, hydrogels can be formulated in a variety of physical forms, including slabs, micro-particles, nanoparticles, coatings, and films. As a result, hydrogels are commonly used in clinical practice and experimental

medicine for a wide range of applications, including tissue engineering and regenerative medicine, diagnostics, cellular immobilization, separation of biomolecules or cells, and barrier materials to regulate biological adhesions. Hydrogels show minimal tendency to adsorb proteins from body fluids because of their low interfacial tension. Further, the ability of molecules of different sizes to diffuse into [drug loading] and out of [drug release] hydrogels allows the possible use of dry or swollen polymeric networks as drug delivery systems for oral, nasal, buccal, rectal, vaginal, ocular and parenteral routes of administration. Several terms have been coined for hydrogels, such as 'intelligent gels' or 'smart hydrogel [23]. The unique physical properties of hydrogels have sparked particular interest in their use in drug delivery applications. Their highly porous structure can easily be tuned by controlling the density of crosslinks in the gel matrix and the affinity of the hydrogels for the aqueous environment in which they are swollen. Their porosity also permits loading of drugs into the gel matrix and subsequent drug release at a rate dependent on the diffusion coefficient of the small molecule or macromolecule through the gel network. Indeed, the benefits of hydrogels for drug delivery may be largely pharmacokinetic specifically that a depot formulation is created from which drugs slowly elute, maintaining a high local concentration of drug in the surrounding tissues over an extended period, although they can also be used for systemic delivery. Hydrogels are also generally highly biocompatible, as reflected in their successful use in the peritoneum and other sites in vivo [24].

Biocompatibility is promoted by the high water content of hydrogels and the physiochemical similarity of hydrogels to the native extracellular matrix, both compositionally (particularly in the case of carbohydrate-based hydrogels) and mechanically. Biodegradability or dissolution may be designed into hydrogels via enzymatic, hydrolytic, or environmental (e.g. pH, temperature, or electric field) pathways; however, degradation is not always desirable depending on the time scale and location of the drug delivery device. Hydrogels are also relatively deformable and can conform to the shape of the surface to which they are applied. In the latter context, the muco or bio adhesive properties of some hydrogels can be advantageous in immobilizing them at the site of application or in applying them on surfaces that are not horizontal. Despite these many advantageous properties, hydrogels also have several limitations [25]. The low tensile strength of many hydrogels limits their use in load bearing applications and can result in the premature dissolution or flow away of the hydrogel from a targeted local site. This limitation may not be important in many typical drug delivery applications [e.g., .subcutaneous injection]. More important, perhaps, are problems relating to the drug delivery properties of hydrogels. The quantity and homogeneity of drug loading into hydrogels may be limited, particularly in the case of hydrophobic drugs. The high water content and large pore sizes of most hydrogels often result in relatively rapid drug release, over a few hours to a few days. Ease of application can also be problematic; although some hydrogels are sufficiently deformable to be injectable, many are not, necessitating surgical implantation [26]. Each of these issues significantly restricts the practical use of hydrogel-based drug delivery therapies in the clinic. In this review, we focus on recent developments addressing three key clinically relevant issues regarding the use of hydrogels for drug delivery: facilitating the in vivo application of drug-eluting hydrogels, extending their duration of drug release, and broadening the range of drugs which they effectively deliver [27].

Classification of hydrogels

1. Based on the method of preparation, hydrogels are classified into:

A] Homopolymer hydrogels

B] Co-polymer hydrogels

C] Multi polymer hydrogels [28]

2. Based on the ionic charges hydrogels can be classified into:

A] Neutral hydrogels

B] Anionic hydrogels

C] Cationic hydrogels

D] Ampholytic hydrogels [29]

3. Based on the structure hydrogels can be classified into:

A] Amorphous hydrogels

B] Semi-crystalline hydrogels
C] Hydrogen bonded hydrogels [30]

4. Based on the mechanism controlling the drug release they are classified into:

A] Diffusion controlled release systems
B] Swelling controlled release systems
C] Chemically controlled release systems
D] Environment responsive systems [31]

Mechanical properties Hydrogel

Mechanical properties of hydrogels are very important for pharmaceutical applications. For example, the integrity of the drug delivery device during the life time of the application is very important to obtain FDA approval, unless the device is designed as a biodegradable system. A drug delivery system designed to protect a sensitive therapeutic agent, such as protein, must maintain its integrity to be able to protect the protein until it is released out of the system. Changing the degree of crosslinking has been utilized to achieve the desired mechanical property of the hydrogel .increasing the degree of cross linking of the system will result in a stronger gel. However, a higher degree of crosslinking creates a more brittle structure. Hence, there is an optimum degree of crosslinking to achieve a relatively strong and yet elastic hydrogels. Copolymerization has also been utilized to achieve the desired mechanical properties of hydrogels. Incorporating a co monomer that will contribute to H-bonding can increase the strength of the hydrogel [32, 33].

Cytotoxicity and in-vivo toxicity

Cell culture methods, also known as cytotoxicity tests can be used to evaluate the toxicity of hydrogels. Three common assays to evaluate the toxicity of hydrogels include extract dilution, direct contact and agar diffusion. Most of the problems with toxicity associated with hydrogel carriers are the unreacted monomers, oligomers and initiators that leach out during application. Therefore, an understanding the toxicity of the various monomers used as the building blocks of the hydrogels is very important. The relationship between chemical structures and the cytotoxicity of acrylate and methacrylate monomers has been studied extensively. Several measures have been taken to solve this problem, including modifying the kinetics of polymerization in order to achieve a higher conversion, and extensive washing of the resulting hydrogel. The formation of hydrogels without any initiators has been explored to eliminate the problem of the residual initiator. The most commonly used technique has been gamma irradiation .Hydrogels of PVA have been also made without the presence of initiators by using thermal cycle to induce crystallization .The crystals formed act as physical crosslinks. These crystals will be able to absorb the load applied to the hydrogels [34].

Common uses for Hydrogels

- Currently used as scaffolds in tissue engineering. When used as scaffolds, hydrogels may contain human cells in order to repair tissue.
- Environmentally sensitive hydrogels. These hydrogels have the ability to sense changes of pH, temperature, or the concentration of metabolite and release their load as result of such a change
- As control-release delivery systems.
- Provide absorption, desloughing and debriding capacities of necrotics and fibrotic tissue [35].
- Hydrogels that are responsive to specific molecules, such as glucose or antigens can be used as biosensors as well as in DDS.
- Used in disposable diapers where they "capture" urine, or in sanitary napkins.
- Contact lenses (silicone hydrogels, polyacrylamides).Common ingredients are e.g. polyvinyl alcohol, sodium poly acrylate , acrylate polymers and copolymers with an abundance of hydrophilic groups. Natural hydrogel materials are being investigated for tissue engineering, these materials include agarose, methyl cellulose, hylaronan, and other naturally derived polymers [36].

Advantages

A. Entrapment of microbial cells within polyurethane hydrogel beads with the advantage of low toxicity.
B. Hydrogel is more elastic and stronger than available hydrogels of similar softness. Poly [methyl acrylate-co-hydroxyethyl acrylate] hydrogel implant material of strength and softness.
C. Hydrogel-based micro-valves have a number of advantages over convention micro-valves, including relatively simple fabrication, no external power requirement, no integrated electronics, large displacement (185 μm), and large force generation (22 mN).
D. Environmentally sensitive hydrogels. These hydrogels have the ability to sense changes of pH, temperature, or the concentration of metabolite and release their load as result of such a change.
E. Natural hydrogel materials are being investigated for tissue engineering, these materials include agarose, methylcellulose, hylaronan, and other naturally derived polymers [37].

Disadvantages

A. The main disadvantages are the high cost and the sensation felt by movement of the maggot
B. Its disadvantages include thrombosis at anastomosis sites and the surgical risk associated with the device implantation and retrieval.
C. Hydrogels are non-adherent, they may need to be secured by a secondary dressing.
D. Disadvantages of hydrogel in contact lenses are lens deposition, hypoxia, dehydration and red eye reactions [38].

Applications of Hydrogels

Applications of hydrogels in Drug Delivery

A number of strategies have been proposed to achieve drug delivery systems for efficient therapy. Among them, hydrogels have attracted considerable attention as excellent candidates for controlled release devices, bio adhesive devices, or targetable device of therapeutic agents. Hydrogel-based delivery devices can be used for oral, rectal, ocular, epidermal and subcutaneous application various sites that are available for the application of hydrogels for drug delivery [39].

Peroral drug delivery

Drug delivery through the oral route has been the most common method in the pharmaceutical applications of hydrogels. In peroral administration, hydrogels can deliver drugs to four major specific sites; mouth, stomach, small intestine and colon. By controlling their swelling properties or bio adhesive characteristics in the presence of a biological fluid, hydrogels can be a useful device for releasing drugs in a controlled manner at these desired sites. Additionally, they can also adhere to certain specific regions in the oral pathway, leading to a locally increased drug concentration, and thus, enhancing the drug absorption at the release site [40].

Drug delivery in the oral cavity

Drug delivery to the oral cavity can have versatile applications in local treatment of diseases of the mouth, such as periodontal disease, stomatitis, fungal and viral infections, and oral cavity cancers. Long-term adhesion of the drug containing hydrogel against copious salivary flow, which bathes the oral cavity mucosa, is required to achieve this local drug delivery. For this purpose, many types of bio-adhesive hydrogel systems have been devised since the early 1980s. Some of these are already on the market. For example, a bio adhesive tablet developed by Nagai et al. is commercially available under the brand name Aftachw. This product is composed of a double layer, with a bio-adhesive. A hydrogel-based ointment can also be utilized for the topical treatment of certain diseases in the oral cavity. It can be used not only as a drug delivery device, but also as a liposome delivery vehicle. The possible advantage of liposome delivery with this ointment is that the use of liposomal formulations with encapsulated drug can lead to an increase of local, and a decrease of systemic, drug concentration, because of then capsulation of drugs with phosphor lipids [41]. This may provide more desirable properties for topical use, such as reduction of

uncontrolled release of drugs into the blood circulation and certain undesirable side effects, compared with the conventional ointment-drug formulations. Pharmaceutical performance of three different hydrogel-based ointments as possible vehicles for liposome delivery into the oral cavity tissues by electron paramagnetic resonance [EPR] can be done. The vehicles employed were Orabasew (a sodium carboxymethylcellulose, pectin and gelatincombination in a polyethylene –paraffinbase), Carbopol 934Pw and neutralized poly[MAA-co-methyl methacrylate[MMA]]. Liposome containing mucoadhesive ointments were prepared by simply mixing multi-lamellar liposomes [42]. The oral cavity can also provide a useful location as a transport route for heavily metabolized drugs, since the drugs absorbed from this route by pass first-pass hepatic metabolism.

A hydrogel ointment containing absorption enhancers for the buccal delivery of 17 b-estradiol (E2) is employed to treat osteoporosis. It is well known that the oral administration of E2 results in very low availability due to its high first pass effect. Ethanol solution containingE2, and glycerylmonolaurate as an absorption enhancer, and an aqueous solution of a commercial carboxyvinyl polymer [Hiviswako 103] and triethanolamine were mixed together to produce the hydrogel ointment. In-vivo studies using hamsters demonstrated that the buccal administration of E2 with this the E2 plasma level at over 300 ng/ml percm3 for 7 h, while no primary morphological change of buccal membrane was observed 7 h after application. New buccal bilayered tablets containing nifedipine and propranolol hydrochloride intended for systemic drug administration [43]. The tablets, comprising two layers, a drug-containing mucoadhesive layer of chitosan with polycarbophil and a backing layer of ethylcellulose, were obtained by direct compression. The double-layered structure design provided a unidirectional drug delivery towards the mucosa, and avoided a loss of drug resulting from wash-out with saliva flow. The striking feature of this device would be the utilization of an in-situ crosslinking action between cationic chitosan and anionic polycarbophil, which progressed upon penetration of the aqueous medium into the tablet. As a result of the crosslinking effect, the tablets showed controlled swelling and prolonged drug release, and an adequate adhesiveness could be obtained [44].

Drug delivery in the GI tract

The GI tract is unquestionably the most popular route of drug delivery because of the facility of administration of drugs for compliant therapy, and its large surface area for systemic absorption. It is, however, the most complex route, so that versatile approaches are needed to deliver drugs for effective therapy. Like buccal delivery, hydrogel-based devices can be designed to deliver drugs locally to the specific sites in the GI tract. For example, stomach-specific antibiotic drug delivery systems for the treatment of Helicobacter pylori infection in peptic ulcer disease. For localized antibiotic delivery in the acidic environment of the stomach, they developed cationic hydrogels with pH-sensitive swelling and drug release properties [45]. The hydrogels were composed of freeze-dried chitosan-poly (Ethylene oxide) [PEO] IPN. pH-dependent swelling properties and the release of two common antibiotics, amoxicillin and metronidazole, entrapped in the chitosan PEO semi- IPN were evaluated in enzyme-free simulated gastric fluid (SGF; pH 1.2) and simulated intestinal fluid (SIF; pH 7.2) [46].

The swelling ratio of the hydrogels after 1 h in SGF was found to be 16.1, while that in SIF was only 8.60. Additionally, the freeze-dried chitosan-PEO semi-IPN demonstrated fast release of the entrapped antibiotics in SGF because of its highly porous matrix structure resulting from freeze drying. More than 65 and 59% of the entrapped amoxicillin and metronidazole, respectively were released from the hydrogels after 2 h in SGF. The rapid swelling and drug release demonstrated by these hydrogel formulations may be beneficial for site-specific antibiotic delivery in the stomach, because of the limitations of the gastric emptying time. Enzymatically degradable gelatin –PEO semi-IPN with pH-sensitive swelling properties for oral drug delivery is employed. In this case, the incorporation of gelatin in the IPN made it possible to swell in the acidic pH of the gastric fluid, due to the ionization of the basic amino acid residues of gelatin. The IPN was found to be degraded by proteolytic enzymes, such as pepsin and pancreatin. However, there are many hurdles, including protein inactivation by digestive enzymes in the GI tract, and poor epithelial permeability of these drugs. However, certain hydrogels may overcome some of these problems by appropriate molecular design or formulation approaches [47]. For example, novel per oral dosage forms of hydrogel formulations with protease inhibitor activities using Carbopol-w (C934P), a poly [acrylic acid] product,

which has been shown to have an inhibitory effect on the hydrolytic activity of trypsin, and its neutralized freeze-dried modification (FNaC934P). They demonstrated that two-phase formulations, consisting of the rapid gel-forming FNaC934P and the efficient enzyme-inhibiting, but more slowly swelling, C934P, had the most profound effect on trypsin activity inhibition. Recently, oral insulin delivery using pH responsive complexation hydrogels [48]. The Hydrogels used to protect the insulin in the harsh, acidic environment of the stomach before releasing the drug in the small intestine were cross linked copolymers of PMAA with graft chains of polyethylene glycol [P[MAAg- EG]]. The insulin-containing P [MAA-g-EG] micro particles demonstrated strong dose-dependent hypo-glycemic effects in in-vivo oral administration studies using both healthy and diabetic rats. The blood glucose levels in these animals were decreased significantly for at least 8 h due to the absorption of insulin in the GI tract. It is worth noting that these effects were observed without the addition of additives, such as absorption enhancers or protease inhibitors. Due to a lower proteolytic activity in comparison to that in the small intestine, the colonic region has also been considered as a possible absorption site for orally administered peptides and proteins. Several hydrogels are currently being investigated as potential devices for colon-specific drug delivery. These include chemically or physically cross linked polysaccharides, such as dextran, amidated pectin, guar gum and inulin, and cross-linked poly(acrylic acid) .They are designed to be highly swollen or degraded in the presence of colonic enzymes or microflora, providing colon specificity in drug delivery [49].

Rectal delivery

The rectal route has been used to deliver many types of drugs, although patient acceptability is variable due to the discomfort arising from administered dosage forms. Its primary applications have been for local treatment of diseases associated with the rectum, such as haemorrhoids. Additionally, it is well known that drugs absorbed from the lower part of the rectum drain into the systemic circulation directly. Thus, the rectal route is a useful administration route for drugs suffering heavy first-pass metabolism. Conventional suppositories hither to adapt as dosage forms for rectal administration are solids at room temperature, and melt or soften body temperature. A problem associated with rectal administration using conventional suppositories is that drugs diffusing out of the suppositories in an uncontrolled manner are unable to be sufficiently retained at a specific position in the rectum, and sometimes migrate upwards to the colon. This often leads to a variation of the bioavailability of certain drugs, in particular, for drugs that undergo extensive first-pass elimination. In this context, hydrogels may offer a valuable way to overcome the problem in conventional suppositories, provided that they are designed to exhibit a sufficient bio adhesive property following their rectal administration. The increased bioavailability of propranolol subject to extensive first-pass metabolism was observed by adding certain mucoadhesive. Polymeric compounds to poloxamer-based thermally gelling suppositories [50]. Among the mucoadhesive polymeric compounds tested, polycarbophil and sodium alginate provided the largest mucoadhesive force and the smallest intrarectal migration to the suppositories, resulting in the largest bioavailability of propranolol [82.3 and 84.7%, respectively] was investigated the potential application of xyloglucan gels with a thermal gelling property as vehicles for rectal drug delivery. Xyloglucan processed by the researchers has the sol-gel transition temperature of around 22- 278C, and thus, it can be a gel at body temperature; on the other hand, it can be easily administered since it can behave as a liquid at room temperature. In-vivo rectal administration of xyloglucan gels containing indomethacin using rabbits showed a well controlled drug plasma concentration-time profile without reduced bioavailability, when compared to commercial indomethacin suppositories.. Avoiding rectal irritation caused by vehicles is another important issue in rectal drug delivery. Both Xyloglucan, propranolol gels products, described above, revealed no evidence of mucosal irritation after rectal administration. A significantly reduced irritation by rectal hydrogels prepared with water-soluble [51].

Ocular delivery

In ocular drug delivery, many physiological constraints prevent a successful drug delivery to the eye due to its protective mechanisms, such as effective tear drainage, blinking and low permeability of the cornea. Thus, conventional eye drops containing a drug solution tend to be eliminated rapidly from the eye, and the drugs administered exhibit limited absorption, leading to poor ophthalmic bioavailability. Additionally, their short term retention often results in a frequent dosing regimen to achieve the therapeutic efficacy for a sufficiently long

duration. These challenges have motivated researchers to develop drug delivery systems that provide a prolonged ocular residence time of drugs. Certain dosage forms, such as suspensions and ointments, can be retained in the eye, although these sometimes give patients an unpleasant feeling because of the characteristics of solids and semi-solids [52]. Due to their elastic properties, hydrogels can also represent an ocular drainage resistant device. In addition, they may offer better feeling, with less of a gritty sensation to patients. In particular, in-situ forming hydrogels are attractive as an ocular drug delivery system because of their facility in dosing as a liquid, and their long-term retention property as a gel after dosing. Cohen et al. developed an in-situ gelling system of alginate with high guluronic acid contents for the ophthalmic delivery of pilocarpine. This system significantly extended the duration of the pressure-reducing effect of pilocarpine to10 h, compared to 3 h when pilocarpine nitrate was dosed as a solution. Rheological evaluation of Gelritew, deacetylatedgellan gum which gels upon instillation in the eye due to the presence of cations. Their study indicated that a high rate of the sol/gel transition of Gelritew in-situ gels results in long precorneal contact times. Silicone rubber/hydrogel composite ophthalmic inserts, Poly[acrylic acid] or poly [MAA]IPN was grafted on the surface of the inserts to achieve a mucoadhesive property. The ocular retention of IPN grafted inserts was significantly higher with respect to ungrafted ones. An in-vivo study using rabbits showed a prolonged release of oxytetracycline from the inserts for several days [53].

Trans dermal delivery

Budama-Kilinc Y, et.al says A Carbopol 934w-basedformulation containing phosphatidyl choline liposomes [liposome-gel]. In their study, the skin absorption behavior of hydrocortisone –containing liposome- gel was assessed Gayet and Fortier [reported hydrogels obtained from the copolymerization of bovine serum albumin [BSA] and PEG. Due to their high water content over 96%, allowing the release of hydrophilic and hydrophobic drugs, their use as controlled release devices in the field of wound dressing was proposed as the potential application of the BSA-PEG hydrogels. Comprehensive studies on in-situ Photo polymerizable hydrogels made from terminally diacrylated ABA block copolymers of lactic acid oligomers [A]and PEG [B] for barriers and local drug delivery in the control of wound healing have been carried out by Hubbell. Recent research trends in transdermal applications are focusing on electrically assisted delivery, using iontophoresis and electroporation. Several hydrogel-based formulations are being investigated as vehicles for transdermal iontophoresis to obtain the enhanced permeation of luteinizing hormone releasing hormone, sodium nonivamide acetate, nicotine and enoxacin. On the other hand, a methylcellulose-based hydrogel was used as a viscous ultrasonic coupling medium for transdermal sonophoresis assisted with an AC current, resulting in an enhanced permeation of insulin and vasopressin across human skin in vitro [54].

Subcutaneous delivery

As described through Sections hydrogels possess a wide variety of possible pharmaceutical applications. Among them, their substantial application may be found in implantable therapeutics. Subcutaneously inserted exogenous materials may more or less evoke potentially undesirable body responses, such as inflammation, carcinogenicity and immunogenicity. Therefore, biocompatibility is a prerequisite that makes materials implantable. Due to their high water content, hydrogels are generally considered as biocompatible materials. They also provide several promising properties, minimal mechanical irritation upon in-vivo implantation, due to their soft, elastic properties, prevention of protein adsorption and cell adhesion arising from the low interfacial tension between water and hydrogels; broad acceptability for individual drugs with different hydrophilicities and molecular sizes; and unique possibilities (crosslinking density and swelling) to manipulate the release of incorporated drugs. Some of these may offer an advantage for the delivery of certain delicate drugs, such as peptides and proteins [55].

Developed new hydrogels originating from the chemical reticulation of a, b- polyasparthydrazide (PAHy) by glutaraldehyde. PAHy is a new water soluble macromolecule, synthesized from a polysuccinimide by reaction with hydrazine. Histological analysis revealed that this hydrogel was inert when implanted subcutaneously into rats. Several hydrogel formulations for the subcutaneous delivery of anticancer drugs have been also proposed. For example, crosslinked PHEMA with good biocompatibility was applied to cystabine [Ara-C] and methotrexate. Poly [AAm-comon methylormonopropylitaconate] developed by Blanco's group was employed for the controlled release

of Ara-C and 5-fluorouracil. Current studies on implantable hydrogels have been directed towards the development of biodegradable systems requiring no follow-up surgical removal once the drug supply is depleted. A bio erodible hydrogel based on a semi-IPN structure composed of a poly(1-caprolactone) and PEG macromer terminated with acrylate groups was devised by Cho et al.. Long-term constant release over 45 days of clonazepam entrapped in the semi-IPN was achieved in vivo. Recently, two types of novel degradable PEG hydrogels for the controlled release of proteins were developed by Zhao and Harris. One type is prepared by a poly-condensation reaction between difunctional PEG acids and branched PEG polyols. Upon hydrolysis of the resulting ester linkages, these gels degrade into only PEG and PEG derivatives. The other is PEG-based hydrogels having functional groups in which protein drugs can be covalently attached to the gel network via ester linkage. Thus, the release of the protein drugs immobilized would be controlled by the hydrolysis of the ester linkage between the gel and the protein, followed by the diffusion of the protein out of the gel, and by the degradation of the gel. Extensive research efforts on degradable dextran hydrogels have been carried out by Hennink and his co-workers. These hydrogels are based on acrylate derivatives of dextran. In their studies, the application of the hydrogels to the controlled release of protein was thoroughly investigated. Biodegradable cross-linked dextran hydrogels containing PEG [PEG-Dex] were reported by Moriyama and Yui. Insulin release from these hydrogels was regulated by the surface degradation of PEG-Dexmicrodomain- structured [56].

Tissue engineering

The micronized hydrogels [micro gels] have been used to deliver macromolecules like phagosomes into cytoplasm of antigen-presenting cells. There lease is because of acidic conditions. Such hydrogels mould themselves to the pattern of membranes of the tissues and have sufficient mechanical strength. This property of hydrogels is also used in cartilage repairing [57].

Topical drug delivery

Hydrogels have been used to deliver active component like Desonide which is a synthetic corticosteroid usually used as an anti-inflammatory. Instead of conventional creams, the hydrogels have been formulated for better patient compliance. These hydrogels have moisturizing properties therefore scaling and dryness is not expected with this drug delivery system. Antifungal formulations like cotrimazole have been developed as hydrogel formulation for vaginitis. It has shown better absorption than conventional cream formulations [58]**.**

Protein drug delivery

Interleukins which are conventionally given as injection are now given as hydrogels. These hydrogels have shown better patient compliance. The hydrogels form in situ polymeric network and release proteins slowly. These are biodegradable and biocompatible also [59].

CONCLUSION

Hydrogels are cross linked polymer networks that absorb substantial amounts of aqueous solutions. these hydrogel have an ability to imbibe or absorb water content recently various types of hydrogel system have been designed in order to meet different applications by this review it is concluded that hydrogel is a promising drug delivery system for the effective transport of the drugs into the eye for the cure treatment of various kind of eye diseases.

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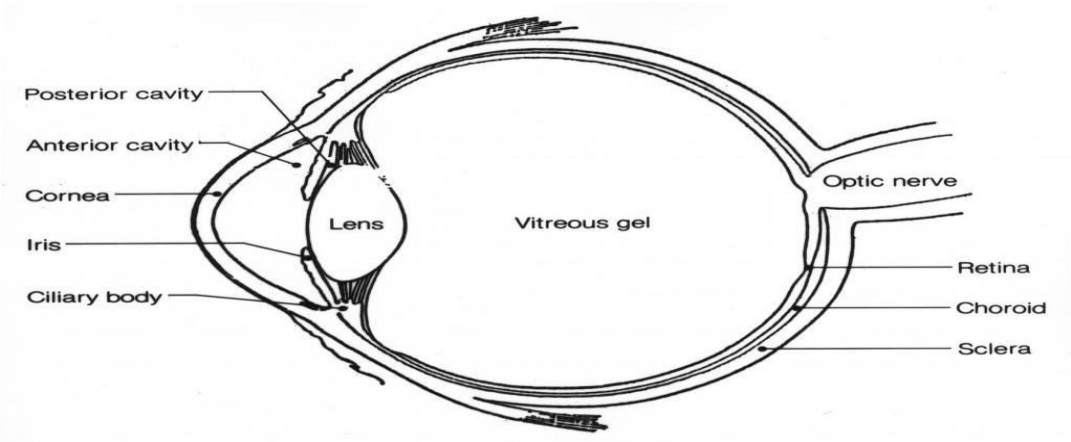

Fig. 1. Anatomy of the Eye

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RESEARCH ARTICLE

Qualitative Phytochemical Screening and Cell-line Study on *Aristolochia indica* Root

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ABSTRACT

Siddha pharmaceutical literatures emphasize the root of *Aristolochia india* should be purified before process as a drug. This concept put forward the researcher to do cell-line study to expedite whether *A.indica* should be used with precaution. The purpose of the research is to find out the antioxidant, reducing power and membrane stabilizing effect of *Aristolochia indica* root. The phytochemical screening chemical test were carried out in root powder extract of *Aristolochia indica* standard procedures to identify the constituents as described by Sofowara (1993),Trease and Evans (1989) and Harbone (1973). The DPPH radical scavenging assay was used to analyze the antioxidant property of aqueous extract of *Aristalochia indica* root powder sample by following Sanchez-Moreno *et al*. (1998) method. The ferric reducing power of extract of *Aristalochia indica* root powder was determined according to the method of Oyaizu (1986). RBC membrane stabilization potential of *Aristalochia indica* root powder extracts were investigated according to the methods proposed by Sakar et al. It is concluded Aristolochia root has toxic effect despite remarkable antioxidant activity and ferric reducing activity. Hence, the root of *A. indica* must be detoxified in a proper way before used in drug formulation.

Keywords: Pharmaceutical, Red blood cell, Phytochemical, *Aristolochia indica*, Antioxidant

INTRODUCTION

Aristolochia indica is one of the plant among five hundred species of the Aristolochaceae family, found in low rocky hill slopes and plains of tropical and sub tropical countries. [1] It is known as Eswaramooli or perumarunthu in

Siddha Medicine. *Aristolochia indica* is a glabrous, shrubby or herbaceous perennial creeper with woody root stock, and long, slender, grooved, glabrous branches. The **leaves** are variable, fiddle shaped to linear with slightly undulate margin. Fruits are six valved dehiscent, ribbed capsule, 1.5 – 2 inches long. Seeds are flat triangular, and winged all around. Root is considerably long, cylindrical. Surface is almost smooth with fine longitudinal wrinkles, and transverse cracks. External surface is light greyish-brown, inner whitish. Odour is camphoraceous [2].

The plant root contains aromatic oil, colouring material, and an alkaloid aristolochine, Aristolochic acid, glycosides, aristolindiguinone, aristololide, 2 hydroxy - 1 - methoxy -4 Halibenzo quinolone – 4 ,5 (6 H) - dione , cephradione aristolactamiia, B –sitosterol – B – D- glucoside aristolactam glycoside 1 stigmastenones 2 and 3 , methylaristolate , iswarol, iswarone and aristolochene and steroids. [3]. Aristolochic acids is a carcinogenic, mutagenic, and nephrotoxic agent which commonly found in the birthwort family of the plants. [4]

Scientific Classification

Kingdom : Plantae – Plants
Subkingdom : Tracheobionta – Vascular plants
Super division : Spermatophyta – Seed plants
Division : Magnoliophyta – Flowering plants
Class : Magnoliopsida – Dicotyledons
Subclass : Magnoliidae
Order : Aristolochiales
Family : Aristolochiaceae – Birthwort family
Genus : *Aristolochia* L. – dutchman's pipe
Species : *Aristolochia indica* – Indian Birthwort [5]

Vernakular Names

Tamil: Adagam, Isuramuli, lyavari, Karudakkodi, Perumaruntu, Perunkilangu, Sarsugadi
Sinhalese: Sapsanda
English: Indian Birthwort, Snake root
Sanskrit: Arkamula, Garuda, Ishvara, Ishvari, Naakuli, Arkmuula Nagadamani
Hindi: Isharmul, Hooka bel
Malayalam: Garudakkoti, Garudakkodi, Karaleyan, Cheriya arayan
Kannada: Isvaberusa, Ishwari Beru, Toppalu,
Telugu: Ishveraveru, Esvaraveru [6]

Organoleptic Character

Suwai(taste) : Bitter
Veeriyam: (Potency): Hot(Ushna)
Vipakam: (transformed state after digestion): Pungent
Gunam: (Character): Lightness (Elaghu), Dry (Ruksham)
Seyal:(Action):Pacifies Kapha, and Vata, De-obstruent, Abortifacient, Emmenagogue, stimulant, Tonic.

Since it is a hot potency herb, subside Vatham (Pain) and Kapham (Mucus), and increases Pitham (Digestion and Metabolism). It has the pharmacological action of digestive, emetic, and purgative, and also gives a feeling of lightness. [7] It shows adverse effect on sperms and fetus. The root bark of the plant are used as antidote for all types of snake poison, spider poison, scorpion stings, etc. The tribal people are using this plant from ancient times to treat cobra poison, and scorpion stings. The root paste is applied to bites of centipedes, and scorpion stings. The purified root is smashed, and placed under the tongue for the neutralization of snake venom. The traditional systems of

medicine that has evolved over the centuries within various communities, are still maintained as a great traditional knowledge base in herbal medicines [8].

Traditionally, this wealth of precious knowledge has been passed through in the form of verse in almost all the traditional system of medicine. In like that, the two main Siddha reputed literatures regarding medicinal plants mentioned, the plant *Aristalochia indica* is effective for swellings due to poison, poisons bites, fever, skin disorders, snake bite, insects bites, hyper tension, Bronchial asthma ,Cough, acute and chronic rheumatism, Indigestion and digestive disorders, Diarrhoea, leocoderma, skin diseases, scabies, Heart disease, Anemia, dropsy [9][10].

The past research findings validate these ancient literatures treatises. The compound isolated from the root of *A.indica* was found to be a potent abortifacient and anti-fertility [11]. Anti- estrogenic and anti- implantation effect also reported for *A.indica* [12]. It is used as an antidote to snake venom [13] *A.indica* root has been confirmed to be effective against snake bite [14]. The plant is used as a decoction for snake bite [15]. Leaf juice of the plant is used for skin disease, scabies and scorpion sting [16]. Anti-inflammatory. Anti-pyretic and analgesic activity against *H.fossilis* venom was reported [17]. Root is beneficial for inflammatory conditions, diarrhea, antispasmodic and asthma.[18] In skin allergies, the paste is applied where as leaf juice is applied to warts also [19]. The plant is used to treat cholera, fever, bowel troubles, ulcers, leprosy, poisonous bites [20]. It is also used as emmenogogue, abortifacient, anti-neoplastic, antiseptic, anti-inflammatory and antibacterial [21]. Root of the species of *Aristolochia* are used as tonic, stimulant and to stops excess menstruation [22].

MATERIALS AND METHODS

Sample Collection and Authentication

The *Aristalochia indica* root (voucher specimen No CARISM/112) sample was collected from Thanjavur and was authenticated by Dr. N. Ravichandran (Botanist), Research officer, Carism, Sastra University, Thanjavur, Tamilnadu, India

Preliminary Phytochemical Screening

The phytochemical screening chemical test were carried out in root powder extract of Aristolochia indica standard procedures to identify the constituents as described by Sofowara (1993)[23], Trease and Evans (1989)[24] and Harbone (1973).[25]

Preparation of Extract

2.5gm of air dried powdered *Aristolochia indica* root digested in alcohol and allowed to stand for 24h.Then filter, filtrate was evaporated to dryness over a water bath. Collected residue screen qualitatively for the presence of following phytochemical constituents as per the standard protocol.

Test for Alkaloids (Dragendroffs Method)

One gram A.indica sample was treated with 2mL of HCl and added 2mL of Drgendroffs reagent, observation noted for red or orange precipitate indicates the presence of alkaloids.

Test for Flavonoid (Shinods method)

One gram of A.indica sample was treated with alcohol and filtered, potassium hydroxide solution 10% were added while yellow colour formation confirms the presence of flavonoids.

Test for Phenol (Ferric chloride test)
One gram of A.indica sample, were added alcohol drops in a scanty amount and $Fecl_3$ solution which turn into bluish green or red denote the availability of phenol.

Test for Carbohydrate (Fehlings Test)
The aqueous solution of A.indica root powder sample was added with Fehlings solution I & Ⅱand heated on boiling water bath for half an hour, brick red appearance precipitate indicates the carbohydrates.

Test for Starch (Iodine test)
One gram of *A.indica* root powder samples was added with iodine and potassium iodide solution. Formation of dark blue colour indicates the presence of starch.

Test for Protein (Biuret Test)
One gram of A.indica sample was treated with 1% solution of copper sulphate followed by 5% solution of sodium hydroxide. Appearance of violet purple colour specify the proteins.

Test for Glycosides (Borntrager"s test)
One gram of A.indica sample was boiled with dilute HCl for two minutes and few dribble solution of $Fecl_3$were added, filtered while hot and cooled. The filtrate was then extracted with benzene and the layer was separated. Equal volume of dilute ammonia solution was added to the benzene extract and shaken well and observed for colour formation.

Test for Sterols (Salkowskis method)
One gram *A.indica* sample was mixed with chloroform; acetic acid and conc.H_2SO_4, formation of blue and green colour specify the availability of sterols.

Test for Terpinoids (Salkowskis method)
One gram of A.indica sample extract was mixed with 2ml of chloroform and 3mL concentrated H_2SO_4 was carefully added to form a layer. A reddish brown colouration of the interface was formed.

Cell-Line Study

Preparation of Extract
Aristalochia indica root powdered sample (10 g) was extracted with 100 ml of solvents (hexane, ethyla acetate, methanol, ethanol and water) and kept for 3 h at room temperature. The extracts were then separated using Whatman No. 1 filter paper and used for further experiments. For antioxidant activity, the solvent was evaporated using a rotovapor (Make: Buchi, Model: R-300) and dry extract was obtained. The extract was then re-dissolved in water at 100 mg / mL ratio and used for the analysis.

Total Phenol Content
The total phenolic content of *Aristalochia indica* root powder extract was estimated according to the method of Singleton et al. (1999).[26] Suitably diluted sample (100 µl) was taken with 250 µl of Folin's-Ciocalteu reagent and 1000 µl of 5% of Na2CO3 was added and incubated for 30 min in dark. Then the absorbance was measured at 720 nm using Spectrophotometer. A calibration curve was prepared using standard gallic acid (16 – 100 mg/L; y = 0.0094x – 0.0585; R2 = 0.9939) and used to calculate the total phenolic content of the extract and the results were expressed as gallic acid equivalents (mg GAE / 100 g sample).

Antioxidant Activity

The DPPH radical scavenging assay was used to analyze the antioxidant property of aqueous extract of *Aristalochia indica* root powder sample by following Sanchez-Moreno *et al*. (1998) method.[27] The extract (100 µl) was added to 0.9 ml of methanolic solution of DPPH (2.5 mg/100 ml) and the reactants were incubated at room temperature for 30 min in dark. Different concentrations of Butylated hydroxyanisol (BHA) were used as a standard and the solvent (distilled water) was used instead of extract in control. After 30 min, the absorbance was measured at 515 nm using a spectrophotometer and the radical scavenging activity of the extract was calculated and expressed on percentage basis.

Ferric Reducing Power

The ferric reducing power of extract of *Aristalochia indica* root powder was determined according to the method of Oyaizu (1986). [28] Samples (2.5 ml) in phosphate buffer (2.5 ml, 0.2 M, pH 6.6) were added to potassium ferricyanide (2.5 ml, 1.0%) and the mixture was incubated at 50°C for 20 min. Trichloroacetic acid (2.5 ml, 10%) was added, and the mixture was centrifuged at 650 x g for 10 min. The supernatant (5.0 ml) was mixed with ferric chloride (5.0 ml, 0.1%), and then the absorbance was read spectrophoto metrically at 700 nm. Based on the absorbency value, the ferric reducing power of extract was expressed.

Membrane Stabilization Potential

RBC membrane stabilization potential of *Aristalochia indica* root powder extracts were investigated according to the methods proposed by Sakar et al. (2010).[29] Human blood (2 mL) was drawn from volunteer in a heparinised tube and centrifuged at 2000 rpm for 10 min. The pellet (RBC cells) was washed twice with PBS (9 ml) and finally the pellet was re-suspended in 10 ml of PBS. The extract (500 µl) were added to 1 PBS, 1 ml of 3% H_2O_2 and incubated for 30 min. In normal control, 1 ml PBS was added instead of extract and in standard group, 1 ml of ascorbic acid was added instead of extract and in negative control only H2O2 was added. After incubation, the contents were centrifuged at 2000 rpm for 10 min and the supernatant was used to measure the absorbance at 520 nm. Based on the absorbance, the percentage of RBC membrane damage and inhibition of membrane damage were calculated.

RESULTS AND DISCUSSION

Plants have primary and secondary metabolites but primary is not essential for sustainability and growth of the plants. The secondary metabolites are synthesized by plants during its development.[30] Preliminary phytochemical investigation, the results was shown in table 1 and it reveals the presence of Carbohydrate, sterol, terpinoids, flavinoids alkaloid and phenol but the same extract shows negative results for Protein, Glycosides and starch. Thus, presence of phenol, Flavinoids, sterol and terpinoids in the *Aristalochia indica* root bark powder might also have therapeutic effect corresponds to stipulated pharmacological action. Specially the phenolic compound is responsible for its remarkable antioxidant activity.

Total Phenolic Content

Aqueous extract of *Aristalochia indica* showed the total phenolic content of 253 mg GAE / 100 g (Figure 2).

Antioxidant Activity

Antioxidant activity of aqueous extract of *A. indica* indicated the remarkable free radical scavenging power (62.19%) at a concentration of 100 mg/ml (Figure 3). However, the antioxidant activity of *A. indica* (IC-50 = 18.75 mg/ml) is lower when compared to the synthetic compounds, gallic acid (IC-50 2.34 mg/ml).

Ferric reducing power of aqueous extract of *A. indica* was analyzed and the results are shown in Figure 4. In this assay, Fe (III) is reduced to Fe (II) by the antioxidant compound through electron transfer. The reduced Fe (II) forms

the Pearl's blue complex, which can be measured at 700 nm. Aqueous extract of *A.indica* exhibited moderate ferric reducing power (58.05%). Conversion of Fe (III) in to Fe (II) form is of great biological significance, because the ferrous form (Fe II) is the only bio-available form and hence, the iron must be converted into ferrous form from ferric state before drug administration.

Membrane Stabilization Potential

RBC used as model cell by a several researchers to the study of interaction of drugs with membrane. [31] Erythrocyte membrane stabilization model has been used to investigate the antioxidant power of aqueous extract of *A.indica*, and the results are given in the Figure 5. In this assay, oxidative stress was induced in RBC cells using H_2O_2 through the production of hydroxyl radicals and the membrane damage was measured calorimetrically and the inhibition capacity of the extracts was determined. But, when we added the aqueous extract of *A.indica*, the extract itself has toxicity and denatured the RBC membrane in the control group. The damage caused by the aqueous extract of *A.indica* was more than the effect of H_2O_2 which was used to damage the RBC membrane and hence the value was negative. Hence, the root of *A. indica* must be detoxified in a proper way before used in drug formulation. The membrane stabilization findings is negative as per Fig 5 indicates the root of *Aristolochia indica* is a toxic part of the plant which was supported by the past research findings. Aristalochic acid is the major active principle responsible for carcino genicity and nephrotoxicity.[32] Species of Aristolochia are known to cause aristolochic acid nephropathy, renal interstitial fibrosis, which is associated with a high incidence of upper urinary tract cancer during chronic use in the treatment of rheumatism as analgesic and diuretic.[33].Geno toxic effect was encountered in cells exposed to Aritolochic acid.[34] The plant *Aristolochia indica* contain some sperm agglutinating compounds contributed to their semen coagulating properties[35] Therefore, Siddha pharmaceutical literatures clearly mentioned it has to be purified before adding as a recipe of a drug.

CONCLUSION

Aqueous extract of *Aristalochia indica* exhibited notable total phenolic content and remarkable antioxidant activity, but it was found to be toxic to RBC cells and produce oxidative stress and thus, induce membrane damage. As mention in Siddha text the purification can overcome the serious safety concerns. If it is purified in proper manner can be beneficial to arthritis, skin disorders, eczema, wounds, gall bladder pain, snake and scorpion bite prevent seizures, increase sexual desire, boost the immune system, and menarche. It is also used to treat snakebite, Intestinal disorders and rheumatism, It is concluded Aristolochia root has toxic effect despite remarkable antioxidant activity and ferric reducing activity. Further traditional medical resources those who prepared drug with *Aristolochia indica* must consider this serious herbal drug hazard impact on patients.

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Table: 1 Preliminary Screening of A.indica root

No	Parameters	Results
1	Alkaloids	+
2	Flavonoids	+
3	Phenol	+
4	Proteins	-
5	Sterols	+
6	Carbohydrates	+
7	Glycosides	-
8	Terpinoids	+
9	Starch	-

Note: Detected (+) Not detected (-)

Figure. 1. ***Aristolochia indica***

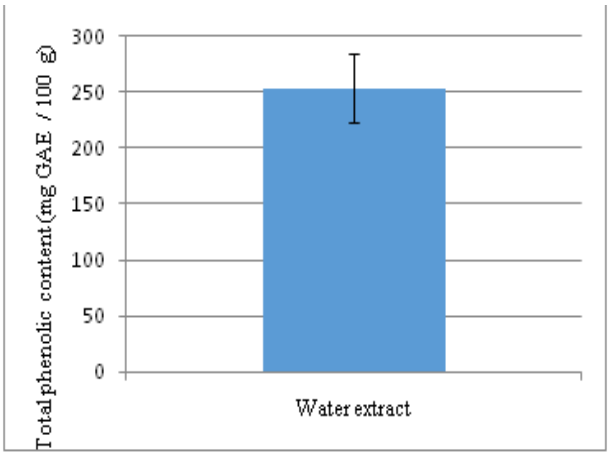

Figure 2. Total phenolic content of aqueous extract of *Aristalochia indica*

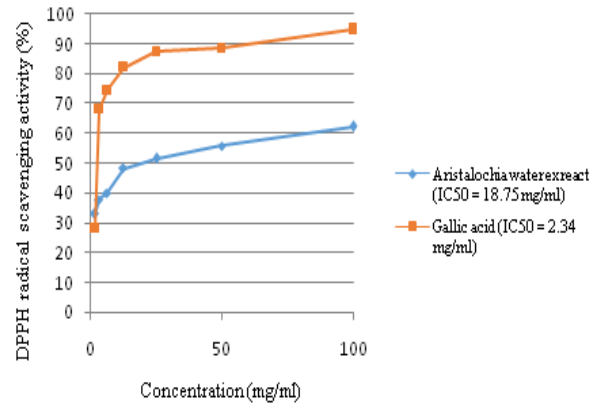

Figure 3. Antioxidant activity of aqueous extract of *Aristalochia indica*

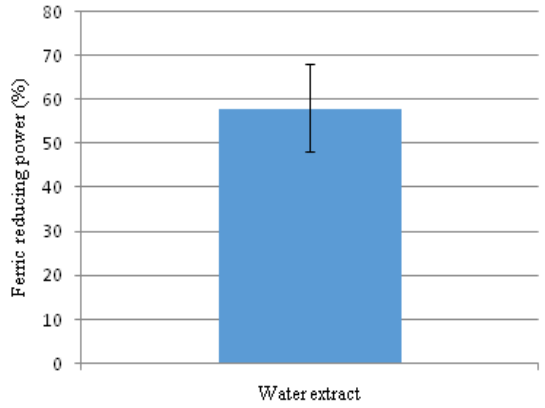

Figure 4. Ferric reducing power of aqueous extract of *Aristalochia indica*

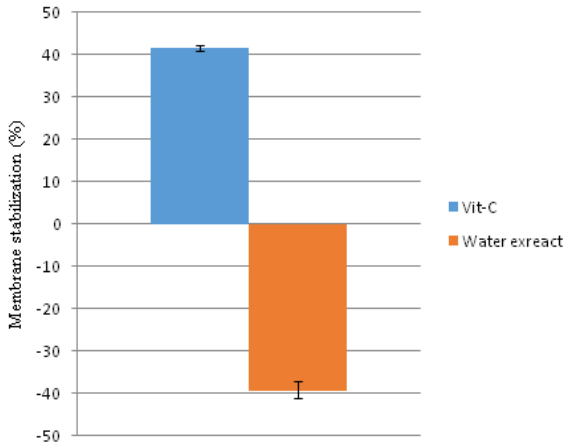

Figure 5. RBC membrane stabilization potential of aqueous extract of *Aristalochia indica*

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RESEARCH ARTICLE

Science Investigatory Projects (SIP) In Schools Division of Siargao

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ABSTRACT

This study aimed to determine the profile and reasons of scarcity of Science Investigatory Projects (SIPs) conducted in the Schools Division of Siargao in the last ten (10) years. The study employed a quanti-qualitative research design. Data were gathered from science teachers using inventory forms and a researcher-made questionnaire for reasons of SIP scarcity. The analysis of data was performed using frequency count and percent, mean and standard deviation, Kruskal-Wallis ANOVA and Dunn Post hoc test with Bonferroni correction, and Friedman Test and Mann-Whitney U Test with Bonferroni Correction. Findings revealed that most of the teacher-respondents are females who are 26-30 years old, and have earned only their Bachelor's degree. They have been in the service for 5 years or less and have not attended a training or seminar relevant to SIP. There are only two SIPs conducted by science teachers and one from the students in the entire Division from 2009-2019. The SIP conducted by the students bagged a 1st prize in the Division level and 3rd prize in the Regional level. They agree that the scarcity of SIP in the Division is due to lack of technical knowledge on SIP, limited time allowance, inadequate logistical support, financial constraints, and anxiety to conduct SIP. The study concluded that those who are at least 31 years old are more affected by financial constraints in conducting SIP than those who are 25 years old or younger. Also, those who have not attended any training or seminar on SIP are more affected by lack of technical knowledge in conducting SIP. Time and financial constraints are topmost reasons of SIP scarcity. Logistical support and technical knowledge are the next concerns while anxiety to conduct SIP is the least of all worries.

Keywords: Science, Investigatory Project, Scarcity, Division of Surigao, Science-Teacher

INTRODUCTION

Science education under K-12 curriculum in the Philippines is adopting new trends of awakening the interest of the students as well as teachers in exploring and discovering something new. One of the trends in science is conducting

an investigatory project or the so-called SIP. This kind of project is an authentic task that science teachers implement in science curriculum (Sanchez,2019). Cuartero (2016) averred that Science teachers are embedded in teaching SIPs to help students understand the problematic issues in the community, be ready on minds-on task through following rigid processes applying scientific method, and have their original work or studies. He added that doing an investigatory project could develop students' interests and process skills like observing, comparing, classifying, measuring, gathering and organizing, predicting, inferring, evaluating, synthesizing, and interpreting data in learning science. And is similarly performing hands-on learning or commonly known as learning by doing. Sanchez and Rosaroso (2019) opined that Science teacher's commitment towards SIP instruction implementation makes them reflective and global teachers. Thus, Science teachers must be strengthened through seminar-workshops and conferences. Further, to motivate the learners and the teachers make quality SIPs, education agencies organize science fairs where competition is exercised (Ndlovu,2019). However, teachers highlight the most common problems in the conduct of SIPs such as lack of computer facilities with internet connection, functional library, and laboratory resources (Sanchez &Rosaroso,2019). Due to limited availability of apparatuses and chemicals, teachers use their own finances, and often go to commercial laboratories for experimentation and analysis. In view of this, the researcher was encouraged to determine the implemented SIPs made by the Junior High School students and Science Teachers in the last ten (10) years from S.Y. 2009-2019 in the Schools Division of Siargao.

Conceptual Framework

This study was anchored on the Republic Act 10533 or commonly known as the Enhanced Basic Education Act of 2013 which is mandated in establishing, maintaining, and supporting a complete, adequate, and integrated system of education relevant to the needs of the people, the country and society-at-large. This means that it is the policy of the state that every graduate of basic education shall be an empowered individual who has learned, through a program that is rooted on sound educational principles and geared towards excellence, the foundations for learning throughout life, the competence to engage in work and be productive, the ability to coexist in fruitful harmony with local and global communities, the capability to engage in autonomous, creative, and critical thinking, and the capacity and willingness to transform others and one's self.

Furthermore, the conduct of the SIPs is the direct application of research in which learners are able to apply and enhance scientific process skills, experience the inquiry approach in learning, and in turn contributing to the national goals towards research and development that serve as the strong backup of the said policy. It was anchored on the concepts that teacher's technical knowledge, skills, and determination are continuing factors to the success of every learner or science enthusiasts. Thus, this study will check the status of SIPs in the Schools Division of Siargao and its association with the profile of the SIP Advisers.

The framework of this study is presented as a research paradigm in Figure 1.The paradigm shows three boxes. First box contains the profile of the respondents in terms of sex, age, highest educational attainment, length of service, and number of trainings or seminars attended relevant to SIP. The second box contains the reasons of SIP scarcity which include technical knowledge, time, teaching support system, financial support, and motivation. These are the dependent variables of the study. The third box indicates the proposed intervention program being formulated that describes the dependent variable of the study.

Statement of the Problem

This study aimed to determine the implemented Science Investigatory Projects (SIPs) in the Schools Division of Siargao in the last ten (10) years.

Specifically, the study sought answers to the following questions:

1. What is the profile of the teacher-respondents as to:
   1.1 Sex,
   1.2 Age,

1.3 District,
1.4 Highest Educational Attainment,
1.5 Years in Service at the time of SIP, and
1.6 Number of SIP trainings/Seminars attended Relevant to SIP?

2. What are the Science Investigatory Projects conducted in the Schools Division of Siargao from 2009-2019?

3. To what extent do the teachers perceive the reasons of scarcity of SIP as to:
   3.1 Technical Knowledge,
   3.2 Time
   3.3 Teaching Support System
   3.4 Financial Support
   3.5 Motivation?

4. Is there a significant difference on the perceived reasons of scarcity of SIP when grouped according to the profile of the teacher-respondents?

5. Is there a significant difference among the perceived reasons of scarcity of SIP?

6. Based from the findings of the study, what intervention program can be proposed?

METHODS

The quantitative research design utilizing a survey method was employed in this study. Since the researcher needs recovery of the SIPs in the Division level, the study was conducted in the Division of Siargao. The respondents of the study were the 40 School Science Coordinators or SIP Advisers and teachers in all public secondary schools in Siargao Division who served as the researcher's direct contact person in gathering the data from 2009 up to present.

The online collaborative platform was utilized in this study. The researcher created an electronic form to be filled in by the School Science Coordinators which can be accessed exclusively through the DepEd e-mail accounts or to be filled in manually especially to those schools without internet connection. Form 1 requires the specifications of the SIPs while Form 2 involves the teacher's profile who conducted SIPs.

A researcher-made questionnaire was also developed to ascertain the profile of the science teachers and the reasons of SIP scarcity. To analyze the data of the study, the Statistical Package for Social Sciences (SPSS), Frequency Count and Percent, Mean and Standard Deviation, Kruskal-Wallis ANOVA and Dunn Test with Bonferroni Correction. Friedman Test and Mann-Whitney U Test with Bonferroni Correction were utilized.

RESULTS AND DISCUSSIONS

On the Profile of Respondents

Table 1 shows the profile of the respondents in terms of sex, age, highest educational attainment, length of service, and number of seminars or trainings attended relevant to SIP. There are 40 Science teachers who responded to the survey on reasons of scarcity of SIP. There are 9 or 22.5% male and 31 or 77.5% are female. They are distributed into four age groups: 8 or 20% are 25 years old and below, 16 or 40% are 26-30 years old, or 22.5% are 1-35 years old, and 7 or 17.5% are 36 years old and above. For their education, there are 19 or 47.5% who only have Bachelor's degree, 17 or 42.5% who have Master's units, and 4 or 10% who have at least Master's degree. There are also 23 or 57.5% of them who have been teaching for 5 years or less, 12 or 30% who have been teaching for 6-10 years, and 5 or 12.5%

have been in the service for at least 11 years. And there are 28 or 70% who have not attended any training or seminar relevant to SIP while 5 or 30% have attended 1-5 seminars or trainings.

On the Conducted Science Investigatory Projects and Achievements

There are only two SIPs conducted by teachers in the entire Division from 2009-2019. One was conducted by a teacher specializing in General Science at Caraga State University on 2016-2018. The other one was conducted by a Biology teacher at Dapa National High School in 2010. Moreover, only one SIP on student category was found. It was an SIP in Physical Science regarding 'Artificial corals made of plastic bottles'. This was conducted in 2016 at Siargao National Science High School by a group of four student-researchers. Such SIP bagged First Prize at the Division level and ranked Third at the Regional level. These results show the scarcity of Science Investigatory Projects in the Division. To have a thorough analysis regarding this scarcity, a follow-up survey was conducted. Results on reasons of scarcity of SIP are shown in the next discussion.

On the Reasons of Scarcity of SIP

The teachers agree that technical knowledge is one of the reasons of the scarcity of SIP. This is based on the average value of 2.81 with a standard deviation of 0.59. It is interesting to note that they agree to all five items ontechnical knowledge as reasons of scarcity of SIP. They got the highest mean value of 2.98 in item 5 "Concepts and skills in SIP making are not well-presented and implemented to science teachers" with a standard deviation of 0.77 while they got the lowest mean value of 2.65 with standard deviation of 0.80 in item 1 "I have no prior knowledge about SIP".
Table 2 shows the extent of reason of scarcity of SIP in terms of technical knowledge.

The results above indicate that the science teachers lack technical expertise in SIP development. This is due to the absence of support system such as lack of trainings or workshop seminars relevant to researches or investigatory projects (Du Plessis, 2017). The inadequate background of researches and knowledge on investigatory projects is one of the contributing factors why science teachers lack technical expertise (Mizzi,2014) in the field of scientific investigations. This will have an impact on the development of the teacher's content knowledge.

Table 3 presents the extent of reason of scarcity of SIP as to time.
Based on the result, the teachers strongly agree that time constraint is one of the reasons why they didn't conduct SIP. This was based on the average value of 3.63 with a standard deviation of 0.51. Specifically, they strongly agree that SIP making demands a lot of time that teachers cannot focus on because they are loaded with paperwork. And this is supported by Vizmanos (2019) that teachers are busy preparing lesson plans and reports that includes paperwork on additional designations.

Such result is based on the highest mean value of 3.78 with a standard deviation of 0.53 in item 3. The mean value of 3.73 with standard deviation of 0.60 in item 5 suggests their strong affirmation that vacant time is not enough to do researches of existing studies. They also strongly agree that not all schools are offering Science Investigatory Project as a subject that burdens the interest of some science teachers to make SIP due to lack of time. This was evident on the mean value of 3.70 with a standard deviation of 0.61 in item 4. On a lighter note, they agree that there is no allocated time intended for SIP development and that there are no weekly assigned teachers for SIP; these are indicated on the obtained mean values of 3.46 and 3.49 on items 1 and 2 respectively.

As revealed by Guzey (2016), science teachers experience various constraints, such as lack of time, equipment, pedagogical content knowledge, and pedagogical skills in implementing investigatory projects. These constraints lead to scarcity of investigatory projects and other scientific researches.
The extent of reason of scarcity of SIP as to teaching support system is shown in the next Table.

Shown in the Table is an average value of 3.25 with a standard deviation of 0.50. This result implies that the teachers agree that the status of teaching support system is also a reason for not conducting SIP. Laboratory is indicated as the

top reason based on the highest mean value of 3.63 with a standard deviation of 0.59 in item 3. Insufficiency of SIP tools and equipment is cited as the next top reason while immediate availability of SIP supplemental materials is third on the list; these are based on the obtained mean values of 3.60 and 3.58 in item 2 and item 1 respectively. Item 5 "The administrator does not regularly monitor and evaluate teacher's performance on SIP" got the lowest mean value of 2.68 with a standard deviation of 0.73 which is described as 'agree'.

The result is supported by Hamidu (2014) that due to lack of materials and equipment to carry out practical work or research studies, science teachers do not usually find it convenient to make laboratory work the center of their instruction or in the process of making SIPs. The absence of the support system (Du Plessis, 2017) such as lack of teacher trainings relevant to SIP making is another reason of scarcity of SIP most specifically in remote areas. In order to increase the quality of SIPs, better laboratory equipment and facilities and trainings are needed.

The extent that financial support is a reason in scarcity of SIP is shown in the next Table. The average value of 3.60 with a standard deviation of 0.64 suggests that the teachers strongly agree that SIP scarcity is also attributed to financial support. They strongly observed that there is no specific program created by the LGU to support the teachers in conducting SIP financially and that SIP making requires laboratory test or analysis of the variable that science teachers cannot afford to pay for the laboratory fees; these are based on the mean values of 3.70 for both items 3 and 5 respectively. They also strongly agree that there is no allocated budget for SIP; this is based on the mean value of 3.60 with a standard deviation of 0.71 in item 1.

At a lower degree of confirmation, they agree that teachers do not have financial capacity to fund their SIP's and school cannot afford to buy materials intended for SIP. These are based on the obtained mean value of 3.49 for both items 2 and 4 respectively.

This may be due to constraints facing of the implemented curriculum such as lack of funds (Brawner,2011). And schools are also affected by lack of funding as well as for the science teachers doing researches. Most of the science teachers revealed that they use their own money for laboratory testing and analysis due to lack of school funding (Jugar,2013).
Table 6 exhibits the extent of reason of scarcity of SIP as to motivation

It can be gleaned that an average value of 2.63 with a standard deviation of 0.53 is obtained. This implies that the teachers agree that lack of motivation is one of the reasons in not conducting SIP's. They indicated that they are anxious thinking about SIP due to lack of experience and lack of encouragement from colleagues. These are based on the obtained mean value of 2.97 with SD=0.77 in item 4 and mean value of 2.78 with SD=0.73 in item 5 respectively. However, they disagree that they are not interested in exploring SIP, their school administrator does not support them in making SIP, and no rewards given to those who conduct SIP. These are based on the obtained mean values of 2.49, 2.40, and 2.48 in items 1, 2 and 3 respectively.

McFarlane (2014) averred that limited knowledge can negatively impact in the SIP instruction. Teachers must be encouraged to attend seminar workshops relevant to SIP making. However, other science teachers are not motivated to attempt SIP making due to lack of encouragement from co-teachers (David,2019) because of the so-called promotion where other teachers start to exhibit attitude and motivation problems. Another reason is lack of support from administrators (Brawner,2011). This may be due to school funding.

On the Difference on Reasons of Scarcity of SIP

Table 7 shows the difference on extent of reasons of scarcity of SIP when grouped by profile.
The Table shows that there is no significant difference on the extent of reasons of SIP when grouped according to sex, highest educational attainment, and length of service. This is due to the p-values obtained which are greater than 0.05 when the extent of reasons on scarcity of SIP across five variables are compared with respect to these above-

mentioned profile factors. Similar results are obtained when extent of reasons on scarcity of SIP as to technical knowledge, time, teaching support system and motivation were grouped according to age. Also, there is no significant difference on the extent of reasons of scarcity of SIP as to time, teaching support system, financial support, and motivation when grouped according to the number of seminars or trainings attended relevant to SIP.

However, an H-value of 16.09 with p=0.001 was obtained when the extent of reasons of scarcity of SIP as to financial support were grouped according to age. Since this value is less than 0.05, the null hypothesis is rejected. Similarly, an H-value of 6.87 with p=0.01 was obtained when the extents of reasons of scarcity of SIP as to technical knowledge were grouped according to number of seminars or trainings attended relevant to SIP. These imply that the extent to which financial support is a reason of scarcity SIP significantly differ between teachers who belong to different age group; also the extent to which technical knowledge is a reason of scarcity of SIP significantly differ between teachers who have not attended seminars or trainings and those who attended 1-5 seminars or trainings relevant to SIP.

Since there are more than two age groups, a Post hoc test using Dunn Test with Bonferroni Correction was conducted for pair wise comparisons. Results showed that the extent to which financial support is a reason of scarcity of SIP among those who are 25 years old and below or less than 26 years old (<26) obtained p-values (Sig.) less than 0.05 like 0.044 with those who are 26-30, 0.006 with those who are 36 and above or older than 35 years old (>35), and 0.000 with those who are 31-35. Also, those who are 26-30 years old have p-value of 0.018 with those who are 31-35. The null hypotheses for these p-values are less than 0.05 but these must be confirmed with Bonferroni Correction or adjusted significance (Adj. Sig.) before rejecting the null hypothesis. Based on adjusted significance, only those who are 25 years old and below or less than 26 years old (<26) got 0.037 with those who are 36 years old and above or older than 35 (>35) and 0.001 with those who are 31-35 years old. Since these adjusted significance values are less than 0.05, then the null hypotheses are rejected. This implies that the extent to which financial support is a reason of scarcity of SIP between these paired age groups significantly differ.

To specifically gauge which group has higher extent of reasons as to financial support by age and technical knowledge by number of seminars or trainings attended relevant to SIP, the mean ranks of the groups are compared as shown in Table 8.

For the difference on extent to which financial support is a reason of scarcity of SIP, those who are 25 years old and below or younger than 26 years old (<26) obtained a mean rank of 9.69 which is less than the mean ranks of those who are 31-35 years old at 29.50 and of those who are 36 and above or older than 35 years old (>35) at 24.79. These results imply that those who are 31 years old or older are more affected by lack of financial support as a reason of scarcity of SIP than those who are 25 years old or younger. Likewise, those who have not attended seminars or trainings relevant to SIP have higher mean rank at 23.64 than those who attended SIP trainings or seminars at 13.17. These imply that those who have not attended seminars or trainings are more affected by lack of technical knowledge as a reason of SIP scarcity than those who have attended at least one training or seminar.
Table 9 shows the difference among the extent of reasons of scarcity of SIP.

Table 9 shows that a Chi-squared value (χ^2) of 80.29 and p=1.51E-16 were obtained when the extents that technical knowledge, time, teaching support system, financial support, and motivation are reasons of SIP scarcity are compared. Since the p-values is less than 0.05, the null hypothesis is rejected. This entails that there is a significant difference on the extent that these five variables are reasons of SIP scarcity. To gauge if which among these variables significantly differ with each other, a post hoc test through Mann-Whitney U test with Bonferroni Correction was performed for. Based on adjusted significance (Adj. Sig.), the extent that motivation is a reason of SIP scarcity got values less than 0.05 when compared with teaching support system, financial support, and time; the obtained adjusted significance values are 0.002, 0.000, and 0.000 respectively. Likewise, the extent that technical knowledge is a reason of SIP scarcity got adjusted significance values which are less than 0.05 when compared with financial support and time. Also, the extent that teaching support system is a reason of SIP scarcity also got adjusted

significance value of 0.033 when compared with extent that time is a reason of SIP scarcity. Since these mentioned adjusted significance or adjusted p-values are less than 0.05, then null hypotheses are rejected. These imply that there is a significant difference on the extents that these paired variables are reasons of SIP scarcity.

Moreover, the mean rank of technical knowledge which is 2.21 is less than the mean rank of financial support at 4.01 and the mean rank of time at 4.06; these imply that technical knowledge is lesser compared to financial support and time as reasons of SIP scarcity. Also, between teaching support and time, teaching support has a mean rank of 3.03 which is less than the mean rank of time at 4.06; this implies that teaching support is lesser than time as a reason of SIP scarcity. All these results imply that time and financial support are the top reasons of SIP scarcity. This is followed by teaching support system, then technical knowledge. Motivation is the least reason of SIP scarcity. As cited in the article of SEI-DOST & UP NISMED(2011) entitled 'Framework for Philippine Science Teacher Education', shortage of qualified science teachers, lack of quality textbooks, inadequate laboratory equipment and facilities, large classes, lack of support from administrators, and lack of funds are some of the constraints faced in the science education in Philippine schools. Thus, framework for science teacher education should pay attention to problems encountered that will address ways to improve SIP instruction and raise teachers training on quality researches.

Proposed Intervention Program to Increase the Number of Science Investigatory Projects (SIP)in Schools Division of Siargao.

Based on the finding and recommendations, a proposed intervention program to give solutions on the scarcity of Science Investigatory Projects in Schools Division of Siargao is herein presented.

Proposed Intervention Program

Rationale

Teachers' expertise in conducting Science Investigatory Projects (SIP) is one of the common problems in Schools Division of Siargao. Most of the teachers often find it difficult to start working a science investigatory projects even in school level. Such occurrence presents financial support, inadequate laboratory equipment and lack of trainings relevant to SIP making. As cited by Dr. Brawner, the Director of Science Education Institute, that shortage of qualified science teachers, lack of quality textbooks, inadequate equipment especially equipment intended for SIPs, large classes, and lack of support from administrators are some of the constraints in the field of science education in the Philippines. And this is really the real concern of other Science Teachers most specifically teachers assigned in remote areas. Thus, the researcher had in mind that the results of the study may serve as basis in developing intervention program that could somehow increase the number of Science Investigatory Projects made by the Science teachers and students in the Schools Division of Siargao. Result of the study revealed that there is scarcity of Science Investigatory Projects (SIPs) in Schools Division of Siargao as to the aspects of technical knowledge on SIP, limited time allowance, teaching support system, and financial support.

Program Objectives

The proposed intervention program is aimed to:

1. Provide a basis that may help the Science Educational Leaders in strengthening Science Program in conducting Science Investigatory Projects (SIP).
2. Serve as a framework for the School Administrators to enhance the skills of teachers and even students in making SIP.
3. Provide solutions to increase the number of quality Science Investigatory Projects made by the teachers and students in the Schools Division of Siargao.

Proposed Intervention Program to Increase the Number of Science Investigatory Projects in Schools Division of Siargao:

Key Activity Matrix - S.Y.2020-2021

Findings

Based on the results of the study, it was found that: Most of the teacher-respondents are females who are 26-30 years old, and have earned only their Bachelor's degree. They have been in the service for 5 years or less and have not attended a training or seminar relevant to SIP. There are only two SIPs conducted by science teachers and one from the students in the entire Division from 2009-2019. The SIP conducted by the students bagged a 1st prize in the Division level and 3rd prize in the Regional level. They agree that technical knowledge, teaching support system, financial support, and motivation are reasons of SIP scarcity. They also strongly agree that time is a reason of SIP scarcity. There is a significant difference on the extent that financial support is a reason of SIP scarcity when grouped according to age. There is also a significant difference on the extent that technical knowledge is a reason of SIP scarcity. There is a significant difference among the reasons of SIP scarcity.

CONCLUSION

Based on the findings of the study, the following conclusions were drawn:

1. The science teaching force of the Division are young professionals who are yet to proceed with their higher professional development and gain more experiences in the field;
2. There are very few SIP's conducted by science teachers and students in the division;
3. The scarcity of SIP in the Division is due to lack of technical knowledge on SIP, limited time allowance, inadequate logistical support, financial constraints, and anxiety to conduct SIP;
4. Those who are at least 31 years old are more affected by financial constraints in conducting SIP than those who are 25 years old or younger. Also, those who have not attended any training or seminar on SIP are more affected by lack of technical knowledge in conducting SIP; and
5. Time and financial constraints are topmost reasons of SIP scarcity. Logistical support and technical knowledge are the next concerns while anxiety to conduct SIP is the least of all worries.

Recommendations

Based on the conclusions of the study, the following recommendations were offered:

1. Educational leaders are encouraged to provide intervention programs to the science teachers to address professional development and the time, financial, and technical constraints in conducting SIP.
2. Public school administrators are encouraged to motivate the science teachers in pursuing graduate studies, motivate them to conduct SIP's, provide them the necessary logistics they need in conducting SIP, and work hand-in-hand with the higher authorities in conducting interventions to teachers. They are also encouraged to promote the culture of research through SIP in their schools.
3. Science teachers are encouraged to pursue graduate studies and attend seminars and trainings relevant to science teaching and SIP for professional development. They need to coordinate with their heads in enabling a culture of research through SIP development in the school.
4. Students are encouraged to cooperate with their science teachers in conducting SIP's and join in competitions.
5. For future researchers, inventory of SIP's in other Divisions is encouraged.

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Table 1. Profile of Respondents

Profile		f(n=40)	Percent
Sex	Male	9	22.5
	Female	31	77.5
Age	25 and below	8	20
	26-30	16	40
	31-35	9	22.5
	36 and above	7	17.5
Highest Educational Attainment	Bachelor's Degree	19	47.5
	With Master's Units	17	42.5
	Master's Degree or Higher	4	10
Length of Service	5 years and below	23	57.5
	6-10 years	12	30
	At least 11 years	5	12.5
Number of Trainings/ Seminars Attended Relevant to SIP	None	28	70
	1-5	12	30

Table 2.Extent of Reason of Scarcity of SIP as to Technical Knowledge

Statement	Mean	SD	Description
1.I have no prior knowledge about SIP	2.65	0.80	Agree
2.I do not have actual experiences in making SIPs	2.83	0.75	Agree
3.There are no SIP trainings implemented	2.68	0.76	Agree
4. Most of the science teachers are not expert in the field of SIP making.	2.93	0.69	Agree
5. Concepts and skills in SIP making are not well-presented and implemented to science teachers.	2.98	0.77	Agree
Average	**2.81**	**0.59**	**Agree**

Table 3. Extent of Reason of Scarcity of SIP as to Time

Statement	Mean	SD	Description
1.There is no allocated time intended for SIPs	3.43	0.71	Agree
2. There are no specified science teachers assigned for SIP per week.	3.49	0.64	Agree
3. SIP making demands a lot of time that teachers cannot focus on because they are loaded with paperwork.	3.78	0.53	Strongly Agree
4. Not all schools offering Science Investigatory Project as a subject that burdens the interest of some science teachers to make SIP due to lack of time.	3.70	0.61	Strongly Agree
5. Vacant time is not enough to do researches of existing studies through online.	3.73	0.60	Strongly Agree
Average	**3.63**	**0.51**	**Strongly Agree**

Table 4. Extent of Reason of Scarcity of SIP as to Teaching Support System

Statement	Mean	SD	Description
1. Supplemental materials for SIP are not readily available anytime.	3.58	0.68	Strongly Agree
2. Tools and equipment used for making SIPs are insufficient.	3.60	0.59	Strongly Agree
3. There is no enough laboratory for the SIP making.	3.63	0.59	Strongly Agree
4. The school administrator does not ensure availability of resources to facilitate the conduct of SIP.	2.78	0.80	Agree
5. The administrator does not regularly monitor and evaluate teacher's performance on SIP.	2.68	0.73	Agree
Average	**3.25**	**0.50**	**Agree**

Table 6. Extent of Reason of Scarcity of SIP as to Motivation

Statement	Mean	SD	Description
1.I have no interest in exploring SIP making.	2.49	0.93	Disagree
2.The school administrator does not support science teacher in making SIP.	2.40	0.74	Disagree
3.There are no rewards given to science teachers who conducted SIP.	2.48	0.72	Disagree
4.I am anxious thinking about SIP as I am not used to it.	2.98	0.77	Agree
5.Collegues do not encourage others to conduct SIP.	2.78	0.73	Agree
Average	**2.63**	**0.53**	**Agree**

Table 7. Difference on Extent of Reasons of Scarcity of SIP when Grouped by Profile

Profile	Reason	H	P	Decision
Sex	Technical Knowledge	1.13	0.29	Not Rejected
	Time	2.34	0.13	Not Rejected
	Teaching Support System	0.64	0.42	Not Rejected
	Financial Support	1.29	0.26	Not Rejected
	Motivation	0.33	0.56	Not Rejected
Age	Technical Knowledge	7.37	0.06	Not Rejected
	Time	7.59	0.055	Not Rejected
	Teaching Support System	6.70	0.08	Not Rejected
	Financial Support	16.09	0.001	Rejected
	Motivation	6.13	0.11	Not Rejected
Highest Educational Attainment	Technical Knowledge	3.14	0.21	Not Rejected
	Time	0.06	0.97	Not Rejected
	Teaching Support System	1.93	0.38	Not Rejected
	Financial Support	0.29	0.86	Not Rejected
	Motivation	5.71	0.057	Not Rejected
Length of Service	Technical Knowledge	2.20	0.33	Not Rejected
	Time	2.72	0.26	Not Rejected
	Teaching Support System	0.20	0.91	Not Rejected
	Financial Support	2.04	0.36	Not Rejected
	Motivation	0.26	0.88	Not Rejected
Number of Seminars or Trainings Attended Relevant to SIP	Technical Knowledge	6.87	0.01	Rejected
	Time	2.12	0.15	Not Rejected
	Teaching Support System	0.41	0.52	Not Rejected
	Financial Support	0.88	0.35	Not Rejected
	Motivation	0.66	0.42	Not Rejected

Table 8. **Mean Ranks on Extent of Reasons of Scarcity of SIP**

Reason	Profile		Mean Rank
Financial Support	Age	25 and below	9.69
		31-35	29.50
		36 and above	24.79
Technical Knowledge	Number of Seminars or Trainings	None	23.64
		1-5	13.17

Table 9. **Difference among Extent of Reasons of Scarcity of SIP**

χ^2	P	Decision
80.29	1.51E-16	Rejected

Proposed Intervention Program to Increase the Number of Science Investigatory Projects in Schools Division of Siargao:

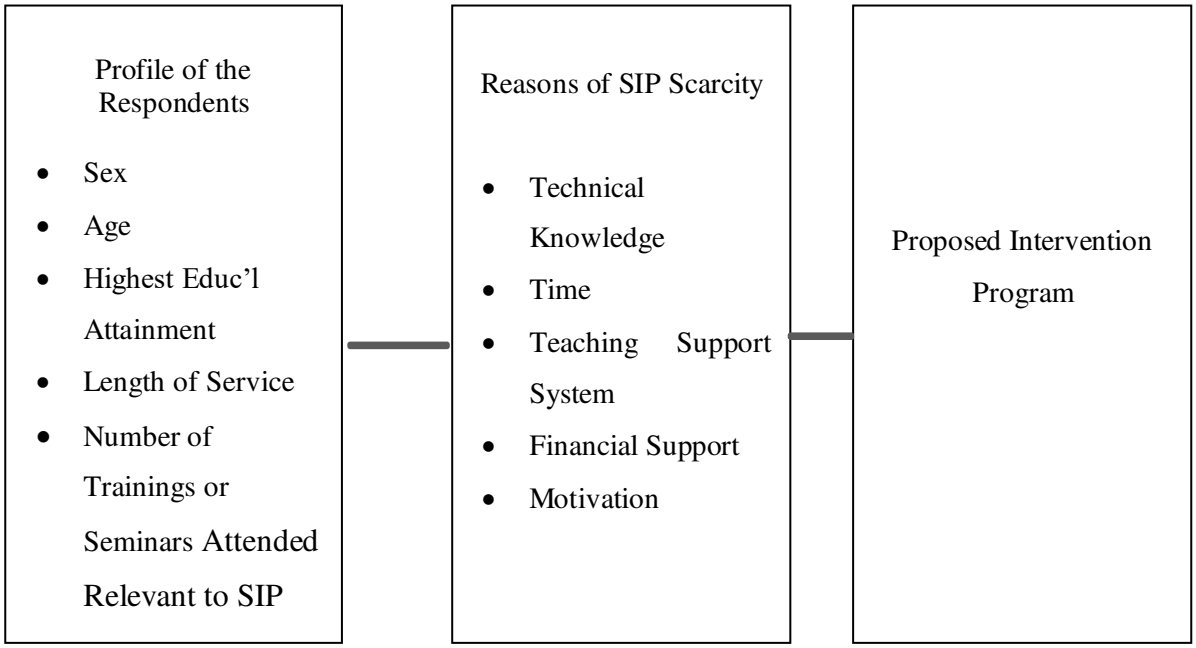
Key Activity Matrix - S.Y.2020-2021

Objectives	Strategies/Activities	Time Frame	Venue	Budget/ Resources Needed	Persons Involved	Expected Output
To train the participants' in writing research skills needed in SIP and challenge them to create SIP proposal	Five (5)-day seminar-workshop in conducting Science Investigatory Project (SIP)	May-June 2021	Division-based	Registration &Transportation costs	Science Education Program Supervisor, School Heads, Teachers	Quality Science Investigatory Project Proposal (Teachers Category)
To enhance the participants skills in applying the scientific method in creating a problem, formulating the hypothesis, testing the hypothesis through proper experimentation, data gathering and drawing conclusion needed in SIP	Four (4)-day seminar-workshop in conducting Science Investigatory Project (SIP)	July-August 2021	School based and District based	Training Materials	Science Education Program Supervisor School Heads, School Science Coordinators, Science Teachers, Students	Quality Science Investigatory Project Proposal (Teachers and Students Category)
To conduct and accommodate investigatory projects with the ultimate aim of empowering young scientist for development	Five (5)-day seminar workshop on the processes of SIP making and proper use of the laboratory apparatuses	August-September 2021	School based and District based	Transportation and Resources costs	Science Education Program Supervisor School Heads, School Science Coordinators, Science Teachers, Students	Quality Science Investigatory Projects ready for Science fair (Students Category)
To develop teaching strategies during laboratory sessions	Classroom Observation	Year-round	School based	Resources costs	Science Education Program Supervisor School Heads,	Increased sensitivity to the teaching and learning environment in the laboratory

To monitor the exposure of the students during their laboratory experiments	Classroom Observation	Year-round	School based	Resources costs	Science Education Program Supervisor School Heads,	Identified the aims of the laboratory learning experiences of the students
To enhance students' performance in research through SIP	Classroom Observation	Year-round	School based	Resources costs	Science Education Program Supervisor School Heads,	Developed Academic Performance in Science through SIP

To enhance the participants skills in applying the scientific method in creating a problem, formulating the hypothesis, testing the hypothesis through proper experimentation, data gathering and drawing conclusion needed in SIP	Four (4)-day seminar-workshop in conducting Science Investigatory Project (SIP)	July-August 2021	School based and District based	Training Materials	Science Education Program Supervisor School Heads, School Science Coordinators, Science Teachers, Students	Quality Science Investigatory Project Proposal (Teachers and Students Category)
To conduct and accommodate investigatory projects with the ultimate aim of empowering young scientist for development	Five (5)-day seminar workshop on the processes of SIP making and proper use of the laboratory apparatuses	August-September 2021	School based and District based	Transportation and Resources costs	Science Education Program Supervisor School Heads, School Science Coordinators, Science Teachers, Students	Quality Science Investigatory Projects ready for Science fair (Students Category)

To develop teaching strategies during laboratory sessions	Classroom Observation	Year-round	School based	Resources costs	Science Education Program Supervisor School Heads,	Increased sensitivity to the teaching and learning environment in the laboratory
To monitor the exposure of the students during their laboratory experiments	Classroom Observation	Year-round	School based	Resources costs	Science Education Program Supervisor School Heads,	Identified the aims of the laboratory learning experiences of the students
To enhance students' performance in research through SIP	Classroom Observation	Year-round	School based	Resources costs	Science Education Program Supervisor School Heads,	Developed Academic Performance in Science through SIP



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RESEARCH ARTICLE

Morphological Characteristics of Seeds of Some Medicinal Plants Used for Treatment of Gastrointestinal Disorders

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ABSTRACT

Present observation has been carried out on the detailed morphological characters of seeds of some plants medicinal used for treatment of gastrointestinal disorders. The analyzed characters in which the study was based on are: shape, color, size (length, width), solidity, brightness, surface, weight per 100 seeds, Appendages. As a result of the study, the shape of seeds is showed a large variation among the investigated species. The shape of seeds is showed a large variation among the investigated species. Most of seeds have oval to oblong shape (*Zea mays* L., *Eleusine coracana* (L.), *Raphanus sativus* L., *Sesamum indicum* L.) and others are Spherical to oval (*Plantago ovata* Forssk., *Cuperus rotundus* L., *Peganum harmal*a L.) , Linear (*Cuminum cyminum* L.) or Rectangular in shape (*Trigonella tibetana* (Alef.)). The color varies from brown to brown dark (*Cuminum cyminum* L., *Plantago ovata* Forssk., *Raphanus sativus* L.), yellow (*Zea mays* L.), black dark (*Allium cepa* L., *Nigella sativa* L.), creamy to yellow (*Lupinusalbus* L.), grayish-green to grayish-yellow (*Eleusine coracana* (L.)), brown (*Cuperus rotundus* L.) and white (*Sesamum indicum* L.). Seeds dimensions vary greatly among the examined species, the largest seeds in *Cuperus rotundus* L. have a length of 12.62±0.48 mm and width of 08.60±0.50 mm and the smallest seeds measure 01.35±0.11 mm, 01.02±0.13 mm in *Plantago ovata* Forssk.The surface shape is smooth in the most of species. Highest weight was observed with seeds of *Cuperus rotundus* L. (3017.75±119.29 mg), while lowest weight was found in seeds of *Plantago ovata* Forssk. (99.75±1.09 mg). The information presented here on various macro-morphological features of seed can serve as a base for the identification of medicinal plants used for treatment of gastrointestinal disorders.

Keywords: Morphological characters, Plants medicinal, Seeds, Gastrointestinal disorders.

INTRODUCTION

Nature is always a golden sign to show the prominent phenomena of coexistence. Natural products from plants, animals and minerals are the basis for treating human diseases [1]. Medicinal plants are used for personal health-care and environmental landscaping. They include annual and perennial species and may be cultivated or occur in the wild. It is important to note that some medicinal plants are rare and limited in their geographical range; if they are not managed appropriately; their existence may be threatened [2]. Medicinal plants are already known as a natural source of a range of bioactive compounds. Therefore, the researchers today are emphasizing on evaluation and characterization of various plants and plant constituents against a number of diseases based on their traditional claims [3]. Undoubtedly, identifying is the first step to consume medicinal plants and one way to protect the perceived loss of cultural heritage is to document it. Knowledge regarding the plant types and discussion over their recognition and preservation are the most important fundamentals in field, and they should be handed down to the next generations [4].

Gastrointestinal disorders are ailments affecting the functions of the digestive tract, i.e., food and liquid absorption, digestion, or excretion [5]. Such disorders are caused by infections by various kinds of bacteria, viruses, and parasitic organisms). Common gastrointestinal disorders are stomach/abdominal pain, diarrhea, dysentery, gastroenteritis, constipation, vomiting, etc. [6]. These disorders cause morbidity and can lead to mortality, especially in the developing world where sanitation is deficient [7]. Seed structure has been used in the understanding of many natural groups of angiosperms. For example, they are significant for the systematics of some legume seeds [8] and for the tribe Hyoscyameae of the Solanaceae [9]. A wider study on the systematic value of seed surface ornamentation and epidermal tissue in general showed the importance of the shape of individual cells [10].The cells are only slightly influenced by environmental conditions, and therefore present helpful characters in the understanding of phylogenetic relationships [11].For identification of medicinal plants many authors consider only leaves of the plants, because leaves are of two dimensional nature and are available at all the time. But less research is done in identification of medicinal plants using flower and fruits/seeds because they are three-dimensional in nature and available only in specific seasons [12]. This paper will give brief review about seeds of medicinal plants identification using different morphological characteristics. Since seed morphology is a heritable trait, the knowledge of seed morphology is an important tool for seed identification for various purposes. The information presented here on various macro-morphological features of seed can serve as a base for the identification of medicinal plant used for treatment of gastrointestinal disorders.

MATERIALS AND METHODS

Plant Material

The dry cleaned physiologically mature seeds of various medicinal species were taken from traditional medical practitioners, herbalist, hawkers in traditional medicines and rural dwellers in the region of Setifian high plateau which situated in the north east of Algeria between the two longitude 5°and 6°and between the two latitudes 35°. 40 and 36°.35.We put the seed in paper bags to keep it dry and to avoid humidity and climatic factors which lead to germinating these seeds; they were kept in normal condition of laboratory.

Seed morphology

The morphological characteristics in which the study was based on were used by different researchers for example the characteristics like size, weight ,color and shape were used as suggested by various workers such as [13,14,15,16,17]. The seed dimensions were taken using Digital Caliper (0-150 mm range) of Fisher Scientific make. The dimensions were taken at the point of maximum length / width / thickness in five replicates of randomly selected seeds and average of same is reported in results while seed color is based on visual examination. Surface pattern or spermoderm pattern of the seeds were studied at 40 x magnification using

hand held Digital Microscope (LER 4416) and digital photographs were taken. Statistically mean values with standard deviations of each species was computed using the SPSS Software package 2003 version-13.0.

RESULTS AND DISCUSSION

Morphological characteristics

In order to identify the different morphological characteristics of seeds species of plants medicinal used for treatment of gastrointestinal disorders, we found that the single character is not enough to distinguish the species because the seeds of more than one species possess same mean value however their standard deviations vary. But the consideration of these characteristics collectively was found unique in this study. The identifying characters described and used in this publication are found only on the external surface of the seeds. Their usefulness for identification varies. Characters of major importance are color, size and shape of the seed [14, 18]. Other characters used in conjunction with these features have limited use. Based on light microscopy observations, the examined species showed variation in qualitative and quantitative seed characteristics. Seeds of plants medicinal included in this study are represented in photos (Photo1 to Photo 08).

Seeds shape

The shape of seeds is showed a large variation among the investigated species. Most of seeds have oval to oblong shape (*Zea mays* L.,*Eleusine coracana* (L.), *Raphanus sativus* L., *Sesamum indicum* L.) and others are Spherical to oval (*Plantago ovata* Forssk., *Cuperus rotundus* L., *Peganum harmala* L.) ,Linear (*Cuminum cyminum* L.) or Rectangular in shape (*Trigonella tibetana* (Alef.)) (Table 1). The seed shape as observed in the present study seems to be diagnostic at the generic level. The data of seed shape is compatible with that mentioned before by Gunes [19].

Seeds color

The color of seeds is of high diagnostic and systematic interest among species. The color varies from brown to brown dark (*Cuminum cyminum* L., *Plantago ovata* Forssk., *Raphanus sativus* L.),yellow (*Zea mays* L.), black dark (*Allium cepa* L.,*Nigella sativa* L.),creamy to yellow(*Lupinus albus* L.), grayish-green to grayish-yellow (*Eleusine coracana* (L.)),brown (*Cuperus rotundus* L.) and white (*Sesamum indicum* L.).The seed color is diagnostic at the generic and specific level for some extent. The data of seed color is compatible with that mentioned before by Cappers and Bekker [20].

Seeds dimensions

Seeds dimensions vary greatly among the examined species, the largest seeds in *Cuperus rotundus* L. have a length of 12.62±0.48mm and width of 08.60±0.50mm and the smallestseedsmeasure01.35±0.11 mm, 01.02±0.13mm in *Plantago ovata* Forssk., while the rest of the studied species have seeds their dimensions from02.17±0.08mm, 01.52±0.29mm to 08.90±0.27mm, 05.70±0.32mm (see Table 2 and Table 3).

Seeds surface

The character of Seeds surface texture can be of considerable diagnostic and systematic value. The surface shape is Smooth in the most of species as *Zea mays* L., *Trigonella tibetana* (Alef), *Lupinus albus* L., *Eleusine coracana* (L.), *Plantago ovata* Forssk., *Raphanus sativus* L., *Sesamum indicum* L. and rough in some species as *Cuperus rotundus* L. and *Nigella sativa* L.. This is in accordance with the work of Rajani and Veena [12].

Seeds Solidity, brightness and Appendages

Table 2 showed that seeds of medicinal plants are rigged in most of species such as *Zea mays* L. *Allium cepa* L., *Trigonella tibetana* (Alef), *Lupinus albus* L., *Eleusine coracana* (L.), *Plantago ovata* Forssk., *Cuperus rotundus* L., *Raphanus sativus* L. and *Nigella sativa* L. While in *Cuminum cyminum* L.and *Sesamum indicum* L. seeds are fragile. Seeds are bright in *Zea mays* L. *Allium cepa* L., *Trigonella tibetana* (Alef), *Lupinusalbus* L., *Eleusine coracana* (L.), *Plantago ovata*

Forssk., *Raphanus sativus* L., and *Nigella sativa* L. and Pale in *Cuminum cyminum* L. and *Cuperus rotundus* L. Seeds can have a short beak in *Cuminum cyminum* L., *Eleusine coracana* (L.), and *Sesamum indicum* L.

Weight per 100 seeds (mg)

Average weight of 100 seeds of species was taken, results are given in table 2. Highest weight was observed with seeds of *Cuperus rotundus* L. (3017.75±119.29mg), while lowest weight was found in seeds of *Plantago ovata* Forssk. (99.75±1.09mg). To sum up, the study shows that seed morphology is an important tool use for the identification and classification of medicinal plants. Variation in seed characters, such as the size (length, width) the shape, the surface sculpturing pattern and the weight, appears to be of high importance value in distinguishing the species of different family [21,22]. However, in some cases, seed morphological characters are useful for distinguishing the studied closely similar species, which are in the same family [23, 24].

CONCLUSION

Previous studies on seed morphology indicate that seed characters are important for the taxonomy of the species. Our study also confirms their importance; it shows that seed features, such as ornamentations of the seed surface, seed shape and color, are useful characters for identification of medicinal plants species. The examined seeds are variable in both shape and size. The size of the smallest seed is about 1 mm in length (*Plantago ovata* Forssk.) and the size of the largest seed is about 13 mm in length (*Cuperus rotundus* L.). Most of the examined seeds are Oval to oblong (*Zea mays* L., *Eleusine coracana* (L.), *Raphanus sativus* L., *Sesamum indicum* L. from brown to brown dark *(Cuminum cyminum* L., *Plantago ovata* Forssk., *Raphanus sativus* L.), yellow *(Zea mays L.),* black dark *(Allium cepa*L., *Nigella sativa* L.), creamy to yellow *(Lupinus albus L.),* grayish-green to grayish-yellow(*Eleusine coracana* (L.)), brown (*Cuperus rotundus L.)* and white (*Sesamum indicum* L.).The information presented here on various macro-morphological features of seeds can serve as a base for the identification of medicinal plant used for treatment of gastrointestinal disorders.

CONFLICT OF INTEREST

We declare that we have no conflict of interest

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Table 1: Morphological characteristics of medicinal plants seeds (Shape, Color and Size)

Name of species	Family	Medicinal use	Shape	Color	Size(mm)
Cuminum cyminum L.	Apiaceae	antispasmodic carminative digestive and stimulant	Linear	Brown to brown dark	04.37±0.63 01.15±0.18
Zea mays L.	Poaceae	Against diarrhea	Oval to oblong	Yellow	08.90±0.27 05.70±0.32
Allium cepa L.	Liliaceae	Against	Reniform	Black dark	02.35±0.21

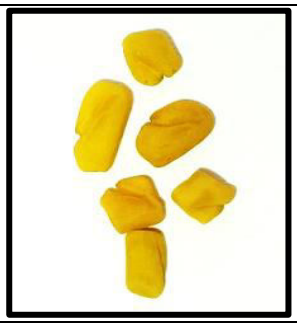
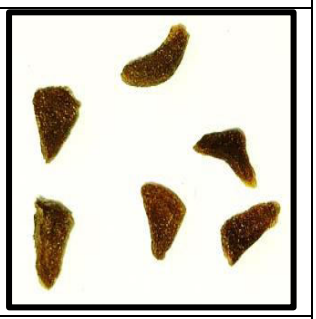
		indigestion			01.27±0.15
Trigonella tibetana (Alef.)	Fabaceae	Carminative	Rectangular	Yellow to brown	03.37±0.78 02.40±0.31
Lupinus albus L.	Fabaceae	Against indigestion	Squarer	Creamy to yellow	07.50±1.20 07.12±1.14
Eleusine coracana (L.)	Poaceae	Antispasmodic	Oval	Grayish-green to grayish-yellow	02.77±0.26 01.30±0.16
Plantago ovate Forssk.	Plantaginaceae	Laxative	Spherical to oval	Brown to brown dark	01.35±0.11 01.02±0.13
Cuperus rotundus L.	Cyperaceae	Against indigestion	Spherical to oval	Brown	12.62±0.48 08.60±0.50
Raphanus sativus L.	Brassicaceae	indigestion	Oval to oblong	Brown to brown dark	02.40±0.27 01.52±0.29
Nigella sativa L.	Rununculaceae	antispasmodic carminative digestive and stimulant	Oval	Black dark	02.17±0.08 00.92±0.11
Sesamum indicum L.	Pedaliaceae)	Laxative	Oval to oblong	White	03.25±0.29 01.07±0.11
Peganum harmala L.	Zygophyllaceae	Against diarrhea	Spherical to oval	Brown dark	03.12±0.04 00.97±0.08

(±SD): Standard deviation

Table 2: Morphological characteristics of medicinal plants seeds (Surface, Solidity, brightness and Weight per 100 seeds (mg)).

Name of species	Surface	Solidity	brightness	Appendages	Weight per 100 seeds (mg)
Cuminum cyminum L.	Rough, distinctly reticulated	Fragile	Pale	Short beak	297.25±04.32
Zea mays L.	Smooth	Rigged	Bright	None	1525.20±36.20
Allium cepa L.	Rough	Rigged	Bright	None	272.75±42.22
Trigonella tibetana (Alef.)	Smooth	Rigged	Bright	None	120.25±07.08
Lupinus albus L.	Smooth	Rigged	Bright	None	3017.75±119.29
Eleusine coracana (L.)	Smooth	Rigged	Bright	Short beak	107.25±9.15
Plantago ovate Forssk.	Smooth	Rigged	Bright	None	99.75±1.09
Cuperus rotundus L.	Rough, distinctly reticulated	Rigged	Pale	None	3982.5±189.92
Raphanus sativus L.	Smooth	Rigged	Bright	None	894.25±8.87
Nigella sativa L.	Rough	Rigged	Bright	None	268.5±39.61
Sesamum indicum L.	Smooth	Fragile	Bright	Short beak	296.25±4.02
Peganum harmala L.	Rough	Rigged	Bright	None	389.75±8.13

(±SD): Standard deviation

			
Photo 1: Seeds of *Eleusine coracana* (L.)	**Photo 2: Seeds of *Trigonellati betana* (Alef.)**	**Photo 3: Seeds of *Plantago ovata* Forssk.**	**Photo 4: Seeds of *Allium cepa*L.**
			
Photo 5: Seeds of *Lupinusalbus* L.	**Photo 6: Seeds of *Cuminum cyminum* L.**	**Photo 7: Seeds of *Zea mays* L.**	**Photo 8: Seeds of *Peganumharmala* L.**

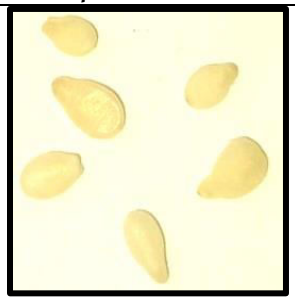



Photo 9: Seeds of *Sesamum indicum* L.	**Photo 10: Seeds of *Nigella sativa* L.**	**Photo 11: Seeds of *Raphanus sativus* L.**	**Photo 12: Seeds of *Cuperus rotundus* L.**

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RESEARCH ARTICLE

Pharmacokinetic Modification of Fast Dissolving Tablets of Irbesartan

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ABSTRACT

The main aim of the present work is to develop and evaluate the Fast Dissolving Tablets of Irbesartan to improve its bioavailability, reduce the dose and frequency of drug administration. Tablet are the most popular among all dosage forms existing today because of its convenience of self administration, dysphasia in case of geriatric patients, the under develop muscular and nervous system in young and in case of uncooperative patients, the problem of swallowing is common phenomenon which leads to poor patient compliance. Irbesartan is used in the treatment of hypertension and to help protect the kidneys from damage due to diabetes. To overcome these drawback, fast dissolving/disintegrating tablets (FDDTs) has emerged as alternative oral dosage forms. An ideal fast dissolving tablets should require no water for oral administration, yet dissolve/disperse/disintegrate in mouth in a matter of seconds. The various technologies adopted to prepare mouth-dissolving tablets are Disintegrant Addition, Freeze drying / lyophillization, Moulding, Sublimation, Spray drying, Mass extrusion, Direct compression. Formulating FDTs Irbesartan by using superdisintegrants as croscarmellose sodium and Sodium Starch Glycolate. To prevent these difficulties during administration, there is need to develop rapidly disintegrating dosage form, which disintegrate and / or disperse in saliva without need of water.

Keywords: Irbesartan, Fast Dissolving Tablets, Direct compression technique.

INTRODUCTION

Tablets are solid preparations each containing a single dose of one or more active ingredients and are obtained by compressing uniform volumes of particles. The objective of the design and manufacture of the compressed tablet is

to deliver orally the correct amount of drug in the desired location and to have its chemical integrity protected to the point. Tablets may vary in size, shape, weight, hardness, thickness, and disintegration characteristics and in other aspects, depending upon the intended use of the tablets and their method of manufacture.

Types of tablets

1. Tablets ingested orally. e.g. standard compressed tablets, enteric coated tablets, delayed release tablets and mouth dissolving tablets
2. Tablets used in the oral cavity. e.g. buccal and sublingual tablets,
3. Tablets used to prepare solution. e.g. effervescent tablets
4. Tablets administered through other routes. e.g. vaginal tablets and implants.

Difficulties with existing oral dosage form

- Patient may suffer from tremors therefore they have difficulty to take powder and liquids .In dysphasia physical obstacles and adherence to an esophagus may cause gastrointestinal ulceration.
- Swallowing of solid dosage form like tablet and capsules may produce difficulty for young adult of incomplete development of muscular and nervous system and elderly patients suffer from dysphasia.
- Liquid medicaments (suspension and emulsion) are packed in multidose container; therefore achievement of uniformity in the content of each dose may be difficult.
- Buccal and sublingual formation may cause irritation to oral mucosa, so patients refused to use such medications.
- Cost of products is main factor as parenteral formulations are most costly and discomfort [1].

Fast Dissolving Tablets

A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue. Tablet are the most popular among all dosage forms existing today because of its convenience of self administration, dysphasia in case of geriatric patients, the under develop muscular and nervous system in young and in case of uncooperative patients, the problem of swallowing is common phenomenon which leads to poor patient compliance. To overcome these drawback, fast dissolving/disintegrating tablets (FDDTs) has emerged as alternative oral dosage forms. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds. According to europian pharmacopoeia, the FDTs should disperse/disintegrate in less than three minutes. The basic approach used in development of FDDTS is the use of Super disintegrants like cross linked carboxymethylcellulose (croscarmilose), sodium starch Glycolate (primogel, Explotab). Polyvinylpyrrolidone (polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. The bioavailability of some drug may be increased due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pas down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets [2]. Researchers have formulated FDTs for various categories of drugs, which are used for therapy in which rapid peak plasma concentration is required to achieve desired pharmacological response. These include nuroleptics, cardiovascular agents, analgesics antiallergics, and drugs for erectile dysfunction [3,4-7].

Technologies for preparing mouth dissolving tablets

The various technologies adopted to prepare mouth-dissolving tablets are:

- Disintegrant Addition
- Freeze drying / lyophillization.
- Moulding.
- Sublimation.
- Spray drying.
- Mass extrusion.
- Direct compression.

Disintegrant Addition [7]

Disintegrant addition technique is one popular techniques for formulating Fast-dissolving tablets because of its easy implementation and cost-effectiveness. The basic principle involved in formulating Fast-dissolving tablets by disintegrant addition technique is addition of superdisintegrants in optimum concentration so as to achieve rapid disintegration along with the good mouth feel. Microcrystalline cellulose and low substituted hydroxypropylcellulose were used as disintegrating agents in the range of 8.2 – 9.1 to prepare fast dissolving tablet. Agar powder is used as disintegrant for the development of fast disintegration tablets by enhancing the porosity of agar by water treatment fast disintegrating tablets of bitter drugs oxybutynin & pirenzepine were prepared by using the taste masked granules and mixture of excipients consisting of crystalline cellulose (Avicel pH 02) and low-substituted hydroxypropy cellulose HPC, LH-11), Ishikawa et al. prepared rapidly disintegrating tablets using microcrystalline cellulose (Avicel pH-M series) that was spherical and had a very small particle size 7-32 μm). instead of conventional microcrystalline cellulose (pH 102). Tablets prepared using microcrystalline cellulose; pH-M06 and L-HPC in the ratio of 9:1 were very rapidly disintegrating) in saliva. They concluded that Avicel pH-M06 was superior to Avicel pH 102 in terms of the feeling of roughness in the mouth. Fast dissolving table of efavirenz (anti HIV agent) were formulated by using combination of microcrystalline cellulose and sodium starch glycolate as super disintegrant.

Gillis et al, prepared a fast-dissolving tablet of galanthamine hydrobromide which comprises of spray dried mixture of lactose monohydrate and microcrystalline cellulose (75:25) as a diluent, a cross linked polymeric disintegrant such as cross povidone and with a direct compression process of preparing such fast-dissolving tablets. Fast-dissolving tablets having analgesic activity was formulated using a combination of superdisintegrants. Rapid oral disintegration tablets were developed by direct compression using co-ground mixture of D-mannitol and crospovidone. CIMA labs patented Orasolv technology by employing the evolution of carbon dioxide or the effervescence as disintegration mechanism in the formulation of fast-dissolving tablets. The OraSolv technology is an oral dosage form, which combines taste-masked drug ingredients with a quick dissolving effervescent excipient system. Taste masking is achieved through a process of microencapsulation, which coats or entraps the active compound in an immediate release matrix. The effervescent excipient system aids in rapid disintegration of the tablet, permitting swallowing of pharmaceutical ingredients before they come in contact with the taste bud. The OraSolv tablet dissolves quickly without chewing or without water and allows for effective taste masking of a wide variety of active drug ingredients, both prescription and non-prescription. Flashtab technology™ is a patented technology of Prographarm, which employ combination of taste-masked multiparticulate active drug substances, a disintegrating agent, a swelling agent and other excipients to form a multiparticulate tablet that disintegrates rapidly. Rapidly disintegrating multiparticulate tablet was prepared by using taste-masked microcrystals of drugs, crosslinked disintegrating agent and soluble diluent with binding properties.

Freeze drying / Lyophillization [8-10]

Freeze-drying or lyophilization has been in existence since the early 1900s. Freeze drying or lyophilization process is one of the first generation techniques of preparing mouth dissolving tablets, in which water sublimes from the product after freezing. This technique creates an amorphous porous structure that can dissolve rapidly. The ideal drug characteristics for this process are relative water insolubility with fine particle size and good aqueous stability in suspension. The drug is entrapped in water soluble matrix which is freeze dried to produce a unit which rapidly disperses when placed in mouth.

Advantages

- Pharmaceutical substance can be processed at non elevated temperature, thereby eliminating adverse thermal effects.
- The tablets made by this process dissolved within seconds after placement on the tongue.

Disadvantages

- High cost of the equipment and processing.

- Lack of resistance, which make the use of conventional packing difficult and poor stability during storage under stressful condition.

Moulding [9]
This type of tablets are prepared by using different moulding techniques

Compression Moulding: The powder mixture previously moistened with a solvent like ethanol/water is compressed into mould plates to form a wetted mass.

Heat Moulding: The moulded forms can be obtained directly from a molten matrix in which the dispersed/ dissolved.

No Vacuum Lyophilization: In this process at standard pressure the solvent from a drug solution or suspension is evaporated. Tablets produced by moulding are solid dispersion .It dissolves in molten/wetted mass. The drug can exist as discrete or micro particles dispersed in the molten matrix.

Advantages
The tablets prepared by moulding offer more rapid disintegration and improved taste.

Disadvantages
- Lack mechanical strength.
- Disintegration property is uncomparable with freeze-dried products.

Sublimation [10]
The slow dissolution of the compressed tablet containing even highly water-soluble ingredients is due to the low porosity of the tablets. Inert solid ingredients that volatilize readily (e.g. urea, ammonium carbonate, ammonium bicarbonate, hexa methelene tetramine, camphor etc.) were added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. Additionally, several solvents (e.g. cyclohexane, benzene) can be also used as pore forming agents.

Spray drying: Spray drying technique produces highly porous and fine powders. The processing solvent is evaporated rapidly by spray drying, which renders the product highly porous and thus can be used in manufacturing fast disintegrating tablets.

Mass extrusion: This technique includes softening of the active blend using solvent mixture of water soluble poly ethylene glycol, using methanol and expulsion of softened mass through extruder or syringe to get a cylinder of the product into segments using heated blade to form tablets. The dried cylinder can also be used to coat granules having bitter taste for taste masking.

Direct compression: The term direct compression is used to define the process by which tablets are compressed directly for powder blend of active ingredients and suitable excipients, which will flow uniformity in the die cavity and forms a firm compact [11-14].

MATERIALS AND METHODS

Materials
Active Pharmaceutical Ingredient (Irbesartan) was received as a gift sample from Arabindho Pharmaceutical Private Limited, Hyderabad, India. Lactose Monohydrates, Microcrystalline Cellulose (MCC Ph103), Croscarmellose

Sodium, Sodium Starch Glycolate, Aspartame, Magnesium Stearate, Talc were used as chemicals and reagents. All reagents and solvents used were of analytical grade.

Methods

Manufacturing method of fast dissolving Tablets [15-17]

Direct Compression Technique

- Weigh the ingredients accurately as given in the table.
- Shift the drug, Crosspovidone, Sodium starch glycolate, through sieve no 60 and mix them for 5min in a poly bag.
- Pass talc and magnesium stearate through sieve no 60.
- Powder blend is lubricated with talc and magnesium stearate and blend it for 20min. it is ready for compression.
- The blend is compressed using multiple tolling twenty station single rotary with single puch (8mm), on labpress machine to produce round shaped tablets. Weighing 200mg each. The compression force is adjusted to obtain tablets with hardness 3-5kg/cm^2.

Solubility studies [15-17]

Organic solubility of Irbesartan as a function of pH was determined in different physiological media. Solubility of drug was studied at different organic solvent like Ethanol, Acetonitrile and Methanol.
The results were shown in table. 2

UV spectrophotometric Analysis

Drug was dissolved in 10 ml of Acetonitrile & Phosphate Buffer pH7.4. Stirred for 15mm, sonicated and filtered through membrane filter paper. Samples were taken from stock solution and serial dilutions were made and UV absorbance was analyzed for λ max.
The results were shown in Fig. 2 & 3

Infra-red sepectrophotometric analysis

The pellets were made by mixing 1gm of drug and 100gm of dried potassium bromide powder. Mixture was then compressed under 10-ton pressure in a hydraulic press to form a transparent pellet. The thin pellet was put on pellet disc to get IR spectra.

Preformulation Studies [15-17]

The preformulation studies include physicochemical characterization of the drug and excipients which are useful in formulating the dosage form.

Organoleptic characters

This includes analysis of color, odour and taste of the drug, record of color is very useful is establishing appropriate of batches.

Density

Powder flow, compressibility, dissolution and other properties may dependent on density.

Bulk density

Bulk density of the granules was calculated using following formula
Bulk density = weight of powder / volume of powder.
The results were shown in table. 3

Tapped Density

Tapped density is determined by placing a graduated cylinder containing same mass of powder used for B.D on a mechanical tapper apparatus which is operated for a fixed number of taps (approx x 500) until powder bed volume has reached a minimum

$$\text{Tapped density} = \frac{\text{weight of powder}}{\text{min volume of powder}}$$

The results were shown in table. 3

Angle of repose

Angle of repose in the tan inverse of angle between height (h) of pile of powder and the radius of the base of conical pile.

The results were shown in table. 3

Evaluation of FDT's tablets of Irbesartan

In process parameters evaluation [18-22]

Hardness Test: The hardness of tablets for fast dissolving tablets is usually kept low for easy disintegration in the mouth. The hardness was measured using shulinger hardness tester

The results were shown in table. 4

Thickness: The thickness of tablets was determined using a Vernier callipers. six tablets from each batch were used and average values were calculated.

The results were shown in table. 4

Friability test: The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%) ten tablets were initially weighed and revolved at 25 rpm for 4 min.

The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated.

The % friability was then calculated by,

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

Acceptance criteria for % friability, % weight loss should be less than 1%

The results were shown in table. 4

Weight Variation Test: Twenty tablets were selected randomly from each batch and weighed individually on electronic balance. The individual tablet is weighed and then compared with average weight for the weight variations.

The results were shown in table. 4

Finished product parameter

Disintegration time Testing: It was determined using tablet disintegration test apparatus, using 900 ml of distilled water without disk at room temperature. Test was performed on 6 tablets. Limit set for the disintegration: not more than 30 seconds.

The results were shown in table. 4

Wetting time of Tablet [18-22]

Wicking time gives the idea on porosity, compressibility as well as absorption capacity of the tablets. Since the dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for the evaluation of tablets.

The results were shown in table. 4

Water absorption ratio [18-22]

Test was done with the same procedure as that of wetting time. In this test, initial weight of tablet was taken before placing on petridish. After complete, wetting, the wetter tablet was then weighed water absorption ratio, R was determined using the equation,

$R=100\ (w_b - w_a)/w_a$

Where w_a is weight of tablet before water absorption w_b is weight of tablet after water absorption.

The results were shown in table. 4

***In-vitro* dispersion time [18-22]**

For determination of *in vitro* dispersion time, one tablet was placed in a beaker containing 10ml of Phosphate Buffer pH7.4 at 37oc ± 5oc and the time required for complete dispersion was determined. The test was repeated on three other tablets of same batch, the average gives *in vitro* dispersion time.

The results are shown in Table. 4

***In-vitro* Drug release study [16, 17]**

The release rate of drug from FDT was determined using USP dissolution testing apparatus. (II paddle method).

The dissolution medium was maintained at 37^0c +0.5^0c the rotation speed was 50 rpm. The sample solutions was measured at 224 nm using a UV – visible double beam spectrophotometer. Cumulative percentage drug release was calculated using linear equation obtained from a standard curve.

The results were shown Fig. 4

Stability Studies [23-26]

The purpose of stability testing is to predict the quality of drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage condition, retest periods and shelf – lives. In the present work, stability study was carried out for the optimized formulation at 40^oc/75% RM for 1 month. After time period of every month sample was collected and analysis is carried out for *In vitro* Drug release study, % Assay and Physical parameters.

RESULTS AND DISCUSSION

Solubility Studies of Irbesartan in Various Media

Solubility studies were performed in distilled water, Ethanol, Methanol, Acetonitrile, Phosphate Buffer pH 7.4phosphate buffer by shaking flask method.

From standard calibration curve of Irbesartan in Acetonitrile & Phosphate Buffer pH7.4 dissolution media, it was observed that the drug obeys Beer-Lamberts law in concentration range of i.e. 01 to 10 µg/ml.

Infra-red sepectrophotometric analysis

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. The samples were taken for FT-IR study.

Preformulation studies

The preformulation studies include physicochemical characterization of the drug and excipients which are useful in formulating the dosage form.

The physical parameters of drug as well as excipients concluded that these were considerably good to formulate the Fast Dissolving Tablets using direct compression technique.

Evaluation of FDT's tablets of Irbesartan

Evaluation parameters of tablets mentioned in the pharmacopoeia need to be assessed, but some, which require special concern or need to be modified, are discussed here.

The tablets were compressed at the average weight of 200mg. The maximum weight variation of the tablets was 199.7 to 203.4 %. Hardness for tablets of all batches was in the range of 3.37 to 3.67 kg/cm². The thickness of the tablets of all the batches was found in the range of 3.25 to 3.36 mm. The friability of the tablets of all batches was found in the range of 0.31 to 0.28 %. All the parameters are indicated that the, physical parameters of formulated tablets were within the Pharmacopeial specifications.

***In-vitro* Dissolution Studies**

Stability studies

Stability study was carried out for the optimized formulation at 40°c/75% RM for 1 month. After time period of every month sample was collected and analysis is carried out for *In vitro* Drug release study, % Assay and Physical parameters.

CONCLUSION

The focus of present investigation is to minimize disintegration time and improved drug release with fast onset of action. Tablets were formulated by using two different superdisintegration such as crosspovidone, sodium starch glycolate at different concentrations 5% and 7% along with micro crystalline cellulose. Various parameters like disintegration time, *in vitro* drug release studies and stability parameters were evaluated. The presence of superdisintegrants helps to complete release of the drug in short time and the effect of superdisintegrants on tablet properties were studied. The result of all the formulations for weight variation , friability, hardness and assay were found to be within the standard pharmacopoeial limits, the formulations F5 contain 5% w/w of sodium starch glycolate, 5% w/w of crosspovidone, was found to be promising and has show an *in vitro* dispersion time of 5sec and disintegration time of 12seconds, wetting time of 6sec,water absorption ratio of 87.83% and cumulative drug release of 99.87% drug with 45min when compare with marketed tablet it shows 58.99% within 45min. The formulation F5 showed fast drug release when compared to a commercial conventional tablet of irbesartan. The stability study performed as per ICH guidelines. The optimized formulation F5 wrapped in aluminium foils and kept in petridish at (40°C+2°c/75% RH +5%) in humidity chamber. The stability study was conducted after 30th day. Formulation F5 was selected as per it content uniformity, disintegration time, wetting time, hardness test and *in vitro* drug release study. The formulation (F5) showed no significant variant in all parameters which was stable for a period of 30 days. Hence, finally it was concluded that the prepared fast dissolving tablet of irbesartan may proved to be potential candidate for effective fast disintegrating tablet dosage form.

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Table 1: Composition of Fast dissolving tablets

Ingredients (mg)	F1	F2	F3	F4	F5
Irbesartan	50	50	50	50	50
Lactose Monohydrates	60	60	60	60	60
Microcrystalline Cellulose (MCC Ph103)	75	72.5	75	72.5	70
Croscarmellose Sodium	5	7.5	-	-	5
Sodium Starch Glycolate	-	-	5	7.5	5
Aspartame	6	6	6	6	6
Magnesium Stearate	2	2	2	2	2
Talc	2	2	2	2	2
Total Tablet Weight	200mg				

Table 2: Solubility Studies of Irbesartan in Various Media

Media	Solubility (mg/mL)
Water	0.0098 (98µg/mL)
Ethanol	0.0128
Methanol	0.0143
Acetonitrile	0.0162
Phosphate Buffer pH 7.4	0.0282

Table 3: Physical characteristics of Irbesartan granules

Formulation Code	F1	F2	F3	F4	F5
Bulk Density (g/ml)*	0.252	0.248	0.247	0.221	0.242
Tapped Density (g/ml) *	0.335	0.321	0.309	0.328	0.325
Carr's Index %	24.77	24.62	24.71	24.06	24.07
Hausner Ratio	1.32	1.30	1.28	1.30	1.28
Angle of Repose (θ)	25º.41′	25º.31′	25º.01′	25º.21′	24º.41′

*Mean±SD, (n=6)

Table 4: Physical Characteristics of FDT'S of Irbesartan

S. No	SPECIFICATION	F1	F2	F3	F4	F5
1.	Weight Variation (mg) **	202.7±0.08	200.9±1.25	203.4±1.18	201.8±1.17	199.7±1.25
2.	Hardness (kg/cm2) *	3.45±0.21	3.51±0.20	3.45±0.14	3.37±0.13	3.67±0.12
3.	Thickness(mm) *	3.23±0.04	3.34±0.04	3.25±0.05	3.28±0.05	3.36±0.04
4.	Friability (%) *	0.29%	0.28%	0.31%	0.28%	0.31%
5.	Disintegration Time (sec) *	18	16	21	20	12
6.	Wetting Time (sec) *	11	9	17	14	6
7.	Dispersion Time (sec)*	7	6	11	8	5
8.	Assay (%) **	98.5	98.7	98.1	98.3	99.1
9.	Water absorbance ratio (%) *	75.30	77.92	65.72	68.96	87.83

*Mean±SD, (n=6) **Mean±SD, (n=20)

Table 5: Stability Parameters of Optimized Formulation F5

Parameters	1st Month	
	RT	40°C/75%RH
Weight variation test**	199.7±1.25	199.21±1.25
Thickness*	3.67±0.12	3.45±0.12
Hardness*	3.36±0.04	3.28±0.03
Friability*	0.31%	0.30%
Disintegration Time (sec) *	12	11
Wetting Time (sec) *	6	6
Dispersion Time (sec)*	5	5
Assay (%) **	99.1	99.0
Water absorbance ratio (%) *	87.83	87.33
% of Drug Release *	99.87	99.17

*Mean±SD, (n=6) & **Mean±SD, (n=20)

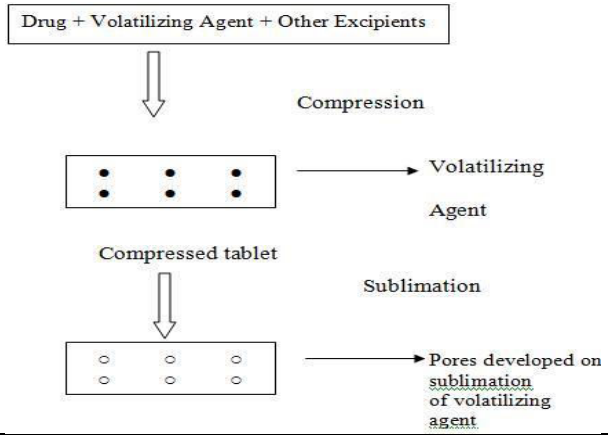

Fig. 1: Steps Involved in sublimation

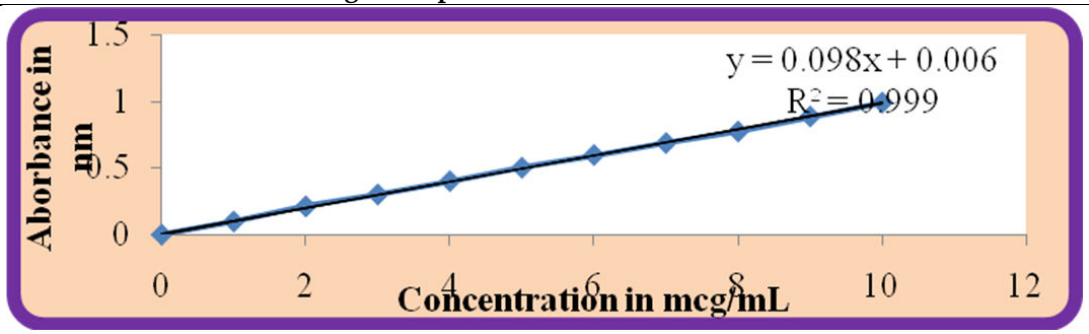

Fig. 2: Absorbance of Irbesartan in Acetonitrile λmax 224

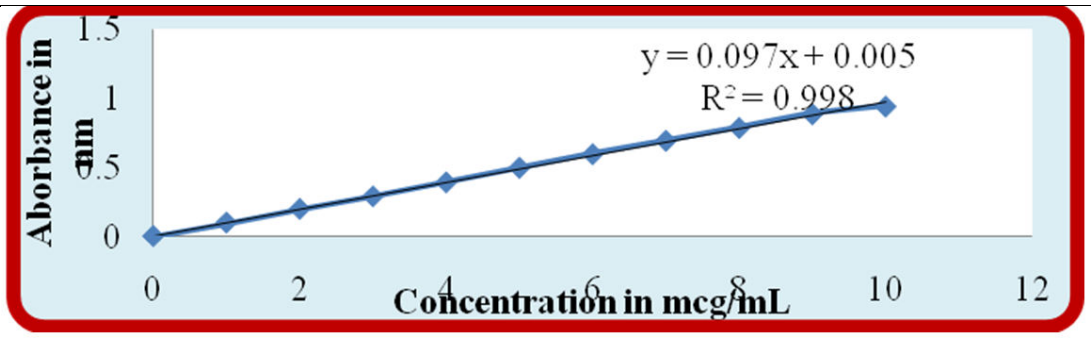

Fig. 3: Absorbance of Irbesartan in Phosphate Buffer pH 7.4 λmax 224

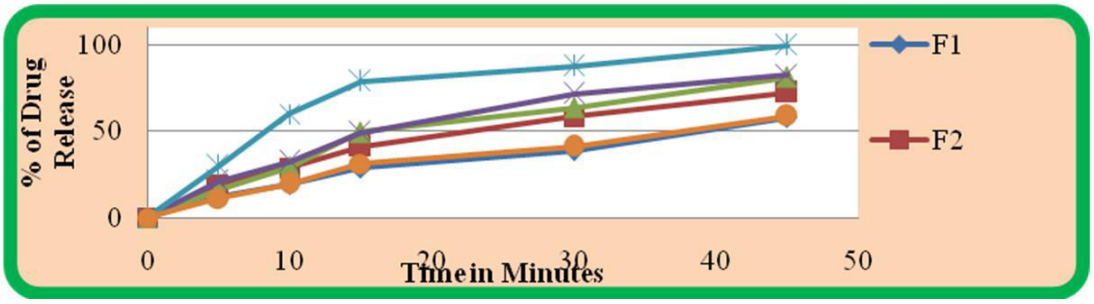

Fig. 4: *In-vitro* percentage dissolution studies of FDT of Irbesartan and Marketed Formulation

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RESEARCH ARTICLE

Parameters for an Imaging System

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ABSTRACT

Presently when anyone visits medical for checkup, doctors immediately refer him/her for diagnosis. Out of many diagnosis medical imaging is one important one. This imaging are important because with the help of this doctors can able see the internal body parts and identify the problem/diseases associated with it. In one line the quality of photograph is important which depends on the gamma camera. In this paper the main parameters of an Imaging system has been described.

Keywords: CT, MRI, X-Ray

INTRODUCTION

To describe the performance of an imaging system for diagnostic are used different benchmark parameters, among which the main are: the spatial resolution, the energy resolution, the acquisition frequency (or temporal resolution) and the sensitivity [1-3]. The bench mark parameters has been discussed below.

Parameters

Spatial Resolution: The spatial resolution of an imaging system is defined as the minimum distance between two radiation sources so that they are distinguishable. Consequently, if two radionuclides are separated by a value inferior to the spatial resolution of the gamma camera, these are shown as a single source in the reconstruction. The intrinsic spatial resolution of a system is calculated in the absence of a collimator and depends only on the characteristics of the crystal and photodetectors and on their coupling. The overall spatial resolution includes in addition the contribution of the collimator and written as $=(R_{intrinsic}^2+R_{collimator}^2)^{0.5}$. A further limit to the spatial resolution, which is present in medical applications and does not depend, however, from the measuring system, is due to the interaction between the gamma rays inside the patient: these can interact within the body with Compton

scatterings before escaping and being detected by the gamma camera and thus contribute to the image formation. The spatial resolution depends therefore also on the distribution of the radionuclide and by its depth of penetration into the patient. In medicine, the need to reduce as much as possible this parameter is due to the necessity to identify lesions and tumor masses as small as possible to prevent their development.

Energy Resolution: The energy resolution of an imaging system is its fundamental benchmark, since it determines its ability to be able to distinguish the primary gamma photons, generated by the photoelectric effect, from those generated by Compton scattering or other radioactive sources. [4-7] The statistical nature of nuclear phenomena means that the energy distribution in the photodetector is typically approximable to a Gaussian: $G(E)=[1/(\sigma\cdot\sqrt{2}\cdot\pi\cdot)]exp[-(E-E^0)^2/(2\cdot\sigma^2)]$. Where E_0 is the mean value of the distribution, and σ is its standard deviation. A typical spectrum is shown in Fig 1, where in red is highlighted the Gaussian fitting of the photoelectric peak: The width of the Gaussian depends on the energy resolution R_E of the photodetector, which may be divisible in four contributions.

Temporal Resolution: After the detection of a scintillation event, the Gamma Camera is not able to immediately detect another one, but it is necessary to wait for a time interval, which is called *dead time*, and whose typical values are around 2.5-4 μs. This latter depends on several factors, but mainly by the spontaneous decay constant of the scintillator. In fact, the temporal dynamic of the light photons emission has an exponential behavior and gamma events that occur during the tail of this latter produce pulses which are summed to the previous ones, causing a phenomenon known as pile-up [8-9]. These pulses can be lost or misinterpreted by the readout electronics: two low-energy events that are piled-up may be indeed considered as one with the right energy and used for the image reconstruction, while two useful events may be discarded because their sum would be outside the energy window considered for a valid signal. The introduction of new scintillators materials, as the LaBr3(Ce), which has a decay time of only 25 ns, makes possible to almost completely eliminate this problem. In this case, the limit to the acquisition frequency is determined by the collection time of the charge in the photodetectors and by the read-out electronics.

Sensitivity: The sensitivity of a device for imaging represents the efficiency of the system in detecting the radiation to which it is exposed. This parameter is calculated as the ratio between the number of events detected and the dose of radiotracer administered to the patient, $S=events/dose$ $[cpm/\mu Ci]$ Where cpm indicates "counts per minute", while μCi is the micro-Curie, a radioactivity measurement unit. This means that, with the same radioactivity, a system with greater sensitivity can acquire more information on the incoming signal. In the medical field, the main advantage of the diagnostic nuclear imaging respect to radiological techniques is indeed the ability to detect very low concentrations of radiopharmaceuticals and therefore to minimize the dose of ionizing radiation transmitted to the patient. The sensitivity depends on: the thickness and characteristics of the scintillator material, the collimator, the energy window and the noise contributions previously discussed [10].

SUMMARY AND CONCLUSION

A description for the performance of an imaging system has been discussed and also the different benchmark parameters has been discussed like: the spatial resolution, the energy resolution, the acquisition frequency (or temporal resolution) and the sensitivity.

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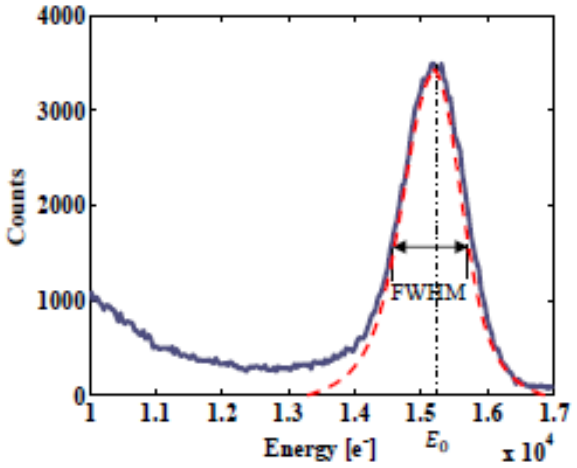

Fig 1: Statistical distribution of the energy peak measured by the system and centered in *E*0

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RESEARCH ARTICLE

Optimal Replenishment Policy for a Two-Warehouse Inventory Model with Fuzzy Demand and Deterioration under Trade Credit Offer

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ABSTRACT

In classical scenario the inventory models are considered with different demands and deterioration rates, which are either constant or time dependent , but they have inherent vagueness and imprecision. To avoid this, we need to incorporate the fuzzy demand and deterioration. So in this article, we are considering a two warehouse inventory model with fuzzy demand and deterioration under the Trade Credit facility. There is no shortages allowed. Further, this article intends to find optimal inventory cost by obtaining optimal replenishment policy. To achieve it, we have developed a mathematical model and is validated with numerical examples.

MSC Code: 90B05, 03E72.

Keywords: Inventory model, Two-Storage facility, Variable holding cost, Time dependent demand, Trade credit offer, Fuzzy inventory model, Defuzzification, Graded mean integration representation.

INTRODUCTION

In day-to-day life, inventory management plays a key role in the most of the business firms, organizations, retail management and etc. The main aim of Inventory management is to run the business without any interruption and avoid the loss of customers. The inventory system depends on many parameters, such as demand, deterioration, inflation, backlogging, trade credit, advertisement, number of warehouses and their types etc. It is observed that most of the retailers use their primary warehouse at busy market places as sales centres. So to attract customers, they display their items; decorates and provide better facilities at primary warehouse. Due to this they can't accommodate all the items in primary warehouse. So there is a need of secondary warehouse, for example, motor vehicle

showrooms, marble houses, construction materials, interior decorates, garment shops etc. Also, when an alternative price discounts for bulk purchase is available, retailers can purchases more items at a time. These items cannot be accommodated in the existing warehouse, so they need another warehouse to keep them. Similarly there are several reasons to have two warehouses in the inventory management. To enhance their business, traders follow many strategies. One of them is trade credit. By offering trade credit to retailer, suppliers can attracts more orders and new customers. Also in-hand stock decreases which results decrease in inventory cost and increase in profit. At the same time, trade credit offer act as an alternative price discount and reduces the ordering cost, investment amount to the retailer. Also, retailer can earn the interest on revenue accumulated by selling the items during the trade credit period.

Recently, Boina Anil Kumar, S. K. Paikray, S. Mishra Jaggi et al. [2], Kaliraman et al. [4], Liang and Zhou [5], Liao et al. [6], Singh and Kumar [8] and Tiwari et al. [9] have developed the inventory model by considering both two-warehouses and trade credit offer. Lee and Yao [10] considered fuzziness in demand and production quantity constraints in their economic production quantity model. Consequently, Kao and Hsu [11], Dutta et al. [12], Wang et al. [13], Sadeghi et al.([14, 15]), and Kundu et al. [16] assumed fuzzy demand in their inventory models. Next, MaitiandMaiti [17], and Rong et al. [18] considered fuzzy lead time in their inventory models. Shabani et al.[19] considered both demand and deterioration as fuzzy numbers for their inventory problem. Further, Singh et al. [20], Samal and Pratihar[21], Mahata and Mahata [22], Jain et al. [23], Shaikh et al. [24]and Pal et al. [25] developed their inventory models in fuzzy environment.

Different costs and parameters associated with inventory are considered as constant, but they have inherent vagueness and imprecision. To deal such type of problems many researchers used the fuzzy technique in their models. In recent years, Indrajitsingha et al. [1], Jayanti and Maragatham [3], and Misra and Mishra [7] and more researchers used fuzzy technique to obtain better results. In this article, authors considered a two-warehouse inventory model with fuzzy demand and deterioration under trade credit offer. Also, the authors assumed that the holding cost of items in RW are higher than of OW, as RW provides better preserving facility, less deterioration than of OW and it includes transportation charges. Further, with the effect of trade credit offer there arises different cases. For each case a mathematical solution was obtained and is illustrated with numerical examples.

Assumptions and Notations

Assumptions

The following assumptions are taken into account to develop the model.

1. All items in the inventory are of same kind.
2. Items in the Inventory have Fuzzy exponential demand and Fuzzy constant deterioration.
3. Inventory designed for Two-Warehouses (i.e. Owned Warehouse (OW), Rented Warehouse (RW)).
4. OW has limited Capacity to store the items, Whereas RW has infinite capacity.
5. There is no loss of customers during the cycle, i.e. shortages are not allowed.
6. The lead time is negligible.
7. The rate of deterioration in RW is less than of OW. Since it provider better facilities than of OW.
8. The holding cost of items in RW is greater than of OW, as it includes transportation Charges and better facilities.
9. The rate of Replenishment is infinite.
10. The maximum no. of deteriorating units in OW should not exceeds the demand at any time.

Notations

Following Notations are used while developing the model.

- $R(t) = \tilde{\alpha}e^{\tilde{\beta}t}$: Demand function. $\tilde{\alpha} > 0, 0 < \tilde{\beta} < 1$.
- N: The maximum number of items can be stored in OW.
- $\tilde{k}$: Fuzzy rate of deterioration in OW.
- $\tilde{\lambda}$: Fuzzy rate of deterioration in RW.

- ϵ_0: Ordering Cost per cycle.
- ϵ_p: Purchase cost per unit item.
- ϵ_s: Selling price per unit item.
- H_0: Holding cost per unit item in OW.
- H_r: Holding cost per unit item in RW.
- τ : At which RW becomes empty.
- T: At which OW becomes empty, i.e. total cycle time.
- $Q_0(t)$: Inventory level at any time t in OW, $t\epsilon[0,T]$.
- $Q_r(t)$: Inventory level at any time t in RW , $t\epsilon[0,\tau]$.
- M: Trade Credit period offered by supplier.
- θ: Rate of interest on payable amount.
- ϑ: Rate of interest earned on revenue accumulated by selling the items.
- $\widetilde{TC}(\tau)$:Fuzzy total cost of the inventory.
- $GTC(\tau)$:Defuzzified total cost of inventory.
- GT: Defuzzified Total cycle time.

Mathematical Model

The inventory cycle is started with W items at $= 0$. Initially, the OW is filled with its maximum capacity N items and rest of the items are kept in RW. To reduce the cost of inventory system items in the RW are depleted first, then the items in the OW depletes. The inventory level in RW decrease due to both demand and deterioration in the interval $t\epsilon[0,\tau]$.]. Also the inventory level in OW decrease due to deterioration in the interval $t\epsilon[0,\tau]$.and decreases due to both demand and deterioration in the interval $t\epsilon[\tau,T]$.Thus at $t = 0$, the RW becomes empty and at $T = 0$, OW becomes empty (i.e. both the Warehouse are empty). Inventory level in RW at any time t,$(0 \le t \le \tau)$ is governed by the differential equation

$\frac{dQ_r(t)}{dt} + \tilde{\lambda}Q_r(t) = \tilde{\alpha}e^{\tilde{\beta}t}$(1)

With boundary condition $Q_r(t) = 0$.

On solving equation (1), we get

$Q_r(t) = -\frac{\tilde{\alpha}e^{\tilde{\lambda}(-t)}}{\tilde{\beta}+\tilde{\lambda}}\left(e^{t(\tilde{\beta}+\tilde{\lambda})} - e^{\tau(\tilde{\beta}+\tilde{\lambda})}\right)$, $(0 \le t \le \tau)$ (2)

Inventory level in OW at any time t, $(0 \le t \le \tau)$ is governed by the differential equation

$\frac{dQ_0(t)}{dt} + \tilde{k}Q_o(t) = 0$, $(0 \le t \le \tau)$(3)

with boundary condition $Q_o(t) = N$.

On solving equation (3), we get $Q_0(t) = Ne^{\tilde{k}(-t)}$, $(0 \le t \le \tau)$ (4)

Inventory level in OW at any time t, $(\tau \le t \le T)$ is governed by the differential equation

$\frac{dQ_0(t)}{dt} + \tilde{\lambda}Q_0(t) = -\tilde{\alpha}e^{\tilde{\beta}t}$, $(\tau \le t \le T)$(5)

with boundary condition $Q_0(\tau) = Ne^{\tilde{k}(-\tau)}$.

On solving differential equation (5),we get

$Q_0(\tau) = \frac{e^{\tilde{k}(-t)}}{\tilde{\beta}+\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N + \tilde{k}N - \tilde{\alpha}e^{t(\tilde{\beta}+\tilde{k})}\right)$(6)

As per our assumption $Q_o(t) = 0$ at $t = T$.so using this in equation (6) and solving for$T$, we get

$T = \frac{1}{\tilde{\beta}+\tilde{k}}\log\left(\frac{1}{\tilde{\alpha}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N + \tilde{k}N\right)\right)$(7)

Now the different costs associated with inventory are

(i)Ordering Cost: $OC = \epsilon_0(8)$

(ii)Stock Holding Cost: Total Stock Holding Cost of inventory is

$$SHC = H_r\int_0^{\tau} Q_r(t)dt + H_0\left(\int_0^{\tau} Q_r(t)dt + \int_{\tau}^{T} Q_r(t)dt\right)$$

$$= \frac{H_r\tilde{\alpha}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{\lambda})} - (\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau} + \tilde{\lambda}\right) + H_0\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}} + \frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N\right) - \frac{e^{-\tilde{k}T}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N(\tilde{\beta}+\tilde{k}) + \tilde{\alpha}\tilde{k}\,e^{T(\tilde{\beta}+\tilde{k})}\right)\right)(9)$$

(iii)Total Deteriorating cost in the inventory is

$$DC = \epsilon_p\left(\tilde{\lambda}\int_0^{\tau} Q_r(t)dt + \tilde{k}\left(\int_o^{\tau} Q_0(t)dt + \int_{\tau}^{T} Q_0(t)dt\right)\right)$$

$$= \epsilon_p\left\{\frac{\tilde{\alpha}\tilde{\lambda}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{\lambda})} - (\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau} + \tilde{\lambda}\right) + \tilde{k}\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}} + \frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N\right) - \frac{e^{-\tilde{k}T}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N(\tilde{\beta}+\tilde{k}) + \tilde{\alpha}\tilde{k}\,e^{T(\tilde{\beta}+\tilde{k})}\right)\right)\right\}(10)$$

(iv)Interest Payable by Retailer:

Case-1: $M \le \tau \le T$

$$IP_1 = \theta\epsilon_p\left(\int_M^{\tau} Q_r(t)dt + \int_M^{\tau} Q_0(t)dt + \int_{\tau}^{T} Q_0(t)dt\right)$$

$$= \theta\epsilon_p\left\{\frac{\tilde{\alpha}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{\lambda})-\tilde{\lambda}M} - (\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau} + \tilde{\lambda}e^{\tilde{\beta}M}\right) + \frac{N}{\tilde{k}}\left(e^{-\tilde{k}M} - e^{-\tilde{k}T}\right) + \frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N\right) - \frac{e^{-\tilde{k}T}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N(\tilde{\beta}+\tilde{k}) + \tilde{\alpha}\tilde{k}\,e^{T(\tilde{\beta}+\tilde{k})}\right)\right\}(11)$$

Case-2: $\tau < M \le T$

$$IP_2 = \theta\epsilon_p\left(\int_M^{T} Q_0(t)dt\right)$$

$$= \theta\epsilon_p\left\{\frac{e^{-\tilde{k}M}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N(\tilde{\beta}+\tilde{k}) + \tilde{\alpha}\tilde{k}\,e^{M(\tilde{\beta}+\tilde{k})}\right) - \frac{e^{-\tilde{k}T}}{\tilde{\beta}\,(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}\,e^{\tau(\tilde{\beta}+\tilde{k})} + \tilde{\beta}N(\tilde{\beta}+\tilde{k}) + \tilde{\alpha}\tilde{k}\,e^{T(\tilde{\beta}+\tilde{k})}\right)\right\}(12)$$

Case-3: $M > T$

$IP_3 = 0.(13)$

(v) Interest Earned by Retailer:

Case-1: $M \le T$

$EI_2 = \vartheta\epsilon_s\left(\int_0^M t\,R(t)dt\right) = \frac{\tilde{\alpha}\vartheta\epsilon_s}{\tilde{\beta}^2 T}\left(e^{\tilde{\beta}M}(\tilde{\beta}M-1)+1\right)$ (14)

Case-2: $M > T$

$$EI_3 = \vartheta\epsilon_s\left(\int_0^M t\,R(t)dt + (M-T)\int_0^M R(t)dt\right)$$

$= \vartheta\epsilon_s\left(\frac{\tilde{\alpha}}{\tilde{\beta}}(M-T)\left(e^{\tilde{\beta}T}-1\right)+\frac{\tilde{\alpha}}{\tilde{\beta}^2}\left((\tilde{\beta}T-1)e^{\tilde{\beta}T}+1\right)\right)$ (15)

Thus, the total relevant fuzzy total cost of the inventory per unit time is

$$\widetilde{TC}(\tau,T)=\frac{1}{T}(OC+SHC+DC+IP-IE)$$

Therefore $\widetilde{TC}(\tau,T)=\begin{cases}\widetilde{TC_1}, M\le\tau\le T\\ \widetilde{TC_2}, \tau<M\le T\\ \widetilde{TC_3}, M>T\end{cases}$ (16)

Here

$\widetilde{TC_1}=$

$\frac{1}{T}\Bigg\{\epsilon_0+\frac{H_r\tilde{\alpha}}{\tilde{\beta}(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{\lambda})}-(\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau}+\tilde{\lambda}\right)+H_0\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}}+\frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right)+\epsilon_p\left\{\frac{\tilde{\alpha}\tilde{\lambda}}{\tilde{\beta}(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{\lambda})}-(\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau}+\tilde{\lambda}\right)+\tilde{k}\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}}+\frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}\tilde{\beta}N\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right)\right\}+\theta\epsilon_p\left\{\frac{\tilde{\alpha}}{\tilde{\beta}(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{\lambda})-\tilde{\lambda}M}-(\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau}+\tilde{\lambda}e^{\tilde{\beta}M}\right)+\frac{N}{\tilde{k}}\left(e^{-\tilde{k}M}-e^{-\tilde{k}T}\right)+\frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right\}\Bigg\}$ (17)

$\widetilde{TC_2}=$

$\frac{1}{T}\Bigg\{\epsilon_0+\frac{H_r\tilde{\alpha}}{\tilde{\beta}(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{\lambda})}-(\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau}+\tilde{\lambda}\right)+H_0\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}}+\frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right)+\epsilon_p\left\{\frac{\tilde{\alpha}\tilde{\lambda}}{\tilde{\beta}(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{\lambda})}-(\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau}+\tilde{\lambda}\right)+\tilde{k}\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}}+\frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}\tilde{\beta}N\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right)\right\}+\theta\epsilon_p\left\{\frac{e^{-\tilde{k}M}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{M(\tilde{\beta}+\tilde{k})}\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right\}--\frac{\tilde{\alpha}\vartheta\epsilon_s}{\tilde{\beta}^2T}\left(e^{\tilde{\beta}M}(\tilde{\beta}M-1)+1\right)\Bigg\}$ (18)

$\widetilde{TC_3}=$

$\frac{1}{T}\Bigg\{\epsilon_0+\frac{H_r\tilde{\alpha}}{\tilde{\beta}(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{\lambda})}-(\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau}+\tilde{\lambda}\right)+H_0\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}}+\frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right)+\epsilon_p\left\{\frac{\tilde{\alpha}\tilde{\lambda}}{\tilde{\beta}(\tilde{\beta}+\tilde{\lambda})\tilde{\lambda}}\left(\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{\lambda})}-(\tilde{\beta}+\tilde{\lambda})e^{\tilde{\beta}\tau}+\tilde{\lambda}\right)+\tilde{k}\left(\frac{N-Ne^{-\tilde{k}\tau}}{\tilde{k}}+\frac{(\tilde{\beta}+\tilde{k})e^{-\tilde{k}\tau}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}\tilde{\beta}N\right)-\frac{e^{-\tilde{k}T}}{\tilde{\beta}(\tilde{\beta}+\tilde{k})\tilde{k}}\left(\tilde{\alpha}\tilde{\beta}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N(\tilde{\beta}+\tilde{k})+\tilde{\alpha}\tilde{k}e^{T(\tilde{\beta}+\tilde{k})}\right)\right)\right\}-\vartheta\epsilon_s\left(\frac{\tilde{\alpha}}{\tilde{\beta}}(M-T)\left(e^{\tilde{\beta}T}-1\right)+\frac{\tilde{\alpha}}{\tilde{\beta}^2}\left((\tilde{\beta}T-1)e^{\tilde{\beta}T}+1\right)\right)\Bigg\}$

(19)

Hear $T=\frac{1}{\tilde{\beta}+\tilde{k}}\log\left(\frac{1}{\tilde{\alpha}}\left(\tilde{\alpha}e^{\tau(\tilde{\beta}+\tilde{k})}+\tilde{\beta}N+\tilde{k}N\right)\right)$ (from equation (7))

Let us take fuzzy parameters $\tilde{\alpha},\tilde{\beta},\tilde{\lambda}$ and $\tilde{k}$ as triangular fuzzy numbers $(\tilde{\alpha}_1,\tilde{\alpha}_2,\tilde{\alpha}_3),(\tilde{\beta}_1,\tilde{\beta}_2,\tilde{\beta}_3),(\tilde{\lambda}_1,\tilde{\lambda}_2,\tilde{\lambda}_3),(\tilde{k}_1,\tilde{k}_2,\tilde{k}_3)$ respectively in the equations (17),(18) and (19). Then defuzzifying them by Graded Mean Integration Representation Method as

$$GTC=\frac{1}{6}(\widetilde{TC_1}+4*\widetilde{TC_2}+\widetilde{TC_3})(20)$$

Here $\widetilde{TC_1},\widetilde{TC_2},\widetilde{TC_3}$ are the fuzzy total costs obtained by replacing 1st,2nd and 3rd fuzzy numbers of the corresponding triangular fuzzy numbers respectively in the i^{th} fuzzy total functions. Using equation (20), we can obtain defuzzified total costs $GTC_i(i=1,2,3)$ in each case. Similarly the total cycle time can be defuzzified as follow.

$$GT=\frac{1}{6}(T_1+4T_2+T_3)\ (21)$$

Here T_1, T_2, T_3 are obtained by replacing 1st, 2nd and 3rd fuzzy numbers of the corresponding triangular fuzzy numbers respectively.

Solution Procedure

Our objective is to find the minimal total cost in each case. The necessary and sufficient conditions for $GTC_i(\tau)$is minimal are $\frac{dGTC_i(\tau)}{d\tau} = 0$ and $\frac{d^2GTC_i(\tau)}{d\tau^2} > 0$ $(i = 1,2,3)$. So find

1.${\tau_1}^*$such that $\frac{dGTC_i({\tau_1}^*)}{d\tau} = 0$ and $\frac{d^2GTC_i({\tau_1}^*)}{d\tau^2} > 0$.

2.${\tau_2}^*$such that $\frac{dGTC_i({\tau_2}^*)}{d\tau} = 0$ and $\frac{d^2GTC_i({\tau_2}^*)}{d\tau^2} > 0$.

3.${\tau_3}^*$such that $\frac{dGTC_i({\tau_3}^*)}{d\tau} = 0$ and $\frac{d^2GTC_i({\tau_3}^*)}{d\tau^2} > 0$.

Find the corresponding ${GT_i}^*$from equation (21) by replacing τ by${\tau_i}^*(i = 1,2,3)$. Among all the minimal solutions the optimal solution can be found as follow.

Step-1 If $M \le {\tau_1}^* \le {GT_1}^*$, then set $\tau^* = {\tau_1}^*, GT^* = {GT_1}^*$ and $GTC^*(\tau) = GTC_1(\tau^*)$

Step-2 If ${\tau_2}^* < M \le {GT_2}^*$, then set $\tau^* = {\tau_2}^*, GT^* = {GT_2}^*$ and $GTC^*(\tau) = GTC_2(\tau^*)$

Step-3 If ${\tau_3}^* < {GT_3}^* < M$, then set $\tau^* = {\tau_3}^*, GT^* = {GT_3}^*$ and $GTC^*(\tau) = GTC_3(\tau^*)$

Step-4 If all the three steps fails, then set$GTC^*(\tau) = min\{GTC_1({\tau_1}^*), GTC_2({\tau_2}^*), GTC_3({\tau_3}^*)\}$ and $\tau^* = argmin\{GTC_1({\tau_1}^*), GTC_2({\tau_2}^*), GTC_3({\tau_3}^*)\}$.$GT^*$can be find from the corresponding τ^*. Then the optimal solutions is τ^*, GT^*&$GTC^*(\tau)$.

Numerical Examples

Example-1: Case-1$(M \le \tau \le T)$

ϵ_0 = 1800, ϵ_p = 9, ϵ_s = 15, H_0 = 1.5, H_r = 3, M= 0.27, θ = 0.18, ϑ= 0.13, N = 110,$(\tilde{\alpha}_1, \tilde{\alpha}_2, \tilde{\alpha}_3)$ = (2000,2500,3000),$(\tilde{\beta}_1, \tilde{\beta}_2, \tilde{\beta}_3)$=(0.1,0.3,0.5),$(\tilde{\lambda}_1, \tilde{\lambda}_2, \tilde{\lambda}_3)$=(0.07,0.09,0.11),$(\tilde{k}_1, \tilde{k}_2, \tilde{k}_3)$=(0.15,0.25,0.35).

Solution The optimal solution isτ^* = 0.421527GT^*= 0.456994$GTC^*(\tau)$ = 6212**.**

Example-2: Case-2 $(\tau < M \le T)$

ϵ_0 = 1620, ϵ_p = 14, ϵ_s = 20, H_0 = 4, H_r = 14, M= 0.15, θ = 0.3, ϑ= 0.18, N = 350,$(\tilde{\alpha}_1, \tilde{\alpha}_2, \tilde{\alpha}_3)$ = (300, 800, 1300), $(\tilde{\beta}_1, \tilde{\beta}_2, \tilde{\beta}_3)$= (0.5, 0.7, 0.9),$(\tilde{\lambda}_1, \tilde{\lambda}_2, \tilde{\lambda}_3)$ = (0.13, 0.15, 0.17),$(\tilde{k}_1, \tilde{k}_2, \tilde{k}_3)$= (0.7, 0.8, 0.9).

Solution The optimal solution is τ^* = 0.0522633GT^*= 0.413442$GTC^*(\tau)$ =7542.8**.**

Example-3: Case-3 $(M > T)$

ϵ_0 = 2500, ϵ_p = 14, ϵ_s = 21, H_0 = 6, H_r = 12, M= 0.45, θ = 0.3, ϑ= 0.25, N = 900,$(\tilde{\alpha}_1, \tilde{\alpha}_2, \tilde{\alpha}_3)$ = (3500, 4000, 4500), $(\tilde{\beta}_1, \tilde{\beta}_2, \tilde{\beta}_3)$= (0.6, 0.8, 0.10),$(\tilde{\lambda}_1, \tilde{\lambda}_2, \tilde{\lambda}_3)$ = (0.15, 0.25, 0.35),$(\tilde{k}_1, \tilde{k}_2, \tilde{k}_3)$= (0.25, 0.45, 0.65).

Solution The optimal solution is τ^* = 0.0464681GT^*= 0.236332$GTC^*(\tau)$ =9752.66**.**

CONCLUSION

Thus, taking in to account of fuzzy demand and deterioration for Two-Warehouse inventory model with Trade Credit offer, we have developed a mathematical model to obtain optimal replenishment time. While developing the model we considered no shortages and the holding cost of items in RW is higher than of OW, as it provides better preserving facility and includes transportation charges. Furthermore, triangular fuzzy numbers and Graded Mean Integration Representation Method are used. The mathematical model is validated with examples in different cases arises due to trade credit offer. This article can be extended by incorporating shortages, different backlogging, inflation, different type of demand and deteriorations.

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REVIEW ARTICLE

Review Paper on Smart Power Generation from Waste Heat using Thermoelectric Generator (TEG).

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ABSTRACT

In this paper our main focus on reducing environmental pollution. As the major source of production of electricity by thermal with the help of fossil fuel, coal. In this electricity conversion Burning of fossil fuel required and during this process environmental pollution occur. During this process lots of heat is wasted. This waste heat we are going to recover. And this waste heat converted into electricity with the help of Thermoelectric Generator (TEG). The basically Thermoelectric Generator work on the principle of see beck effect. In This project Waste heat into electricity from various Appliances like Automobile, Industries, And Power plants etc. Also waste heat from Automobile like (Cars, Trucks, etc). Thermoelectric Generator (TEG) device, which are semiconductor system that can be directly convert thermal energy with medium cooling or heating or Recover Waste heat and convert into Electrical Power. And it also helps to reduce CO_2 and Beneficial for Environment.

Keywords: Thermoelectric Generator (TEG), Waste Heat, Power Generation, Seebeck Effect.

INTRODUCTION

As per the demand of electricity increase because of consumption of electricity more than the generation of power. Generation electricity from Renewable as well as Non-renewable resources. 70% of electricity generated by thermal power plant which requird coal, But this is limited, so full-fill demand of electricity we required renewable source like solar, Wind. But the solar, Wind is not generated electricity all the time. Besides this we have another new technology option to generate electricity from waste heat; this waste heat may be from Automobile, Industrial, Generating plant, by using thermoelectric generator direct conversion of thermal energy into electrical energy.

In thermal power plant wastage of heat from duct (i.e. Fly Ash to remove into environment) where heated gases. And also thermal power plant (TPP) the steam from turbine generally fed towards the cooling purpose to convert into water for reuse. This steam is fed by using pipes. So this pipes are get heated because of highly temperature heated steam, so we convert into electrical energy by placing our thermoelectric generator (TEG)

From automobile in internal combustion engine useful for mechanical work and reaming heat is to be waste heat enter into environment from the silencer or any medium by placing thermoelectric generator (TEG) this waste heat to convert into electrical energy

METHODOLOGY

Thermoelectric power generation offer a potential application in the direct conversion of waste-heat energy into electrical power where it is unnecessary to consider the cost of the thermal energy input. The application of this alternative green technology in converting waste-heat energy directly into electrical power can also improve the overall efficiencies of energy conversion systems. In this paper, a background on the basic concepts of thermoelectric power generation is presented and recent patents of thermoelectric power generation with their important and relevant applications to waste-heat energy are reviewed and discussed [5].

Principle of Working

See beck Effect (1821) When two ends of a conductor are held at different temperatures electrons at the hot junction at higher thermal velocities diffuse to the cold junction. The see beck Effect is the conversion of temperature difference directly into electricity .It is classic example of an electromotive force (emf)and leads to measurable currents or voltage .[1]The magnitude of the emf V produced between the two junctions depends on the material and on the temperature ΔT12 through the linear relationship defining the See beck coefficient S for the material.

$\Delta V = S \Delta T12$

The See beck coefficient can be measured Figure.1 by connecting wire-A in a circuit with 2 wire-Bs. The two junctions (ends of wire-A) are held at two temperatures, and V measured as T1 or T2 is vary.

Project Working

In this particular project by using thermoelectric generator (TEG), thermal energy i.e. waste heat consists of thermal energy convert into electrical energy. Here we are trying to increases overall efficiency. The working of our project are showing in block diagram .It consist of Waste heat resources, Heat resources ,Thermoelectric generator Temperature **sensor** ,Dc fan with motor ,8051 micro controller ,Energy storage battery ,Inverter ,LCD display. From waste heat resources ,the heat is going to be recover with heat recovery device and heat is given to thermoelectric generator which is convert thermal energy into electrical energy .this is known as smart power generation. Temperature sensor is to measure the temperature of input side of thermoelectric generator .DC motor it is used to represent the power is utilized from thermoelectric generator as temperature increases flow of fan is also increases. As the power is generated in is DC power and if we want to drive AC load.

Firstly this DC power is stored into the battery and converted it into Alternating Current (AC) power with the help of inverter. Microcontroller 8051(AT89s52) allow dynamic and faster control and it is interfaced and output voltage. In this way whole system work starts from wastage of heat from thermal power plant turbine section, in automobile silencer in vehicle convert to electricity with the help of thermoelectric generator.

Resistor: The property of circuit that opposes the flow of current is called resistance. The electronic device is commonly used to reduce the power or current in an electronic device. Resistors operate on the principle that energy can be neither created or destroyed, only cone state to another. A resistor is made of a material that has a specific

amount of resistance to current flow. Resistors are selected for the amount of resistance they possess. This value is measured in Ohm's (Ω).

Dc Motor: It is used to represent the power obtained from thermoelectric generator. When heat is release the sped of motor is increase, it indicates the power obtained from thermoelectric generator.

LCD (2*16); the term LCD stands for liquid crystal display. It is one kind of electronic display module used in an extensive range of applications like various circuits & devices like mobile phones, calculators, computers, TV sets, etc. This device can be use to display any message, status of name of project and voltage. In this project it indicates the status power. It works on 5v

Inverter Module: It is used to converts the DC voltage e into AC voltage. It converts the 12v dc At the output AC load is obtain. This AC load is again supply to run the same machine which will use in production of products in industry. Else it can used to run the other load.

Thermoelectric Generator: A thermoelectric generator (TEG), also called a See beck generator, is a solid state device that converts heat flux (temperature differences) directly into electrical energy through a phenomenon called the See beck effect (a form of thermoelectric effect).

Battery: It have capacity of 12v 1.3 AMP , it is used to stored the electric energy through thermoelectric generator module. Also it supply the power to other components like, Microcontroller, LCD display , inverter etc.

ULN2003:ULN2003 is a 16-pin IC. It has seven Darlington Pairs inside, where each can drive loads up to 50V and 500mA. For these seven Darlington Pairs we have seven Input and Output Pins. This is because when the input pin of the IC gets high the respective output pin will get connected to ground.

Application

1. Thermoelectric Generators are basically used in where the power production is less.
2. In many industries amount of heat is executed and been wastage. We can used this hear for electricity using TEG.
3. In automobile vehicle produce heat that can be used for generating electricity by using TEG.
4. Recharge the battery where ever waste heat is obtained.
5. Self charging battery by fixing the TEG at radiator or two wheeler silencers pipe.

Advantages

1. This is a Non-conventional system, No fuel is require.
2. Easy maintenance, portable, charging time is less (maximum temp).
3. Promising technology for solving power crisis to an affordable extent.
4. We can charge any electronic devices
5. Electricity can used for many purposes

Disadvantages

1. Improper variation of temperature gradient difference may damage the TEG.
2. Complex design.

CONCLUSION

In this review paper on "smart power generation from waste heat using thermoelectric generator (TEG) "this conclude that the waste heat from thermal power plant (boiler section), Automobile silencer or vehicle convert into electricity with the help of TEG.

To increase overall efficiency of any plant if is more beneficial and it is an appropriate conversion of waste heat into electricity using thermoelectric generator to improve the efficiency .and TEG required very low maintenance very less vibration and notice, TEG is a next step for great contribution forwards green earth .Also result into reduction in pollution that occur in thermal power plant as well in automobile.

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Table 1 : Component Details

NAME OF COMPONENT	NO OF UNIT	VALUE
Resister	6	100ohm
DC motor	1	5V
Relay	3	5V
UIN2003	1	500mA, 50V
LCD 16*2	1	4.7V-5.3V
CFL inverter	1	12DC to 230 AC
Battery	3	4V , 2A
Peltier Module (TEG)	4	1.4V DC Each
Capacitor	2	100 micro Farad,
Temprature Sensor	1	

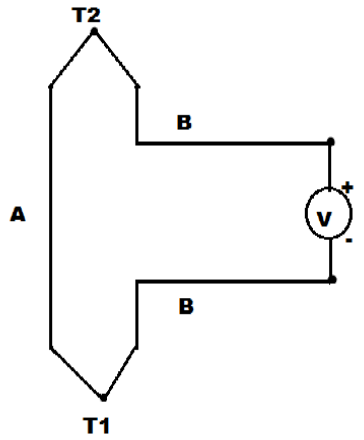

Fig.1 see beck coefficient measurement.

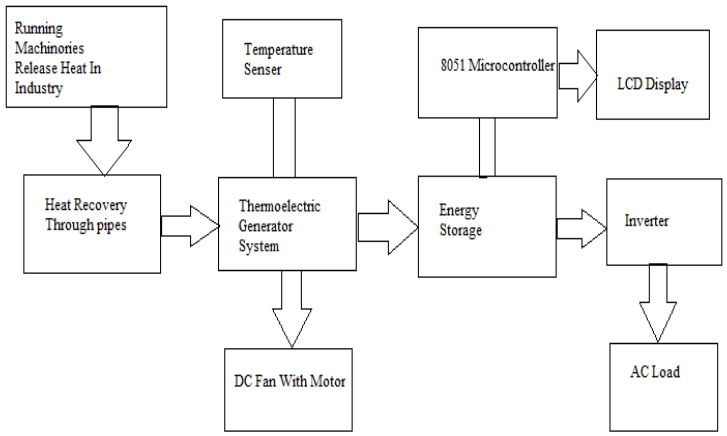

Fig.2 Working Block Diagram of Project.

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RESEARCH ARTICLE

Development and *In-vitro* Evaluation of Oxybutynin Chloride Extended Release Tablets

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ABSTRACT

In the present study, an attempt was being made to formulate and evaluate extended release tablets containing of oxybutynin Chloride to improve its bioavailability with reduction in dosing frequency and dose related side effects. 9 formulations were developed with varying concentrations of excipients other than drug and Opadry yellow. Binder solutions and solvents were used to make up to required volume. Drug-Excipient compatibility studies were conducted using FT-IR by Potassium Bromide pellet technique. Quality of drug-excipient powder was analyzed for the flow properties. The finished product is evaluated for hardness test, friability test, disintegration test and dissolution studies. FT-IR studies showed no evidence on interactions between drug, polymers and excipients. The final batch (F9) shows the maximum drug release of 93.45% after 24 hours. So, the final batch (F9) was optimized and was compared with innovator batch in terms of in-vitro dissolution studies. The optimized formulation batch (F9) was compared with reference standard batch. Stability studies were conducted for the formulation F8and F9. The stability study was performed at 40°C /75 % RH for a specific time period. The selected formulation (F9) showed that there was no significant change observed during the time period. Results of this study reveal that the tablets of optimized formulation (F9) containing drug: polymer (1:1) hypermellose showed better extended release when compare to the other formulation.

Keywords: oxybutynin, extended, tablet, oral.

INTRODUCTION

Tablets may be defined as solid pharmaceutical dosage forms containing medicament (or) medicaments with or without suitable excipients & prepared either by compression ormolding. Extended release as a dosage form designed to release the medication in a controlled manner during an extended period of time, at a predetermined rate, duration, and location following administration [2,4,5]. There are various advantages of extended release medications like enhancement of adherence, reduction in dose frequency, improvement of patient compliance, etc. [2-4]. There are various types of extended release tablets like sustained release, Repeated action, etc. The extended release tablets can be prepared by using hydrophilic polymers, solvents, etc.[6,7].There are different mechanisms in formulating extended release formulations like chemical, pH, diffusion, etc[7-9]. Each drug must fulfill some criteria in order to be formulated into extended release like lesser $T_{1/2}$ (2-3 hrs), chronic disease state, lower solubility, etc. [10-12] They can be delivered in ocular cavity, dermally or even orally.Extended release products help in maintaining the constant Levels of the drug in the bloodstream increases the therapeutic effectiveness of the drug [5]. The drug release is generally resembles zero-order kinetics. Drugs of this type release the same amount of drug by unit of time and it is the ideal method of drug release in order to achieve a pharmacological prolonged action [13,14].

MATERIALS AND METHODS

PRE-FORMULATION STUDIES

UV- ANALYSIS

Drug (Oxybutynin) stock solution is prepared and diluted with phosphate buffer pH 6.8 and 0.1N HCl. The diluted drug sample is analyzed in UV-spectrophotometer (Shimadzu-UV-1601) at wavelength of 220 nm. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

FT-IR

FT-IR studies of the drug and excipients are conducted using Potassium Bromide (KBr) pellet technique. The discs were scanned over a wave number range of 400 to 4000 cm^{-1} in FT-IR instrument. This is also used for analysis of drug-excipient compatibility.

BULK DENSITY

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve #20) into a measuring cylinder. The bulk density is calculated using bulk volume according to the formula mentioned below. It is expressed in g/ml and is given by

$$D_b = M/V_b$$

Where,
M is the mass of powder
V_b is the bulk volume of the powder.

ANGLE OF REPOSE

It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\theta = \tan^{-1}(h/r)$$

Where,
θ is the angle of repose
h is the height in cms
r is the radius in cms.
It is performed by fixed funnel method. Angle of repose helps in determination of flow properties.

CARR'S INDEX

Carr's index helps in determination of compression parameters. It is also known as compressibility. It is determined as follows:

$$C.I. = \frac{D_t - D_b}{D_t} \times 100$$

Where,
D_t is the tapped density of the powder
D_b is the bulk density of the powder.

PROCEDURE

Ofoxybutynin Hydrochloride, microcrystalline cellulose and lactose monohydrate which are co-sifted at #40 are mixed and granulated for 10 minutes at low impeller speed. Hydro alcoholic solvent is added for 1 minutes uniformly and gradually. Granulated wet mass was kneaded and air-dried for 15 min followed by drying at 55ºC±5ºC in fluid bed dryer. It is again sieved at #40 followed by addition of lubritab and magnesium stearate. The resultant mixture is subjected to compression into tablet form. Methyl acrylic acid co-polymer Dispersion USNF was used for Enteric coating.

EVALUATION OF FINISHED PRODUCT

APPEARANCE

Tablets from each formulation were randomly selected and organoleptic properties such as color, odour, taste, and shape were evaluated.

HARDNESS TEST

Hardness tester (Electrolab) was employed for this test. Force required to break the tablet is determined in this testof 20 tablets was determined using digital hardness tester and the average hardness was calculated. It is expressed in N or kg/cm^2.

FRIABILITY TEST

Friability of the tablets determined using Roche friabilator at 25 rpm and dropping height is 6 inches. This process is done until the friabilator completes 100 rotations in total. The friability (F)is given by the formula.

$$F = W_{initial} - W_{final} \times 100 / W_{initial}$$

The acceptance criteria of friability is not more than 1%.

DISSOLUTION STUDIES (*IN-VITRO*)

It is performed using USB dissolution testing apparatus II (paddle assembly). The drug is added into the dissolution basket containing the phosphate buffer pH 6.8. the rotation speed and temperature of the paddle assembly is maintained at 75 RPM and 30 7.5 plus or minus 4.5 degree Celsius respectively. Sample is withdrawn from the dissolution apparatus up to 24 hours at an interval of 2 hours. Drug content in the collected sample is analysed using UV double beam spectrophotometer (Shimadzu UV-1601).

STABILITY STUDIES

This is performed for prediction of the quality of prepared batch of finished product. The stability studies are conducted as per ICH Q1A guidelines. The parameters for various types of stability studies are mentioned as below: In the present work stability study was carried out for the optimized formulation at40ºC±2ºC/75%RH±5%RH for three months. Results obtained in these tests are subjected to analysis of statistical significance using the unpaired student t-test.

KINETIC RELEASE STUDIES

These studies are used for calculation of uniformity of drug release in extended release products. This type of studies are highly useful in formulation of controlled release dosage forms. Kinetic models such as Higuchi diffusion model, Hixson-Crowell model, etc.

RESULTS AND DISCUSSION

PREFORMULATION STUDIES

UV-ANALYSIS

Standard graph of drug (Ofoxybutynin) using UV-spectrophotometry at 220 nm in phosphate buffer pH 6.8 is as follows: Based on the above studies, it is confirmed that this drug obeys Beer-Lambert's law successfully.

FT-IR STUDIES

The FT-IR studies was conducted for the drug successfully using Fourier Transform Infra-Red Spectrometer (Electrolab). The FT-IR spectrum of drug (Ofoxybutynin) is as follows: The studies showed no evidence on interactions between drug, polymers and excipients. The FT-IR studies infer that there are no drug-excipient interactions.

BULK DENSITY

The bulk density was evaluated for 9 different batches and is as follows:
It infers that the 2nd batch (F2) has the highest bulk density, while the 4th batch (F4) has the lowest bulk density.

ANGLE OF REPOSE

The angle of repose was determined using fixed funnel method for 9 different batches. The angle of repose for 9 different batches was as follows:
Based on the above data, it is observed that 4th batch (F4) has the lowest angle of repose stating the free flow property; while, the 7th batch (F7) has the highest value relating to least inter particulate friction.

CARR'S INDEX

Carr's index was determined for 9 different batches. The angle of repose for 9 different batches was as follows:
Based on the above data, it is observed that 8th batch (F8) has the lowest value of Carr's index resulting in free flow property; while, the last batch (F9) has the highest value relating to least inter particulate friction.

EVALUATION OF FINISHED PRODUCT

APPEARANCE

The appearance and other properties like texture and other organoleptic properties were done as specified in monograph. The appearance and other organoleptic properties is in compliance with the criteria specified under monograph.

HARDNESS TEST

The hardness test was performed for different batches of finished product. The data of hardness of various batches is as follows: It is observed that the 2 batches (F5 & F7) share the lowest hardness level. The 2nd batch (F2) has the highest hardness quality.

FRIABILITY

The friability test was performed for different batches of finished product using Roche friabilator. The data of friability of various batches is as follows:
It is observed that three batches (F6, F7 & F9) exhibits no friability. Highest friability is present in the 1st batch (F1).

DISSOLUTION STUDIES

The dissolution studies are conducted for several batches of finished product. The dissolution studies of various batches are as follows:

STABILITY STUDIESD

The dissolution studies suggest that the first batch (F1) has the slowest drug release when compared to other batches. But, the final batch (F9) shows the maximum drug release (93.45%) of all batches after 24 hours. So, the final batch (F9) was optimized and was compared with innovator batch in terms of *in-vitro* dissolution studies.

KINETIC RELEASE STUDIES FOR EXTENDED RELEASE

The Kinetic release of extended release product was calculated using several models like higuchi diffusion, zero order release, KorsmeyerPeppa model, Hixson Crowell. The graphical representation of these models are presented below:

CONCLUSION

The oral extended release matrix tablet containing 15mg of Oxubutynin chloride provided extended release for 24 hours. The hydrophilic polymer Pharmatose 200M alone have a satisfied release profile compared incombination with Kollidon. The optimized formulation followed zero order kinetics while the drug release mechanism was describing Case 11 transport drug release mechanism. A 3-month stability study data revealed no marked changes in the physical parameters and drug release profile.

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Table 1. The parameters for various types of stability studies

Study	Storage condition	Time period
Longterm	$25^0C\pm2^0C/60\%RH\pm5RHOR$ $30^0C\pm2^0C/65\%RH\pm5\%RH$	12 month
Intermediate	$30^0C\pm2^0C/65\%RH\pm5\%RH$	6 month
Accelerated	$40^0C\pm2^0C/75\%RH\pm5\%RH$	03 month

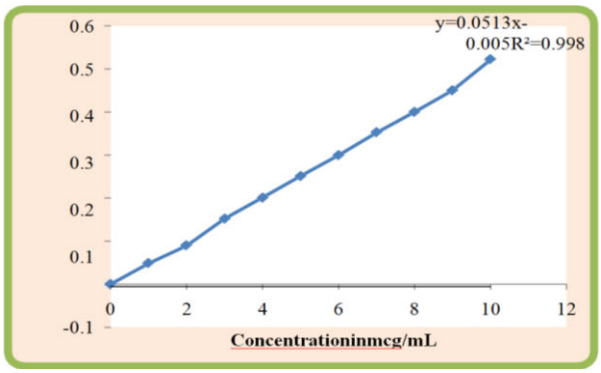


Fig.1. UV-ANALYSIS

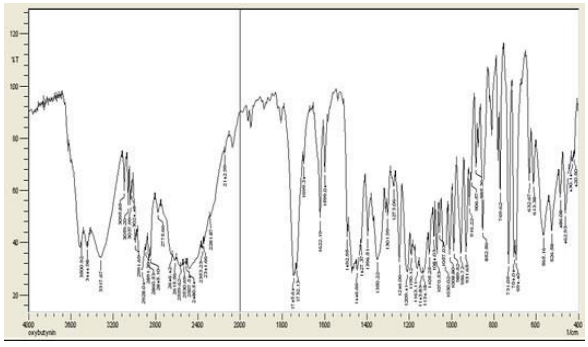


Fig.2. FT-IR STUDIES

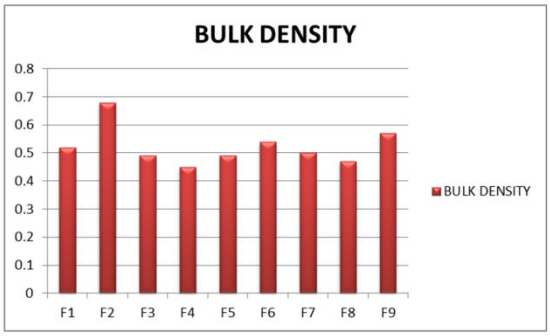


Fig.3.BULK DENSITY

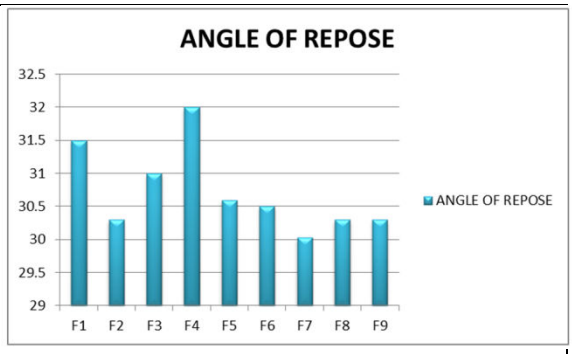


Fig.4.ANGLE OF REPOSE

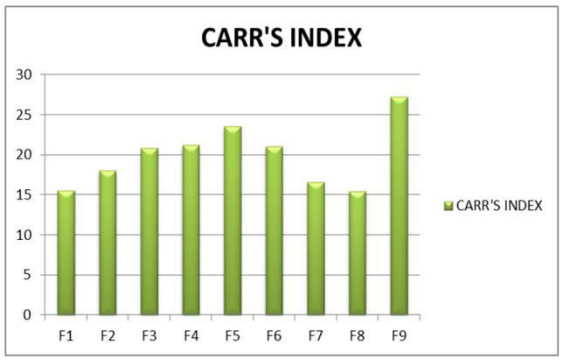


Fig.5.CARR'S INDEX

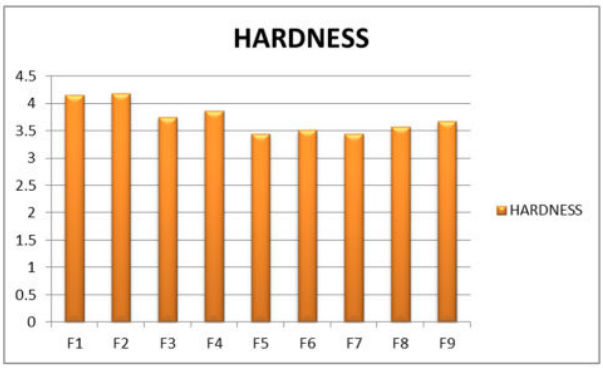


Fig.6.HARDNESS TEST

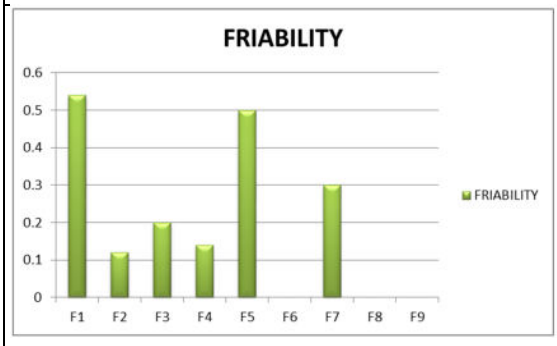


Fig.7.FRIABILITY

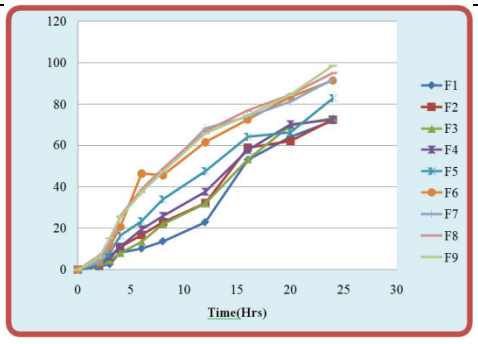


Fig.8.DISSOLUTION STUDIES

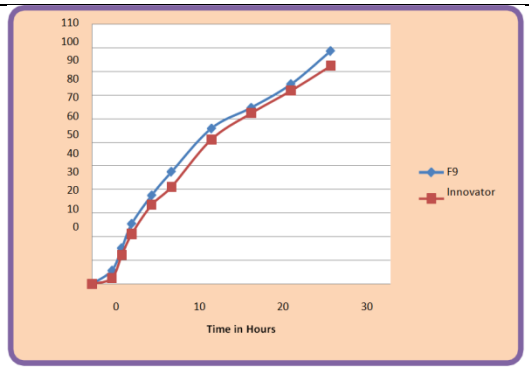
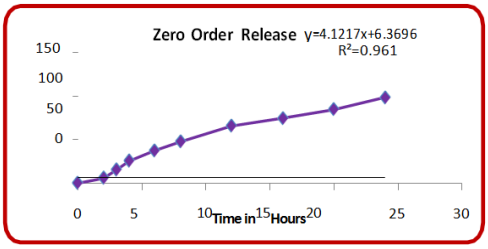
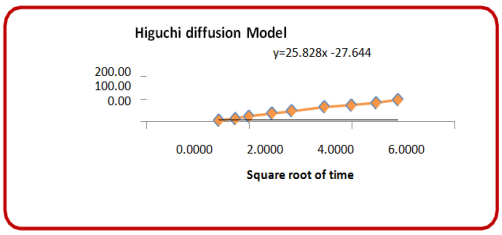
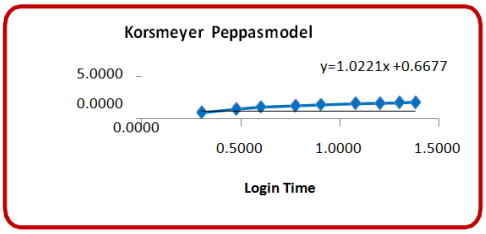
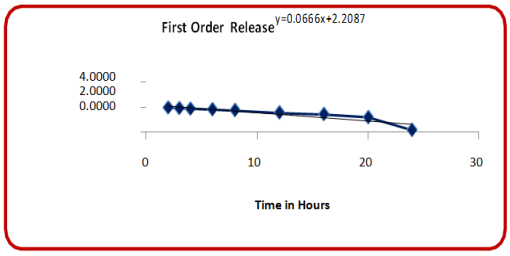


Fig.9.compared with innovator batch in terms of *in-vitro* dissolution studies









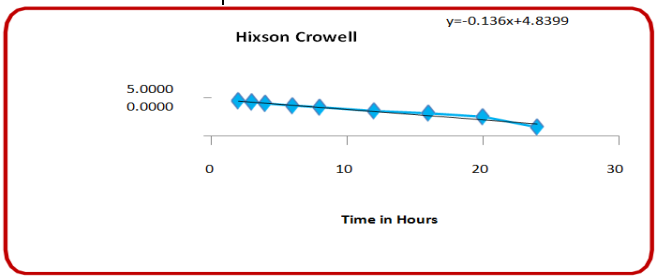


Fig.10.KINETIC RELEASE STUDIES FOR EXTENDED RELEASE

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RESEARCH ARTICLE

Experimental Study of Ethanolic Extract of *Populus deltoides* Leaves to Evaluate the Antipyretic Activity in Mice

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ABSTRACT

The occurrence of different phytoconstituents in the ethanolic leaves extract of *Populus deltoides* was examined, and the analgesic effect in mice was evaluated. Brewer's yeast mediated pyrexia was used to test the antipyretic effect of ethanolic leaves extract of *P. deltoides* (250 and 500 mg/kg). *P. deltoides* leaves extract contained a wide range of chemical constituents, including alkaloids, saponins, flavanoids, terpenes, and steroids. The rats given *P. deltoides* leaves extract were compared to the control (normal saline) group and standard (Paracetamol). The yeast elevated rectal temperature was found to be significantly reduced. We concluded from our research that the leaves extract of *P. deltoides* has antipyretic potential. This research shows that it can be used in management of temperature and provides a scientific foundation for its conventional use.

Keywords: Antipyretic, Paracetamol, Flavanoid, *P. deltoides*, Brewer's yeast.

INTRODUCTION

Fever is characterized as an increase in core body temperature above normal; the average oral temperature in healthy adults is 37°C (98.6°F). A single temperature of more than 38.3°C (101°F) or three temperature readings (at least one hour apart) of more than 38.3°C (100.4° F) was considered important in oncology practice[1]. Lower temperature elevations are found rare in the very young and elderly, as well as in people taking steroids or other immune suppressants. Fever of uncertain origin (FUO) is described as a febrile fever lasting more than three weeks, with temperatures above 38.3°C on several occasions, with no conclusive diagnosis after one week of hospital assessment [2].

Pathophysiology of Fever

The febrile response, of which fever is a part, is a dynamic physiologic response to illness that includes a cytokine mediated increase in body temperature, the production of acute phase reactants, and the activation of various physiologic, endocrinologic, and immunologic processes [3]. Maintaining a balance between heat output and dissipation is important for maintaining body temperature. Heat is produced internally during metabolic processes or when external ambient temperatures surpass those of the body under normal circumstances. Increased skeletal muscle activity, such as that seen in shivering, may also emit heat. Heat is lost mostly by evaporative losses from the skin and, to a lesser degree, from the lungs [4]. Interleukin-1b (IL-1b), tumor necrosis factor (TNF), and interleukin-6 (IL-6) are examples of pyrogenic cytokines that act directly on the hypothalamus to cause a fever response [5, 6]. Exogenous pyrogens, such as microbial surface elements, typically cause pyrexia by activating pyrogenic cytokines. The outer membrane lipopolysaccharide (endotoxin) of gram-negative bacteria, on the other hand, will behave at the hypothalamic level in a similar way to IL-1b [7].

Populus deltoides is a large tree in the *Salicaceae* family that grows to a height of 20 to 40 meters and has a diameter of 1.8 meters. The leaves are large, measuring 4 to 10 cm long, 4 to 11 cm wide, and triangular, with a 3 to 12 cm long petiole with a flattened base.The leaves are dark green and coarsely toothed, and sinuate teeth with glandular tips and a smooth petiole[8]. Many parts of the *Populus deltoids* are used for analgesic, antipyretic, and anti-inflammatory properties, and their effectiveness is well-known.

MATERIAL AND METHODS

The leaves of *Populus deltoides* were collected from the village yard (Jaunpur District, Uttar Pradesh 222001). Dr. K. Ravi Kumar, Senior Botanist at FRLHT Yelhanka Banglore, taxonomically described the species. For future reference, a herbarium specimen was preserved in the college museum. The leaves were powdered and placed in an airtight jar after drying in the shade at room temperature.

Method of Extraction

The coarse powder was subjected for extraction with 70% ethanol by Soxhlet apparatus. The ethanolic extract was concentrated under vacuum and resulting dried extract kept in a dessicator until further use.

Preliminary Phytochemical Studies

The existence of active constituents such as alkaloids, saponins, flavanoids, terpenes, and steroids was determined using an ethanolic leaves extract of *Populus deltoides*, as per standard procedure[9, 10].

Test for Steroid

Libermann- BurchardTest : One ml of chloroform was combined with ten mg of leaf extract, and one ml of acetic anhydride was added after two ml of concentrated sulphuric acid. The existence of steroids was shown by the appearance of a reddish violet coloration[11].

Test for Triterpenoids

Noller Test : Filter the extract by adding a few ml of chloroform. Tin powder and thionyl chloride were added to the filtrate and gently warmed. The existence of terpenoids is shown by the pink hue[12].

Test for Alkaloids

Mayer' Test: In a test tube, one ml of alcoholic extract was mixed with 0.02 ml of dilute hydrochloric acid and 0.1 ml of Mayer's reagent. The occurrence of alkaloid is shown by the development of a yellowish buff coloration precipitate[13].

Dragendroff's Test: In a test tube, 2 ml alcoholic extract solution was mixed with 0.1 ml hydrochloric acid and 0.1 ml Dragendroff's reagent. The formation of an orange brown colored precipitate suggests the presence of alkaloid[14].

Test for Flavonoids

Shinoda's Test: The extract was combined with ethanol and a small amount of magnesium was incorporated; then, drop by drop, concentrated hydrochloric acid was added and heated. Flavonoides existences were reported by the formation of magenta coloration[15].

Test for Tannin: In a test tube, put 5 ml of extract solution and 1 ml of ferric chloride 5 percent solution. The presence of tannin is shown by the development of a greenish black pigment[16].

Test for Saponin: In a graduated cylinder, one ml of extract solution was placed, then purified water was added and the volume was raised to 20 ml. For 15 minutes, the cylinder was shaken. The presence of saponins is shown by the formation of solid foam. When 1 ml of extract is mixed with 1% lead acetate solution in a test tube, a white precipitate forms, indicating the presence of saponins [17].

Determintation of acute toxicity (LD50): The ethanolic extract of *P. deltoides* was tested for acute toxicity using a standard approach (OECD/OCDE No: 425). In albino mice, an ethanolic extract of *P. deltoides* was observed to be harmless up to 5000 mg/kg body weight. Hence in the present study 500mg/kg was taken as effective dose for the ethanolic extract of *P.deltoides*for antipyretic activity.

Pathogenesis of Fever: In recent years, several of the mediators that cause pyrexia have been identified. Polypeptide cytokines are important "endogenous pyrogens" implicated in generating a strongly regulated inflammatory response to tissue injury and infection[18].Evaluation of antipyretic activity of leaves extract of *P. deltoides* by Brewer's-yeast-induced pyrexia test in rat: The extract of *Populus deltoides* was tested for antipyretic activity in a yeast-induced pyrexia procedure[19].The Institutional Animal Ethics Committee (Registration no. 1432/PO/a/11/CPCSEA) approved the research procedure. The animals' daily body temperatures were measured using a digital clinical thermometer (Ranbaxy, DT-01B India) through rectum, and the tails were fastened with adhesive tape.Pyrexia was nurtured in rats by injecting 10 ml/kg of a 20% suspension of Brewer's yeast (*Saccharomyces cerevisiae*) into their housing cages. After 19 hours of yeast injection, each mouse's rectal temperature was tested once more. Animals were chosen for the experiment if their temperature increased by at least 0.50C, 19 hours after yeast injection.The animals were divided into six classes (n = 6) and given saline (10 ml/kg) as a control, extracts (250 and 500 mg/kg), or paracetamol (100 mg/kg) as a normal treatment. Following drug therapy, each animal's rectal temperature was measured at 1 hour intervals for up to 5 hours.The percentage reduction in rectal temperature was calculated using the data obtained. The capacity of test drugs to reverse induced pyrexia was characterized as antipyretic action and represented as percentage reduction in temperature.

$$\text{Reduction in temperature (\%)} = \frac{B-Cn}{B-A} \times 100$$

Where, B represents temperature after pyrexia induction; Cn temperature after 1,2,3,4 and 5 h and A is normal body temperature.

Statistical Analysis: The data are provided as means of standard deviations (SEM). Graph and prism version 6 was used to do the statistical study, which included a one-way analysis of variance (ANOVA) and Turkey multiple reference analyses. P values of less than 0.05 were deemed meaningful.

RESULT AND DISCUSSION

Phytochemical Studies: To ascertain the existence of phytoconstituents, the ethanolic extract of *P. deltoides* was subjected to a qualitative examination. Table1 presented the findings, which indicated the existence of alkaloids, saponins, flavanoids, and terpenes, which have been shown antipyretic efficacy in yeast induced pyrexia. There were no steroids in the extract.

Effects of Ethanolic Leaves Extract of *P. deltoides* on Extracts in Yeast Induced Hyperthermia in Rats:
The effect of *P. deltoides* on yeast-induced pyrexia was investigated, and it was discovered that at doses of 250 mg/kg and 500 mg/kg, *P. deltoides* caused significant body temperature reductions up to the four hour after application. This effect peaked at 500 mg/kg and was dosage dependent, causing substantial body temperature reduction up to the fourth hour after administration.At the nineteenth hour after administration, a subcutaneous infusion of yeast suspension significantly raised rectal temperature. The findings revealed that the ethanolic leaves extract of *P. deltoides* has a strong antipyretic effect in rats when exposed to yeast, and that its effect is similar to that of paracetamol (standard drug).

The antipyretic influence began to manifest within the first hour of administration and lasted for four hours. At a dosage of 100 mg/kg, the standard drug paracetamol greatly decreased the yeast induced rise in body temperature. When the effects of the standard drug and *P. deltoides* extract treated rats were compared to the control (normal saline) sample, it was discovered that the yeast elevated rectal temperature was significantly reduced (Table 2), (figure1).

P. deltoides had a mild antipyretic effect at low doses (250 mg), but it had a strong antipyretic effect at higher doses (500 mg/kg) in Brewer's yeast-induced pyrexia in rats. Antipyretic medications work by inhibiting prostaglandin synthetase in the hypothalamus, which produces antipyretic effects. The first hour the antipyretic effect of leaves extract of *P. deltoides* shown significant ($p< 0.05$).The extract also has anti-inflammatory effects, which may be related to flavonoids in the extract, as flavonoids are noted for their anti-inflammatory, analgesic, and antipyretic properties due to their effect on arachidonic acid metabolism. In general, non-steroidal anti-inflammatory drugs produce their antipyretic action through the inhibition of prostaglandin synthetase within the hypothalamus.

CONCLUSION

The ethnolic leaves extract of *P. deltoides* was shown to be effective in treating pain, fever, and inflammation in laboratory animals in this study. The antipyretic function of *Populus deltoides* ethanolic leaves extract is thought to be due to inhibition of prostaglandin synthesis in the hypothalamus. At both 250 and 500 mg/kg doses, extract decreased hyperthermia after1 hour administration, providing a theoretical justification for its conventional application.

ACKNOWLEDGEMENT

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Ethics Support: The Institutional Animal Ethics Committee (Registration no. 1432/PO/a/11/CPCSEA) approved the research procedure.

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Table1 :Phytoconstituents present in 70% ethanolic leaves extract of *P.deltoides*.

Phytoconstituents	Ethonolic leaves extract of ***P.deltoides***
Alkaloids	+
Saponins	+
Flavonoids	+
Terpenoids	+
Tannin	+
Steroids	-

NOTE: +Presence, -Absence

Table 2 : Effects of ethanolic leaves extract of *P. deltoides* on yeast induced pyrexia in rats

Treatment groups	**Dose (mg/kg)**	**Rectal Temperature in °C at various time (hr)**				
		0	**1**	**2**	**3**	**4**
Control	N.S 5ml/kg	36.2±0.22	36.32±0.21	36.32±0.20	36.4±0.19	36.27±0.25
Paracetamol	100 mg/kg, p.o.	37.02±0.31	36.3±0.27	36.02±0.39	35.8±0.35	36.35±0.39
P. deltoides	250 mg/kg, p.o.	36.47±0.26	36.05±0.13	36.05±0.13	35.72±0.19*	35.85±0.22
P. deltoides	500 mg/kg, p.o.	37.4±0.09	37.22±9.4	36.82±0.60	36.62±0.1**	36.85±0.2

Values represent the Reaction time mean ± S.E.M, (n = 6). *p < 0.05 different from control group

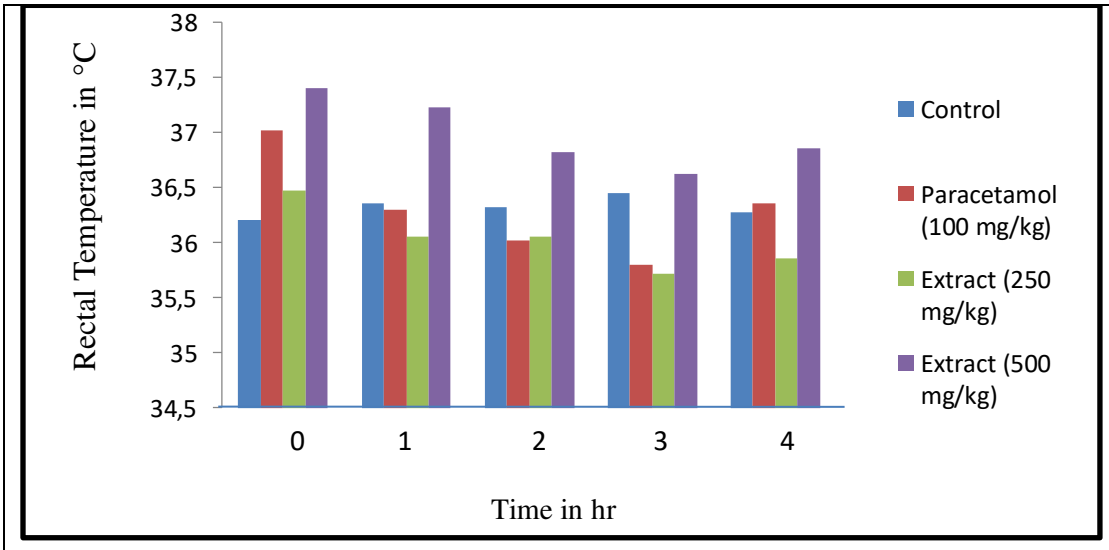

Figure 1. Effect of ethanolic leaves extract of *P.deltoides* on yeast induced pyrexiya in rat

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RESEARCH ARTICLE

Eco Friendly Reduction of Heavy Metals in Tannery Waste Water using Green Synthesized Silver Nanoparticles

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ABSTRACT

Nanotechnology enables a way for the more indistinguishable approach (eco-friendly approach). High chemical content in drinking water causes severe and adverse effects. Water contains various types of heavy metals, among them lead and chromium is considered as the major waste present in tannery waste water. The present study favored this innovation as a result of its advancement. This biological approach is undertaken to diminish toxicity and to reduce pollution. Here, we are intended to target on some challenges regarding eco-friendly approach on water treatment, mainly the improvement of control of these radicals on water including green synthesized nanoparticles. Synthesized silver nanoparticles using *Strychnos potatorum* were characterized by using UV-visible spectroscopy, FTIR, SEM, EDAX and Zeta analysis. The colloidal solution of silver nanoparticles was found to exhibit efficient tool used for the reduction of lead and chromium present in tannery water treatment.

Keywords: *Strychnos potatorum*, UV-visible spectroscopy, FTIR, SEM, EDAX, DLS and Zeta analysis.

INTRODUCTION

Water is essential for living beings it must be protected and saved for the next generation. The fast diminishing of water resources in recent days is due to the rapid increase in the world population and global warming also organic, inorganic and biological pollutants contaminate water resources [47]. When the concentration of heavy metals present in naturally occurring water is increased or due to manually induced chemical species in groundwater will

become contaminated which will not be suitable for drinking. Heavy metals like arsenic, chromium, zinc, copper, cadmium, nickel, mercury, lead are extremely toxic and they are harmful to agriculture and the ecosystem. The presence of impurity in drinking water, especially from dangerous substantial metals and metalloids, is a significant ecological and social issue [61]. The same number of these components are steady they are bio-aggregate, and appraisal of their protected cut-off points is troublesome in the environment [62]. For example, Pb, Hg, Cd and As, are not appropriate for biological activities and are emphatically harmful. During the recent decades researchers have been creating modest and eco friendly innovations for the treatment of wastewater produced at the family unit and up to the mechanical scale. Developments in nanotechnology have been magnificent in this decade. Nanotechnology involves green synthesis methods and starting resources with less cost of production and pollution**.** Nanoparticles exhibit higher efficiency as they act as a bridge between fine particle and macroscopic particles. Unusual methodologies involve chemicals that are toxic to the environment and large scale production is highly complicated. In drinking water the degree of chromium is typically low also, yet contaminated water may contain the hazardous chromium (IV); hexavalent chromium [66]. Lead is a dangerous metal that is destructive to human wellbeing. The level of subjection relies upon the amount of lead, source of subjection (air, water, nourishment), and age [63]. Significant levels of lead sullying in a adults can bring about spasms, major neurological harm, organ dysfunction, unconsciousness, and at last death. The fundamental significance of the plant in bio-based conventions for the metal nanoparticle by utilizing the plants has been discussed. The present study mainly focuses on the biological synthesis of silver nanoparticle using aqueous extract of *Strychnos potatorum* and its application on water treatment which incited the route for future research including green science for the union of different nanoparticles.

Sample Collection

Freshseeds of *Strychnos potatorum* seedswere collected from Thiruchendurai Village, Trichy district. Water sample had been collected from Maathur village, Trichy district-India. The sample had been stored in a plastic bottle which is pre-treated with acid to avoid any contamination.

Preparation of Plant Extract

Aqueous extract of *Strychnos potatorum* seeds had been prepared by using water as a solvent. Plant seeds were washed with fresh water and allowed to dry in shade for 20-25 days. Dried plant seeds were grind into powder using mortar and pestle. Definite amount of the plant sample was taken in a dry beaker and were added with sufficient amount of double distilled water. This solution is kept for boiling for 15-20 minutes by random stirring. Solution was kept aside and allowed it to cool at room temperature for one hour. Then it is filtered using Whatman No.40 filter paper through funnel into a clean beaker. The extract obtained is stored in refrigerator for further analysis.

Synthesis of Silver Nanoparticles

An aqueous solution of 5mM of $AgNO_3$ is prepared. 25ml of 5mM $AgNO_3$ solution is added with 2ml of the aqueous leaf extract. The color of the solution changes from colourless to dark brown color after the addition of leaf extract to the silver nitrate solution. This color change indicates the formation of silver nanoparticles.

Characterization of Silver Nanoparticles

UV-Visible Spectral Analysis

UV–Vis retention spectroscopy is the estimation of the weakening of a light emission after it reflects from an example surface of the analyte. The grouping of an analyte in arrangement can be controlled by estimating the absorbance at a specific frequency and applying the Beer–Lambert Law. UV–Vis ranges the scope of human visual keenness somewhere in the range of 400 and 750 nm, and manages the investigation of electronic changes between orbital's or groups, particles or atoms in every phase. Formation of nanoparticle in the aqueous solution was confirmed by the UV- Visible spectroscopy.

FTIR- Technique

FT-IR measurements were carried out to identify the major functional groups in the plant extract and their possible involvement in the synthesis and stabilization of silver nanoparticles. The existence of bio molecules responsible for the reduction of ions to nanoparticles in the sample was analyzed in FTIR.

Scanning Electron Microscopy

Scanning Electron Microscopy is a characterization technique where the morphology and surface topography of the can be obtained. The SEM image obtained for the synthesized nanoparticle gives complete information about its morphology and predicts the shape of the nanoparticle synthesized.

Energy Dispersive X-Ray Analysis (EDAX)

It is a quick, non-ruinous diagnostic strategy that is moderately economical and promptly adjusted to most SEM instruments. EDS is very helpful in the examination of particulate and other confined types of impurities. Pictures of the impurities dissemination might be acquired by observing the distinguished X-beam power as an element of the examined electron pillar position.

X-Ray Diffraction Study

This technique is used to find the crystallinity or amorphic nature of synthesised particles. The interplanar d-spacing and the relative intensities of the strongest peak of XRD pattern were characterized. The fingerprint region of relative intensity are found using the data with respect to d-spacing values.

Zeta Potential

Zeta potential is a truncation for electrokinetic potential in colloidal frameworks. From a hypothetical perspective, zeta potential is the electric potential in the interfacial twofold layer of a scattered molecule or bead versus a point away from the interface. As it were, zeta potential is the potential contrast between the portable scattering medium and the stationary layer of the scattering medium appended to the scattered molecule. The most significant factor that influences zeta potential is the pH of the medium. Different components incorporate ionic quality, the convergence of any added substances, and temperature.

Heavy Metal Analysis

Lead and Chromium in the collected water sample were determined quantitatively using Atomic Adsorption Spectrophotometer. Water tests with various centralizations of lead and chromium were set up by precisely calibrating the instrument by Lead and Chromium Standard Solutions separately with deionised water containing 0.1% nitric corrosive. 10 ml of each spiked water test in a test tube was balanced to pH 10 with ammonium hydroxide and included 5 ml of 0.01% dithizone in chloroform. The blend was energetically shaken for 10 minutes and the lower chloroform stage was gathered, washed with deionised water and vanished to dryness. Accelerated dithizone-lead complex at the base of a tube was reconstituted by including 0.25 ml of chloroform and followed by 2 ml of 5% nitric corrosive. The examples were then vortexed for 3 minutes. The last grouping of lead in 5% nitric corrosive was controlled by AAS. This run of the mill extraction system brings about 5-crease advancement of lead nuclear assimilation signal in water tests. The institutionalized working conditions were set up as a frequency of 283.3 nm; low cut of 0.7; pre-treatment temperature of 700 °C; atomization temperature of 1700 °C; and read time of 5 seconds.

RESULTS AND DISCUSSION

Visual Observation

Visual observation of color change primarily confirms the formation of nanoparticles. The colourless silver nitrate solution after the addition of plant extract, changes to dark brown. The color change confirmed the formation of silver nanoparticles. The color change of silver nitrate solution is shown in the figure 1.

UV-Visible Spectroscopy

UV-Visible spectroscopy is used to determine the optical properties of a solution. A quantity of light absorbed by the sample gives information about the formation of nanoparticles. The absorbance of synthesized silver nanoparticles using aqueous extract of *Strychnos potatorum* was observed at 426 nm. The absorption peak of synthesized silver nanoparicles shown in figure 2. The SPR band of UV-Vis spectroscopy around 400-480 nm shows the characteristic peak of silver nanoparticles.

FT-IR Spectrum of Plant Sample and Synthesised Nanoparticles

The obtained FT-IR spectrum of aqueous leaf extract of *Strychnos potatorum* showed bio molecules present in the plant extract. The spectrum obtained is useful for determining the functional groups which act as reducing and capping agent. These agents are responsible for the reduction of the selected precursor. The obtained frequencies of *Strychnos potatorum* leaf extract is shown in the table. FTIR spectrum of synthesized silver nanoparticles using aqueous plant extract of *Strychnos potatorum* was taken to identify the biomolecules and functional groups present in the leaf extract of *Strychnos potatorum*. The FTIR spectra of synthesized silver nanoparticles using leaf extract of *Strychnos potatorum* was shown below. The table shows the band and the frequencies absorbed in synthesized silver nanoparticles.

Scanning Electron Microscope.

The SEM image obtained for the synthesized nanoparticle gives complete information about its morphology and predicts the shape of the nanoparticle synthesized. Pseudo-spherical shape of nanoparticles had been confirmed from the result obtained from the SEM analysis, in the size range of 12-50 nm as appeared in the figure 5. The biomolecules present in the extract of *Strychnos potatorum* seed influenced the shape and size of the nanoparticles, where the organic compounds interlink with nanoparticles and diminish them.

EDAX Analysis

A solid signal for the Ag particles is demonstrated in the EDAX profile along with the strong peak of aluminium, and capping of elements like C, O and Cl on the synthesized nanoparticles. The regular adsorption peak of the silver nanoparticle, is observed at 3 keV which is the characteristic for silver nanoparticles. The incorporated Ag nanoparticles were additionally portrayed by EDAX investigation, which gave extra proof for the reduction of Ag(II) answer for Ag(0). The EDAX examination result affirmed that the main component present was silver. This outcome was predictable with the XRD examination result. The recognizable proof of Al was because of the coating of synthesized silver nanoparticle on a aluminium foil.

X-Ray Diffraction Pattern

The obtained XRD pattern for silver nanoparticles synthesized using *Strychnos potatorum* seed extract in figure 7, showed the characteristic peaks (at 2Θ). The planes obtained in XRD are represented in Table 3. All the miller indices showed face centred cubic structure for the synthesized silver nanoparticles using aqueous extract of*Strychnos potatorum*.

Bragg reflections with 2ø values of 38.07°, 42.36°, 64.34° and 77.33° were obtained from the XRD pattern of synthesized silver nanoparticles. This indicate miller indices (1 0 0), (1 1 0), (2 0 0) and (2 1 1) reflections respectively of metallic silver. This confirmed the cubic crystalline face-centred cubic structure of silver. This is further confirmed by the JCPDS No: 04-0783

ZETA Potential

A key pointer of the stability of colloidal scatterings can be given only by Zeta potential. The greatness of the zeta potential demonstrates the level of electrostatic force of attraction or repulsion between nearby, and also charged particles in scattering. For atoms and particles that are sufficiently little, a high zeta potential will give dependability, i.e., the arrangement or scattering will oppose conglomeration. At the point when the potential is little, alluring powers may surpass this repugnance and the scattering may break and flocculate. In this manner, colloids with high zeta potential (negative or positive) are electrically balanced out while colloids with low zeta possibilities will in general coagulate or flocculate. The conductivity behaviour of the colloid is shown in the figure 8. As per the data introduced here, with -5.71 mV in our outcome confirmed silver nanoparticles demonstrated great stability.

Water Treatment Using Synthesized Silver Nanoparticles

The synthesized silver nanoparticles were analysed and treated for treating domestic water which is inedible to drink. The water was analysed for both the acid and basic radical such as lead, chromium and fluoride respectively who may cause harmful effects to both human health and environment.

Heavy Metal Analysis

The experiments were carried out for both the sample and synthesized silver nanoparticle using *Strychnos potatorum* extract. The collected water sample shows higher concentration (Pb, Cr) than the permissible concentration guided by World Health Organisation. Table 10 shows the permissible concentration of heavy metals in drinking water. The concentration of heavy metals in the collected water sample has been determined quantitatively using Atomic Absorption Spectroscopy. The values are expressed in mg/L. The untreated water sample shows a very high concentration of both lead and chromium which is 2.03 and 6.32 mg/L respectively. When water sample was added with aqueous extract of *Strychnos potatorum* seed, the concentration of lead and chromium reduced to a smaller extent which was 1.89 and 5.22 mg/L respectively. Similarly, Water sample is treated with synthesized silver nanoparticle. This mixture is read on Spectrophotometer at 600nm and eventually the concentration of lead and chromium had been further reduced to 1.12 and 2.19 mg/L respectively. The data obtained in the analysis is shown in table 5.

Among lead and chromium, the synthesized nanoparticle shows better treatment on chromium in which chromium is reduced to 6.32 mg/L to 2.79 mg/L. This is about 55.85 % curtailed treatment of synthesized nanoparticles on water treatment. And eventually chromium in the water sample could be reduced by using *Strychnos potatorum* seed mediated silver nanoparticles. However, the concentration of lead could also be reduced but only to a smaller extent.

CONCLUSION

The technique does not require any synthetic chemicals. The precursor used in the present study is silver nitrate and silver nanoparticles were synthesized using aqueous extract of *Strychnos potatorum*. Synthesis of nanoparticles using plant extract is eco-friendly and it is achieved successfully. The technique is inexpensive and practically possible. The aqueous extract of *Strychnos potatorum* showed high efficiency to synthesize the silver nanoparticles. The SPR band in the UV-Visible spectrum shows absorption peak at 426 nm clearly indicates the formation of silver nanoparticles. The FTIR analysis showed the biological material and functional groups present in the aqueous extract of *Strychnos potatorum* seeds. The SEM analysis showed that the synthesized silver nanoparticles have definite shape and surface morphology. Synthesized silver nanoparticles are of Face Centred Cubic (fcc) structure and the crystal nature of the

synthesized nanoparticle had been confirmed using XRD. The stability of synthesized nanoparticles was further confirmed by Zeta potential Analysis. This study also suggested the good precursor for the water treatment more particularly for the eradication of heavy metals like lead and chromium to a greater extent.

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Table 1: Observed Frequencies of FT-IR spectral data of plant extract and the synthesised nanoparticles Scanning Electron Microscope.

BAND	FREQUENCIES	FREQUENCIES
3434.85 cm^{-1}	Strong, broad, OH Stretching alcohol	Strong, broad, OH Stretching alcohol
2988.01 cm^{-1}	Medium, CH stretching alkane	Medium, CH stretching alkane
2916.58 cm^{-1}	Strong CH stretching alkene	----------
1981.56 cm^{-1}	C=C=C stretching allene	----------
1795.36 cm^{-1}	Strong C- O stretching acid halide	----------
1725.48 cm^{-1}	Strong C=O stretching aldehyde	Strong C= O stretching aldehyde
1392.18 cm^{-1}	Medium OH bending alcohol	Medium OH Bending alcohol
1383.42 cm^{-1}	Strong CH bending aldehyde	----------
1292.00 cm^{-1}	Strong CN stretching aromatic amine	----------
1142.00 cm^{-1}	Strong CO stretching aliphatic ether	Strong C- O stretching aliphatic ether
1078.00 cm^{-1}	Strong S=O stretching sulphoxide	Strong S=O stretching sulphoxide
1020.00 cm^{-1}	C=C bending alkene	----------
845.36 cm^{-1}	Strong C-Cl Stretching halo compound	Strong C-Cl stretching halo compound
642 cm^{-1}	Strong C-I stretching halo compound	----------

Table 2: Data obtained from EDAX analysis

El	AN	Series	unn. C [wt.%]	norm. C [wt.%]	Atom. C [at.%]	Error (1 Sigma) [wt.%]
Ag	13	K-series	57.62	80.97	94.45	2.95
Al	47	L-series	13.55	19.03	5.55	0.53
		Total:	71.16	100.00	100.00	

Table 3: XRD Analysis of synthesized silver nanoparticle

2θ of the intense peak (deg)	θ of the intense peak (deg)	FWHM of intense peak (β) radians	Size of the particle(D) nm
38.07	19.03	0.7718	1.899
44.24	22.12	0.5924	2.525
64.34	32.17	0.6306	2.59
77.33	38.66	1.1227	1.44
Average size			2.11

Table 4: Zeta Potential Analysis of Synthesized silver nanoparticles

Parameters			Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV):	**-5.71**	**Peak 1:**	-5.71	100.0	5.52
Zeta Deviation (mV):	3.52	**Peak 2:**	0.00	0.0	0.00
Conductivity (mS/cm):	0.0210	**Peak 3:**	0.00	0.0	0.00

Table 5: Treatment of water using sample and synthesized silver nanoparticles

Heavy metals	Untreated Water Sample (mg/ L)	Sample treated with Extract (mg/ L)	Treated water sample (mg/ L)	Permissible Concentration by WHO (mg/ L)	Curtailment Percentage (%)
Lead	2.03	1.89	1.12	0.05	20.19
Chromium	6.32	5.22	2.19	0.01	55.85

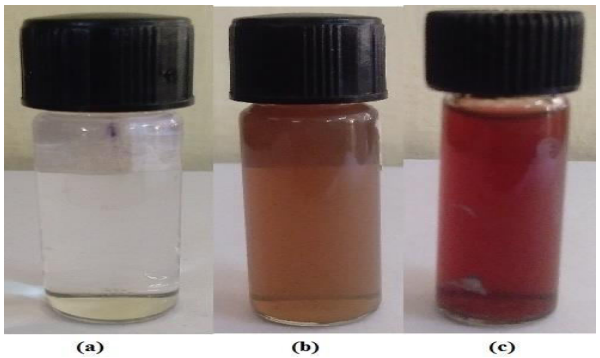

Fig 1: (a) Silver Nitrate Solution (b) Leaf extract of *Strychnos potatorum* (c) Synthesized Silver Nanoparticles

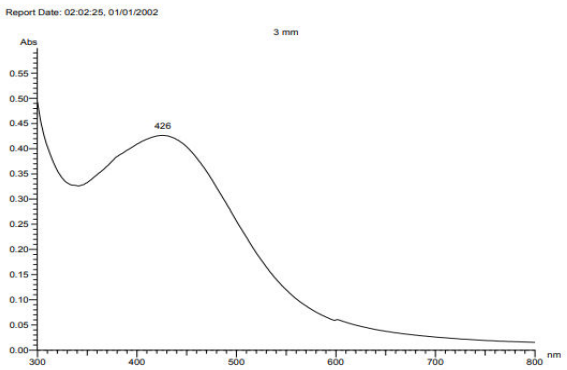

Fig 2: UV-Visible spectrum of syntheized silver nanoparticles using aqueous extract of *Strychnos potatorum*

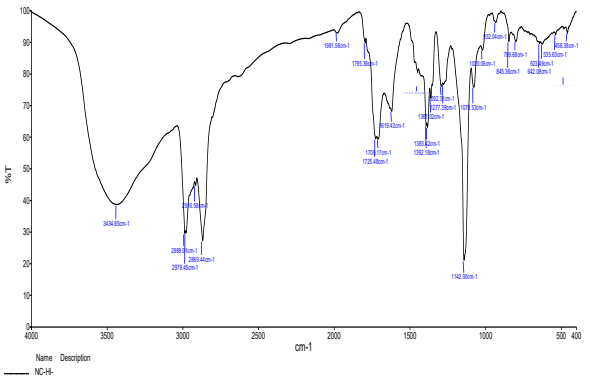

Fig 3 : FT- IR Spectrum of aqueous extract of *Strychnos potatorum*

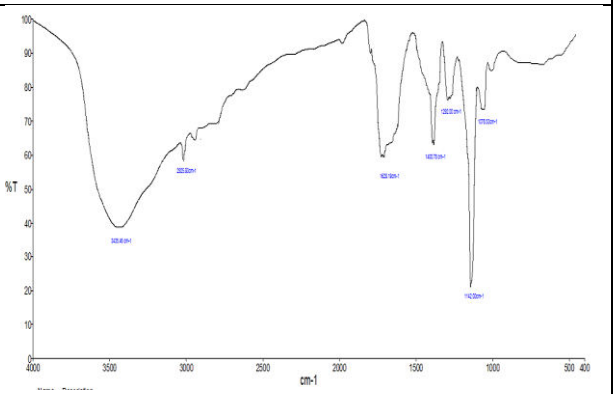

Fig 4 : FT- IR Spectrum of synthesised silver nanoparticles

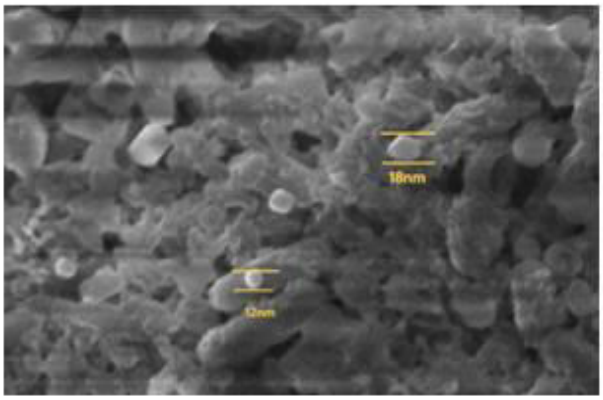

Fig 5 : SEM image of synthesised silver nanoparticles

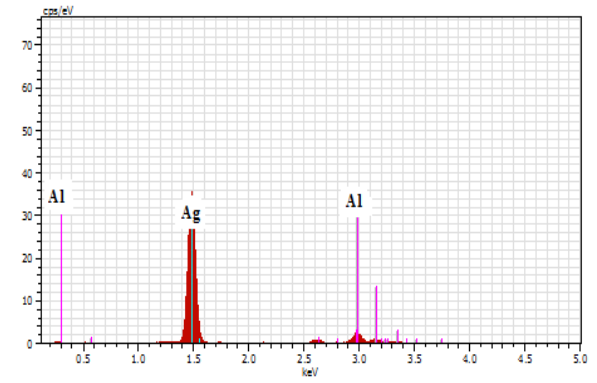

Fig 6: EDAX Analysis of syntheised AgNPs using *Strychnos potatorum* seed

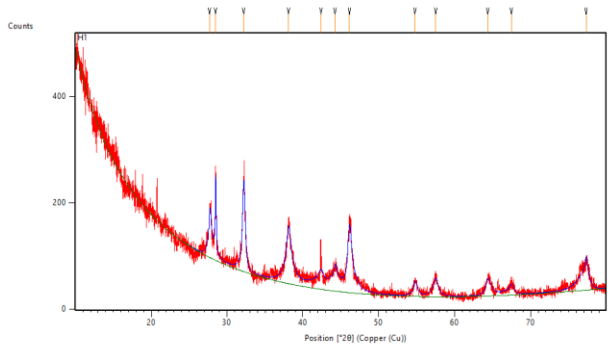

Fig 7: XRD Pattern of synthesised AgNPs from *Acalypha indica*

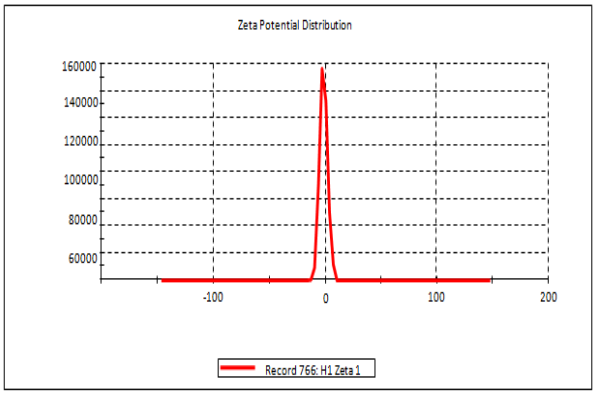

Fig 8: ZETA Potential analysis of synthesized silver nanoparticle

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RESEARCH ARTICLE

Effect of Entrance Channel to the Cross Section

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ABSTRACT

The cross section measurement is one of the important quantity in nuclear physics in fact in almost all the experiment people measured the cross section. According Bohr the formation of a compound nucleus is independent of entrance channel i.e. the formation and the decay of the compound nucleus is independent phenomena. But whether that is applicable to a loosely bound case where the projectile is a loosely bound nucleus. A calculation has been done using a loosely bound nuclei and compared with the Bohr compound nucleus hypothesis and found that for loosely bound nuclei the situation is different.

Keywords: CN, CS, HPGe, SSB

INTRODUCTION

The study of Nuclear reaction including the instrumentation is very important and interesting [1-3]. Nuclear reaction involving weekly bound nuclei is of current interest [4-5] . Many experimental and theoretical investigation has been done for the loosely bound nuclei (the loosely bound nuclei are a group of nuclei which are very loosely bound, say ^{6}Li, ^{7}Li…etc). [6-7]. The break threshold of alpha+deuteron for ^{6}Li is 1.46 MeV similarly for ^{7}Li also it is very less compared to the binding energy per nucleon (8 MeV). So the loosely bound nuclei are of interest as they are very loosely bound and can simulate the situation close to the halo nuclei (a special type of nuclei where the number neutron to proton ration is very high. i.e the number of neutron is more then proton like ^{11}Li but these type of nucleus are not stable) [8]. There is a core and some extra nucleon are far from it, makes an extended shape distribution. The radioactive ion beam is also not stable and expect that it will behave like a loosely bound nuclei up to certain extent. Since the availability of loosely bound nuclei are there so it is possible to measure the experimental data (cross section (CS)) using the loosely bond nuclei and compared it with the strongly bound system case. In the present report a statistical analysis model calculation has done for the formation of a compound nuclei and then

studied the decay channel to see that the Bohr hypothesis of compound nucleus (CN). An experimental comparison has also done for few cases.

CALCULATION AND RESULTS

For the calculation of the cross section a target has been choosed as ^{144}Sm and a beam of ^{6}Li with a beam energy 36 MeV in lab. frame. The barrier height is ~24 MeV and the barrier radius is ~9.65 fm . The beam energy is above the coulomb barrier which provides an excitation energy of ~37.786MeV to the compound nucleus. In this case the compound which will form after reaction is ^{150}Tb. Once the compound nucleus will form then the excitation energy will be under go de- excitation through the particle emission and it has been found that 2n and 3n channel of evaporation is important for this case. A cross section calculation has been performed with the channel number and shown in Fig.1. Similarly on the second theoretical situation a different target and projectile has been chosen such that the same compound nuclei will form (^{150}Tb) but with the nearly same excitation energy. For this purpose a beam of ^{12}C has been chosen with the target nucleus ^{138}Pr. When the carbon will strike the ^{138}Pr it will form the same compound nucleus and the excitation energy was ~37.758 MeV same as the excitation of ^{6}Li +^{144}Sm. With the beam energy of ^{12}C having 55.2 MeV is the beam energy. Since the beam energy has been maped to form the same excitation and as the compound nucleus is same the formation and decay mode should independent. Now the excited compound nucleus will decay by particle emission and it has shown in same Fig.1. One can see that 2n and 3n channel is important for this case also with nearly same cross section.

One can see from the Fig.1 that the cross section is more for the 2n and 3n evaporation where as for other channel it is very small. One can also see that same compound nucleus has formed by two different entrance channel and the decay mode is also same with the predictions provided by the statistical method. So the compound nucleus obey the Bohr hypothesis of compound nucleus which tells that the formation and the decay are the two independent process. Now the experimental data has been collect from the paper [9] and compared with the cross section calculation for the energy where the data are there and it has shown in Fig.2. It has found from the Fig.2 that the cross section of 2n and 3n channel is nearly same (calculated one) which clearly indicated that the Bohr hypothesis is correct whereas when we compared that data with the calculation one can found that the data is not matching with the calculation in fact the experimental measured cross section is less compared to the predicated one which indicated that there are some other mechanism is there which need to be investigated and it has the breakup channel effect

SUMMARY AND CONCLUSION

A calculation has been performed using the statistical model calculation by the code LISE ++ and found that for the same compound nucleus formed by the two independent method the cross section is same which clearly shows the Bohr hypothesis where as the comparison of data with the calculation shows that the measured cross section is less compared to prediction which indicated the presence of other reaction mechanism which need to be investigate

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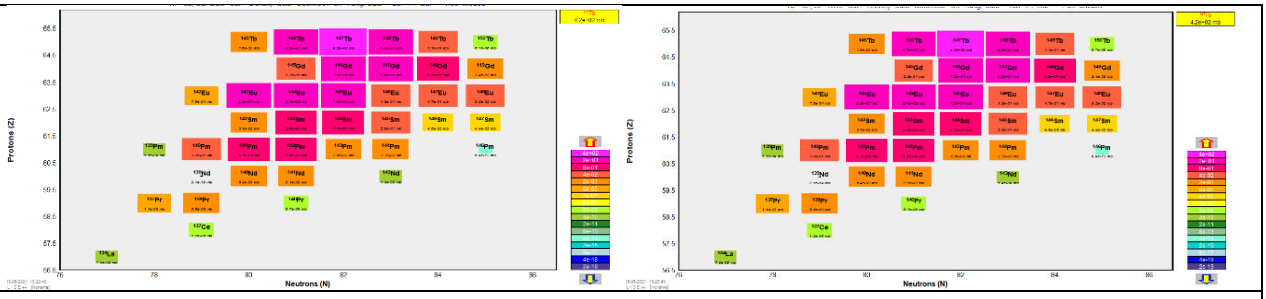

Fig. 1. The Statistical model calculation of the decay of the compound nucleus ^{150}Tb .one can see the various channel formation and their contribution (left) CN ^{150}Tb has formed by ^{6}Li+^{144}Sm and (Right) the same CN has formed by ^{12}C+^{138}Pr

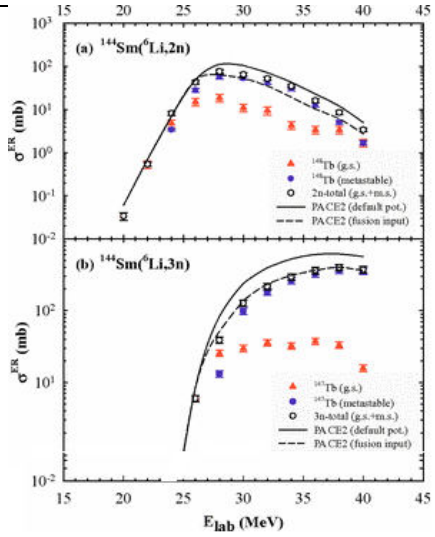

Fig. 2. The comparison of the cross section collected from the paper for 2n and 3n evaporation from the CN ^{150}Tb having the energy bellow and above the coulomb barrier.

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RESEARCH ARTICLE

Development and Comparative Evaluation of Solid Oral Tablets against USP Standard Reference Composed of Hepatoprotective Moiety

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ABSTRACT

In this experimental study, solid oral tablets were formulated and evaluated against reference standard based on United States Pharmacopeia (USP). 5 formulations were prepared with varying concentrations of Microcrystalline Cellulose, Sodium starch glycollate and magnesium stearate in each formulation batch such that total weight of tablet sums to 164.8 mg. The quality of drug was confirmed using Ultra-Violet spectroscopy, solubility studies and organoleptic studies. Drug-Excipient compatibility was checked. Evaluation studies of finished product were evaluated by hardness test, friability, disintegration and dissolution studies followed by short term stability studies.F1 formulation showed a much closer drug release profile value in comparison with reference standard. Therefore, F1 was considered to be better formulation with 81% of similarity factor compared to Reference Standard product and hence F1 is subjected to optimization. Optimized F1 batch is subjected to short term stability studies, content uniformity, assay and water content and is compared with Reference product. The results were found to be satisfactory and within the specification limit for both the temperature conditions. Thus, on the basis of our research findings it could be concluded that the proposed design for the development of immediate release tablets of fluffy, low soluble molecule was extensively evaluated and the process was demonstrated to be flexible enough for improving the rate and extent of drug release. Additionally, a cost-effective quality product can be delivered to the patients, which is equivalent to the reference standard.

Keywords: Pharmacopeia, formulation, standard, evaluation, oral, coating.

INTRODUCTION

Oral Drug Delivery System is one of the widely accepted pharmaceutical route of administration [1]. Tablet is a pharmaceutical oral solid dosage (OSD)form or solid unit dosage form, which consists of a combination of active substances and excipients, typically in the form of powders, pressed or compacted from powder to solid[2]. It should be noted that tablets are not only for oral purpose, but also for other routes like vaginal, parenteral (Highly dispersible tablets), etc[2,3].These tablets are formulated by various techniques like granulation and direct compression[4,5,6]. There are some defects which can occur as a result of poor processing or formulation quality like chipping, cracking, lamination, etc[7].There are various pharmacopeias for preparation & evaluation of tablet form of various drugs. Hepatoproctective drugs are considered as an essential pharmacological class of high importance [8-10].

MATERIALS AND METHODS

EVALUATION STUDIES

ORGANOLEPTIC PROPERTY

The drug is analyzed for organoleptic properties like taste, odour, color, etc.

PARTITION CO-EFFICIENT

Equal quantities of n-octanol (previously saturated with water) and distilled water was taken in a conical flask and add the drug. The mixture was shaken for 24 hours at 25°C in a shaker water bath. The two phases were separated carefully and drug content was analyzed. The experiment was carried out in triplicate.

UV SPECTROSCOPY

5 mg of drug was taken and acetonitrile was used as a solvent. The resultant solution was then scanned for the determination of λ max (absorption maxima) in the spectral range of 100-400 nm of ultra violet visible region.

DRUG-EXCIPIENT STUDIES

Drug excipient compatibility study was performed in which the drug excipient mixtures were observed for any physical changes and the observations are recorded in table 8.7. Initially API and individual excipients as placebo was taken. Then, Physical mixture of API and excipients was evaluated for Drug-Excipient Compatibility (DEC).

SOLUBILITY

It is performed using vortex mixer with (or) without Polysorbate-80 in case of immediate release tablets in various pH media. HPLC is used for analysis of drug.

LOSS ON DRYING

The drug was weighed (1g) and evenly spread in an aluminum tray and placed in the LOD assembly for the determination of its water and volatile substance content under the pre-set conditions of 105ºC for 3 minutes and then the observed LOD was compared with standard range (NMT 2 %).

ANGLE OF REPOSE

Angle of repose of granules was determined by Funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of powder cone was measured and angle of repose was calculated using the following equation.

$\theta = \mathbf{Tan^{-1}(h/r)}$

Where, h- Height of pile

r- Radius of the base pile

θ- Angle of repose.

PROCEDURE

The qualitative and quantitative composition of tablets is as follows in the following table:

- ✓ The drug (API), sodium starch glycollate and Microcrystalline Cellulose are sifted through #40, while, Magnesium stearate alone is sifted through #60 and are dispensed by clean spoons into vessel, which are calibrated and validated.
- ✓ The resultant mixture except magnesium stearate is blended via octagonal blender at 10 rpm for 10 minutes. Magnesium stearate is added for lubrication and blending is continued for another 5 minutes.
- ✓ Prepared blend was processed for compression using 7.6 mm X 7.4 mm, triangular, INT on one side & 10 on another side punches and dies in 16 stations tablet compression. Each tablet was punched with the total a weight of 160 mg.
- ✓ The tablets are spray coated using Novomix Yellow MR and is evaluated at later stages.

FRIABILITY

Tablets equivalent to 6.5g was weighed and placed in friability apparatus. The machine submits the tablets to the combined influence of shock and abrasion by using a plastic chamber that spins at 25 rpm, where the tablets are dropped from a height of 6 inches for 100 revolutions then the sample was weighed again. Percentage of friability should be not more than 1.0% and it should be calculated by following formula,

% Friability = Initial Weight – Final Weight / Initial Weight *100.

HARDNESS

Hardness tester (Electrolab) was employed for this test. Force required to break the tablet is determined in this testof 20 tablets was determined using digital hardness tester and the average hardness was calculated. It is expressed in N or kg/cm2.

DISINTEGRATION TEST

Disintegration test is performed using USP Disintegration apparatus at 37 ± 0.5°Cat a frequency of 28 to 32 cycles per minute, over a distance of 5 to 6 cm. This test is performed for at least 16-18 tablets.

DISSOLUTION STUDIES

The mobile phase consists of Trifluoroacetic acid and acetonitrile. Phosphate buffer is used as the dissolution medium. 20 µl of blank, standard preparation and sample preparation is injected into the chromatograph. The drug content is analyzed quantitatively using HPLC (Waters UV) at regular intervals.

SHORT-TERM STABILITY STUDIES

Accelerated Stability studies are conducted at given conditions (40°C/75%RH). After one month it is taken and tested for its description, pH, assay, related substance and water content. All these parameters are compared with the initial sample and also checked whether it complies with specifications or not only if it complies with specifications the batch pass the test.

RESULTS AND DISSCUSION

PRE-FORMULATION STUDIES

ORGANOLEPTIC PROPERTIES

Organoleptic properties of the drug (API) were observed as per monograph and was in compliance with USP.

PARTITION CO-EFFICIENT

The partition coefficient of the drug at 37° C was found to be 5.11 for the drug, reported value: 4.81. Therefore, it is confirmed that the drug is practically insoluble in water, which is well distributed in octanol. Hypothetically, it is assumed it has higher permeability in GI tract.

UV SPECTROSCOPY

The obtained spectrum was compared with standard API (195 nm) and confirmed that the drug shows maximum absorbance at 195 nm and was in good agreement with working standard, as shown in below figure:

DRUG-EXCIPIENT STUDIES

From the study, it can be confirmed, no extra peaks were observed in physical mixture and can be concluded that all the excipients are compatible with APIat 40°C/ 75% RH and RTit was found that excipients don't have interaction with API.

SOLUBILITY

The solubility of API in various physiological pH media (1.2, 4.5 and 6.8) was analyzed.The solubility of the drug was equally shows low solubility in all buffer media. So, Polysorbate 80 was selected in the increment of 0.04%, 0.06% and 0.08% to increases the solubility of the drug in medium. pH of media including Polysorbate-80 of different concentrations (0.04%, 0.06%, 0.08%) is 6.8.

LOSS ON DRYING

The LOD was found to be 1.42% and found in line with standard range of LOD given in the COA (NMT 2 %). According to the data and poorly soluble nature of the drug shows that the sample is less likely to absorb moisture which does not have any impact on stability issue related to moisture and shall be considered as safe to expose in high humid condition during process development.

ANGLE OF REPOSE

From the flow consolidation study, the value for angle of repose was found to be 32.15, which indicates that powder has good flow.

FINISHED PRODUCT STUDIES

FRIABILITY

The friability of prepared tablets are analysed as per monograph. The data obtained are given in graphical presentation as follows:

All the in-process parameters was evaluated and all parameters are equally good and were within the limits for the formulations F1-F5.Amongst the formulations, F1 exhibited a closer values for all the in-process parameters compare to the values of RLD.

HARDNESS

The hardness test of tablets was performed as per monograph. A control batch was included as a standard batch for comparison purpose. The data obtained for hardness test is given as follows:

Based on the given data, it is observed that the 2nd batch has the highest hardness level, meanwhile, 3rd has the lowest hardness property.

DISINTEGRATION TEST

The disintegration test was performed in 5 different batches and was compared with standard batch. The disintegration time taken for each batch is as follows.

By performing disintegration test, it is confirmed that concentration of Sodium Starch Glycollate and Magnesium stearate is inversely proportional to the disintegration time of the prepared tablet. The 1st batch (F1) is in compliance with standard batch.

DISSOLUTION STUDIES

The samples are subjected to dissolution in Phosphate buffer pH 6.8. The samples are withdrawn at successive intervals and analyzed for drug content using HPLC (UV waters).

Dissolution profile of reference product was faster in FDArecommended dissolution media (0.08% Polysorbate 80 in 50 mM sodium phosphate dibasic buffer, pH 6.8) with USP apparatus II (paddle) at 75 RPM paddle speed and 900mL media volume.From the above dissolution study it can be concluded that 0.08% Polysorbate 80 in 50 mM sodium phosphate dibasic buffer, pH 6.8 shall be an ideal dissolution media for the selected drug.F1 formulation showed a much closer release profile value. Therefore, F1 was considered to be better formulation with 81% of similarity factor compared to RLD product (100%).

SHORT-TERM STABILITY STUDIES

The 1st batch (F1) was selected as the ideal batch in compliance with standard batch. It is then optimized and is subjected to Short-term stability studies. The results of short term stability studies are as follows:

From the study, there is no significant changes were observed and found that all the parameters are within the limit and are stable.

SUMMARY AND CONCLUSION

Aim of the current research was to develop an Immediate Release Tablets, of robust quality equivalent to USP standard Reference Listed Drug (RLD), for the selected hepato-protective drug. The primary physico-chemical characterization (Physical description, Partition coefficient, pH, Spectral analysis) for the API were studied and confirmed. Further evaluation of RLD was performed for optimizing the standard reference values to be used while developing and optimizing various study formulations. The pre-formulation studies LOD, Solubility study, DEC, Flow and consolidation properties was performed for the API and excipients. The flow and consolidation properties studied for the drug and excipient blend indicates that the blend has a Good flow property, thus the blend was selected for tablet preparation by Direct compression method. After the initial pre-formulation studies, optimization process for the formulation variables were carried out by varying parameters involved in the formulation development. The parameters such as Blending time and Lubrication time were optimized to obtain desired blends assay value and blend uniformity. Optimization results showed that blending time of 10 min had a better blend uniformity and blend assay values as desired. Similarly, Lubrication time optimization performed for pre-optimized blended mixture with 60# mesh passed lubricant showed a desired blend uniformity and blend assay values after 5 min of blending time.

The drug-excipient concentration or ratio variation (Formulations F1 – F5), which has impact on dissolution and disintegration was studied for the formulation trials. Among the various formulations optimized, the F1 formulation with 8 mg Sodium starch glycolate and 1.6 mg Magnesium stearate exhibited the desired drug release profile. Based on the similarity factor for the formulations F1-F5 in comparison to RLD it was observed that formulations F2, F3, F4 & F5 exhibited a comparable amount of percentage release difference from the RLD value, whereas F1 formulation showed a much closer release profile value. Therefore, F1 was considered to be better formulation with 81% of similarity factor compared to RLD product. Thus, the optimized F1 formulation was further subjected to evaluate the content uniformity, assay and water content, to ascertain the stability of the formulation on storage, which were within the standard reference limit.

Short-term Stability studies performed for the optimized F1 Formulation for a time period of one month at room temperature and 40°C/75%RH. The results were found to be satisfactoryand within the specification limit for both

the temperature conditions. Thus, on the basis of our research findings it could be concluded that the proposed design for the development of immediate release tablets of fluffy, low soluble molecule was extensively evaluated and the process was demonstrated to be flexible enough for improving the rate and extent of drug release. Additionally, a cost- effective quality product can be delivered to the patients, which is equivalent to the reference standard.

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Table 1: Qualitative and quantitative composition of tablet

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**
	mg/ Tab				
API	10	10	10	10	10
Microcrystalline Cellulose PH102	140.4	142.4	138.4	140.5	140.3
Sodium Starch Glycolate	8	6	10	8	8
Magnesium Stearate	1.6	1.6	1.6	1.5	1.7
Novo mix Yellow MR	4.8	4.8	4.8	4.8	4.8
Purified Water	q.s	q.s	q.s	q.s	q.s
Total Weight (Coated)	**164.8**	**164.8**	**164.8**	**164.8**	**164.8**

Table 2: Disintegration test

Formulation Code	Disintegration Time (Mins)	RLD Disintegration time
F1	0' 42" – 0' 60"	0' 43" – 0'60"
F2	0' 47" – 0' 61"	
F3	0'37" – 0'62"	
F4	0' 41" – 0'62"	
F5	0' 44" – 0' 66"	

Table 3: Short term Stability studies

S. No	Tests	Limits	Initial	1st Month (40±2°C/75±5% RH)
1	**Description**	Pale yellow colour, triangular shape, INT on one side &10 on another side.	Pale yellow colour, triangular shape, INT on one side &10 on another side.	Pale yellow colour, triangular shape, INT on one side &10 on another side.
2	**Water content (w/w)**	NMT 8.0 %	5.1 %	6.52%
3	**Dissolution (% Drug Release)**	NLT 70% (Q) of Product is dissolved in 45minutes.	93%	91%
4	**Assay**	90.0% to 110.0%	100.5%	100.4 %
5	**Related Substance**			
	Impurity A	NMT 0.5%	0.092%	0.095%
	Impurity B	NMT 0.5%	0.322%	0.306%
	Impurity C	NMT 0.5%	0.019%	0.027%
	Unidentified Impurity	NMT 0.5%	0.169%	0.185%
	Total Impurity	NMT 2.0%	0.602%	0.613%

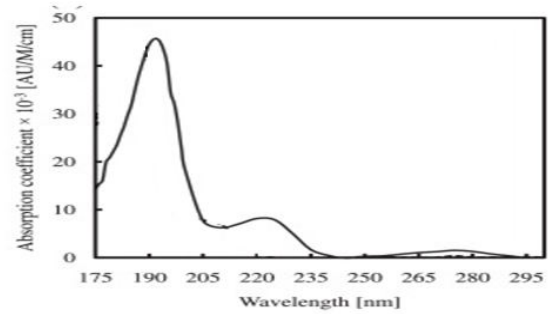

Fig.1. UV Spectroscopy of API

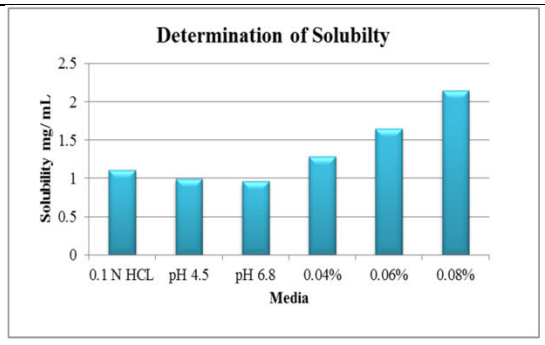

Fig.2. Solubility data of Active Pharmaceutical Ingredient (API)

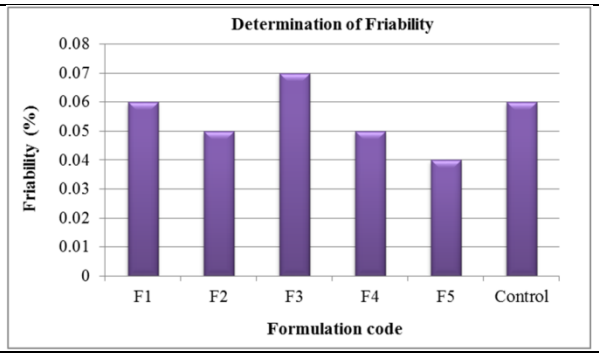

Fig.3. Graphical representation of Friability of prepared solid oral tablets

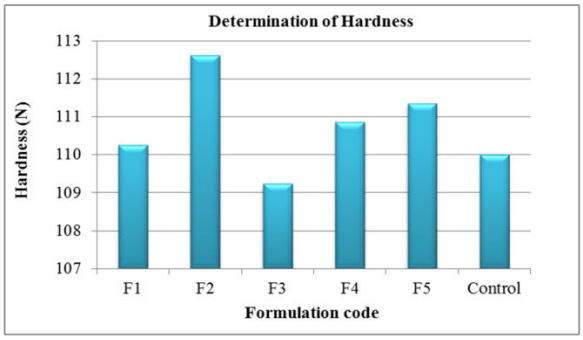

Fig.4.Graphical representation of Hardness of prepared solid oral tablets

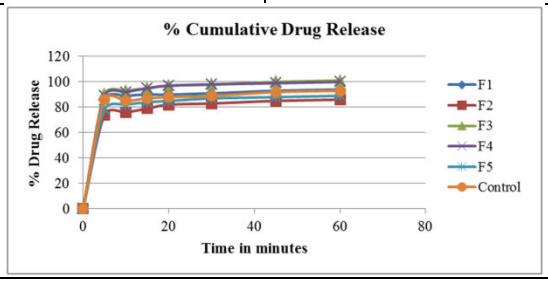

Fig.5. Graphical representation of Dissolution of various batches of prepared solid oral tablets

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RESEARCH ARTICLE

Equitable Detour Global Domination Number of Some Special Graphs

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ABSTRACT

A subset D of V(G) is a detour global dominating set if for each vertex of G is contained in a longest path between any pair of vertices in D and global dominating set. A detour global dominating set D of V(G) is called an equitable detour global dominating set if for each vertex $a \in V$ not in D, there exists a vertex $b \in D$ such that ab is an edge of G and $|deg(a) - deg(b)| \leq 1$.In this paper, we discuss the detour global domination number and equitable detour global domination number of graphs such as lollipop $L_{n,m}$,Windmill $Wd(n,m)$, Friendship F_n, Jellyfish J(n, m) and subdivision of Jellyfish $S(J(n,m))$.
Mathematical subject classification: 05C12, 05C70

Keywords: Detour global domination number, equitable detour global domination number

INTRODUCTION

By a graph G = (V, E), we consider a finite undirected connected graph without loops or multiple edges. The order and size of G are denoted by n, m respectively. The concept of Detour Global Dominating graphs was introduced in [3]. For underlying definition and results, see references.

Preliminaries

Definitions and Notations 2.1

- A lollipop graph $L_{n,m}$ is the graph obtained by joining K_n to P_m with a bridge.

- A windmill graph$Wd(n,m)$ is obtained by taking m copies of K_n with a vertex in common, where $n \geq 2$ and $m \geq 2$
- A friendship graph F_n can be obtained by joining n copies of C_3 with a common vertex.
- The jellyfish graph $J(n,m)$can be constructed from a 4- cycle a_1,a_2,a_3,a_4 by add an edge with a_1 and a_3 and appending n pendent edges to a_2 and m pendent edges to a_4.
- The subdivision of a graph$S(G)$ is obtained from G by a sequence of edge subdivision operations.

Theorem 2.2. For any connected graph G of order n. Then,
(a) Every equitable detour global dominating set of G contains its pendant vertices, full vertices and equitable isolates
(b) If the set D contains only pendant vertices, full vertices and equitable isolates is a $\gamma_{dng}^{e} - set$ of G. then D is the unique minimum $\gamma_{dng}^{e} - set$ of G.

Detour Global Domination and Equitable Detour Global Domination Numbers

Theorem 3.1. If $G \cong L_{n,m}$ then$\gamma_{dng}(G) = 2 + \left\lceil \frac{m-2}{3} \right\rceil$, where $n, m \geq 2$.

Proof: Let G be a lollipop graph with $V(G) = \{a_1, a_2, \ldots, a_n, b_1, b_2, \ldots, b_m\}$. For $j = 1\ to\ n-1, D_j = \{a_i, b_m /$ a_i is not attached by a path$\}$. Then D_j are detour sets of G and dominating set of complement of . But D_j are not a dominating set of . The vertex b_m will dominate only the vertex b_{m-1} in G and a_i will dominate all the vertices of K_n in G. Let D be a minimum dominating set of P_{m-2}. Therefore, $D_j \cup D$ is a γ_{dng} −set of G.

$\gamma_{dng}(G) = |D_j \cup D|$
$= |D_j| + |D|$
$= 2 + \left\lceil \frac{m-2}{3} \right\rceil$.

Theorem 3.2. If $G \cong L_{n,m}$ then $\gamma_{dng}^{e}(G) = 2 + \left\lceil \frac{m-2}{3} \right\rceil$, where $n, m \geq 2$

Proof: Let G be a lollipop graph with $|V(G)| = n + m$ and D be a $\gamma_{dng} -$ set of G. Then, for every vertex $a \in (V - D)$, there exists a vertex$b = N(a) \in D$ such $|deg(a) - deg(b)| = 0\ or\ 1$.Since there is no equitable isolated vertex in G. Hence D itself is a minimum equitable detour global dominating set of G and so $\gamma_{dng}^{e}(G) = |D| = 2 + \left\lceil \frac{m-2}{3} \right\rceil$.

Example 3.3. For the lollipop $L_{4,6}$, $\gamma_{dng}(L_{4,6}) = 4$ and $\gamma_{dng}^{e}(L_{4,6}) = 4$.
In Fig 3.2. $D_1 = \{a_2, b_2, b_4, b_6\}$, $D_2 = \{a_3, b_2, b_4, b_6\}$, $D_3 = \{a_4, b_2, b_4, b_6\}$ are the only three $\gamma_{dng} -$ sets of$L_{4,6}$ so that $\gamma_{dng}(L_{4,6}) = |D_1| = |D_2| = |D_3| = 4$. Also, the set D_1 itself is an equitable. Since $|\deg(a_1) - \deg(a_2)| = |4 - 3| = 1$, $|\deg(a_3) - \deg(a_2)| = |3 - 3| = 0$, $|\deg(a_4) - \deg(a_2)| = |3 - 3| = 0$, $|\deg(b_1) - \deg(b_2)| = |\deg(b_3) - \deg(b_2)| = |2 - 2| = 0$ and $|\deg(b_5) - \deg(b_6)| = |2 - 1| = 1$. Similarly, the sets $D_2\ and\ D_3$ are minimum equitable detour global dominating sets of G. Therefore, $\gamma_{dng}^{e}(L_{4,6}) = 4$.

Remark 3.4. If $n \geq 2, \gamma_{dng}(L_{n,1}) = \gamma_{dng}^{e}(L_{n,1}) = 3$

Theorem 3.5. If $G \cong Wd(n,m), n, m \geq 2$. then $\gamma_{dng}(G) = m + 1$.

Proof: Let G be a windmill graph $Wd(n,m)$ with $|V(G)| = (n-1)m + 1$ and $|E(G)| = m\left(\frac{n(n-1)}{2}\right)$. The graph $Wd(n,m)$as shown in Figure 3.3. Let $\{b_{i1}, b_{i2}, \ldots, b_{i(n-1)}, b\}$ be the vertex set of $i^{th}(1 \leq i \leq m)$ copy of K_n and b be a full degree vertex of G. Obviously, for $j = 1\ to\ n-1$, $D_j = \{b_{1j}, b_{2j}, \ldots, b_{(m-1)j} b_{mj}\}$ are some detour sets of G. Then D_j will dominate all the vertices in G. Also, they dominate all the vertices in $\bar{G}$ other than b. Since a vertex b dominates itself in $\bar{G}$. Therefore each $D_j \cup \{b\}$ is a $\gamma_{dng}(G) - set$ of G so that $\gamma_{dng}(G) = |D_j \cup \{b\}| = |D_j| + |b| = m + 1$.

Theorem 3.6. If $G \cong Wd(n,m)$ where $n,m \geq 2$ then $\gamma_{dng}^{e}(G) = m+1$.

Proof: Let G be a windmill graph $Wd(n,m)$. Then G has one full degree vertex say b and every vertex of G has degree $n-1$. Let D be a$\gamma_{dng}-$ set of G. Then $\gamma_{dng}(G) = |D|$. Let $a \in V-D$, then there exists a vertex $b \in D$ such that $ab \in E(G)$, $\deg(a) = n-1$ and $\deg(b) = n-1$ or $m(n-1)$. Therefore $|deg(a) - deg(b)| = 0$. Hence $\gamma_{dng}^{e}\big(Wd(n,m)\big) = |D| = m+1$.

Corollary 3.7. If $G \cong F_n$then $\gamma_{dng}(G) = n+1$ where $n \geq 2$.

Proof: Let G be a friendship graphF_n with$|V(G)| = 2n+1$and $|E(G)| = 3n$ edges. Let $\{a, b_{2i-1}, b_{2i}\}$ be the vertex set of $i^{th}(1 \leq i \leq n)$ copy of C_3. Then$G$ can be obtained by joining n copies of C_3 with a common vertex a. In a graph G the vertex a is adjacent to all the other vertices $\{b_1, b_2, b_3, \dots, b_{2n}\}$.Therefore. Every global dominating set of G must contains a vertex a. Since$a$ is an isolated vertex in $\bar{G}$. Then $D_1 = \{a, b_2, b_4, \dots, b_{2n}\}$ and $D_2 = \{a, b_1, b_3, \dots, b_{2n-1}\}$ are some detour sets and dominating all the vertices in G and $\bar{G}$so that $\gamma_{dng}(G) = n+1$.

Corollary 3.8. If $G \cong F_n$ then $\gamma_{dng}^{e}(G) = n+1$, where $n \geq 2$

Proof: Let G be a friendship graphF_n with$2n+1$ vertices $\{a, b_1, b_2, b_3, \dots, b_{2n-1}, b_{2n}\}$ and $3n$ edges and $D = \{a, b_2, b_4, \dots, b_{2n}\}$ be a $\gamma_{dng}-$ set of G. Then,for every vertex $b_{2i-1} \in (V-D)$, there exists a vertex $b_{2i} \in D$ such that $b_{2i-1}b_{2i} \in E(G)$, where $1 \leq i \leq n$. Since D is a dominating set of G. Also, $deg\,(b_{2i-1}) = deg\,(b_{2i}) = 2$ so that $|deg(b_{2i-1}) - deg(b_{2i})| = 0$. Therefore D itself is an equitable. Hence, $\gamma_{dng}^{e}(G) = n+1$,

Example 3.9. For the Friendship graphF_4, $\gamma_{dng}(F_4) = 5$ and $\gamma_{dng}^{e}(F_4) = 5$.

In Fig 3.4. $D_1 = \{a, b_2, b_4, b_6, b_8\}$, $D_2 = \{a, b_1, b_3, b_5, b_7\}$are $\gamma_{dng}-$ set of F_4 so that $\gamma_{dng}(F_4) = |D_1| = |D_2| = 5$. Also, $deg(b_1) = deg(b_2) = 2, deg(b_3) = deg(b_4) = 2$, $deg(b_5) = deg(b_6) = 2$ and $deg(b_7) = deg(b_8) = 2$. Therefore, $|deg(b_{2i}) - deg(b_{2i-1})| = 0$, for all i, $1 \leq i \leq 4$. Then D_1 and D_2 are itself equitable set of F_4 so that $\gamma_{dng}^{e}(F_4) = 5$

Theorem 3.10. If $G \cong J(n,m)$then $\gamma_{dng}(G) = n+m+1$ where $n,m \geq 1$

Proof: Let G be a Jellyfish graph $J(n,m)$. Let $\{a, b, c, d, a_1, a_2, \dots, a_n, b_1, b_2, \dots, b_m\}$ be the vertex set of G and $E(G) = \{ac, cb, bd, da, cd\} \cup \{aa_i, bb_j / 1 \leq i \leq n, 1 \leq j \leq m\}$. The set of all end vertices $D' = \{a_1, a_2, \dots, a_n, b_1, b_2, \dots, b_m\}$is a minimum detour set of G and dominating all other vertices in $\bar{G}$ but which is not dominating ser in G. SinceD' dominating only the vertices a, b not the vertices c and d. Therefore, D' along with any one of the vertices in C_4 is a minimum γ_{dng} −set of G. Hence $\gamma_{dng}(G) = |D' \cup \{c\}| = |D'| + |\{c\}| = n+m+1$.

Corollary 3.11. If $G \cong J(n,m)$ then $\gamma_{dng}^{e}(G) = n+m+3$, where $n,m \geq 3$

Proof: Let G be a Jellyfish graph $J(n,m)$ as shown in figure 3.5.

Let $D = \{a_1, a_2, \dots, a_n, b_1, b_2, \dots, b_m, c\}$ be a $\gamma_{dng}-$ set of G. Further the vertices a and b are equitable isolated vertices. Therefore $D \cup \{a, b\}$ is a minimum equitable detour global dominating set. Hence $\gamma_{dng}^{e}(G) = |D \cup \{a, b\}|$

$= |D| + \{\{a, b\}\}$

$= n+m+1+2$

$= n+m+1+3$

Example 3.12. For the Jellyfish graph $J(6,4)$, $\gamma_{dng}\big(J(6,4)\big) = 11$ and $\gamma_{dng}^{e}\big(J(6,4)\big) = 13$.

In Figure 3.6, The set $D = \{a_1, a_2, a_3, a_4, a_5, a_6, b_1, b_2, b_3, b_4, c\}$ is a $\gamma_{dng}-$ set of G and so $\gamma_{dng}\big(J(6,4)\big) = 11$. Then $D' = \{a_1, a_2, a_3, a_4, a_5, a_6, b_1, b_2, b_3, b_4, a, b, c\}$ is a minimum equitable detour global dominating set of G and so $\gamma_{dng}^{e}\big(J(6,4)\big) = 13$.

Remark 3.13. For any Jellyfish graph $J(n,m)$with $n = m = 1(or = 2)$ $then\ \gamma_{dng}\big(J(n,m)\big) = \gamma_{dng}^{e}\big(J(n,m)\big) = n+m+1$. If $n \geq 3$ and $m = 1(or = 2)$ then the equitable isolated vertex a must be included in any minimum equitable detour global dominating set. Hence $\gamma_{dng}^{e}\big(J(n,m)\big) = n+m+2$.

Theorem 3.14: For any subdivision of jellyfish graph $S(J(n.m))$,
$(i)\gamma_{dng}\left(S(J(n.m))\right) = n + m + 3.(ii)\gamma^{e}_{dng}\left(S(J(n.m))\right) = n + m + 4$ where $n, m \geq 2$.

Proof: $(\boldsymbol{i})$Let $S(J(n,m))$ be the subdivision of jellyfish graph as shown in Figure 3.7. Then $\left|V\left(S(J(n,m))\right)\right| = 2n + 2m + 9$ and $\left|E\left(S(J(n,m))\right)\right| = 2n + 2m + 10$. Let $D_1 = \{a_1, a_2, \dots, a_n, b_1, b_2, \dots, b_m\}$ be the set of all end vertices. Clearly every vertex of $S(J(n,m))$ lies on a detour joining a pair of vertices of D_1 and dominate all the vertices in $\overline{S(J(n,m))}$. Also, D_1 will dominate the set of vertices as $\{a_1', a_2', \dots, a_n' b_1', b_2', \dots, b_m'\}$. Therefore $D_1 \cup \{a, b, i\}$ is a minimum detour global dominating set of $S(J(n,m))$ so that $\gamma_{dng}\left(S(J(n,m))\right) = |D_1 \cup \{a, b, i\}| = n + m + 3$.

(ii) Let $D_1 = \{a_1, a_2, \dots, a_n, b_1, b_2, \dots, b_m\}$ be the set of all end vertices and $D_2 = \{a, b\}$ be the equitable isolated vertices. Then by theorem 2.2, the set D_1 *and* $D_2$are subsets of every equitable detour global dominating set also the set $D_3 = \{a_1', a_2', \dots, a_n' b_1', b_2', \dots, b_m'\}$ are equitably dominated by $D_1 \cup D_2$. Then,the vertices in $V(G) - D_3$ are equitably dominated by the vertices c and d. Therefore, $D = D_1 \cup D_2 \cup \{c, d\}$ is a minimum equitable detour global dominating set so that $\gamma^{e}_{dng}\left(S(J(n.m))\right) = |D|$
$= |S_1| + |S_2| + |\{c, d\}|$
$= n + m + 2 + 2$
$= n + m + 4.$

Remark 3.15. For subdivision of jellyfish graph $(J(1,1))$, $\gamma_{dng}\left(S(J(1.1))\right) = \gamma^{e}_{dng}\left(S(J(1,1))\right) = 5$

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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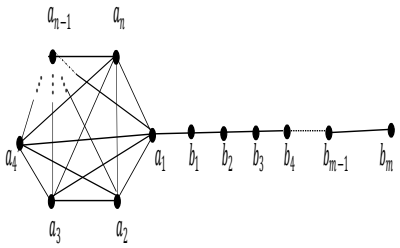

Figure 3.1- Lollipop graph $L_{n,m}$

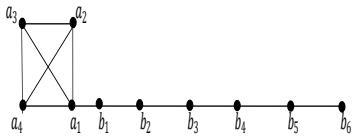

Figure 3.2- Lollipop graph $L_{4,6}$

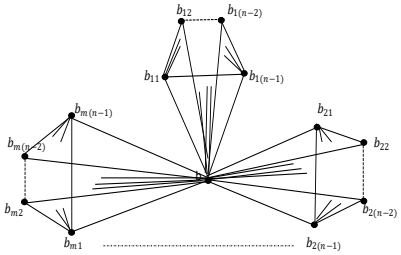

Figure 3.3- Windmill Graph $Wd(n,m)$

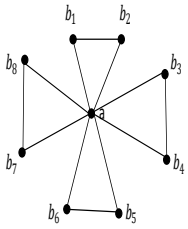

Figure 3.4- Friendship graph F_4

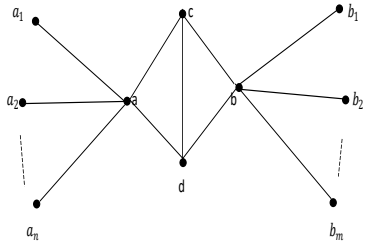

Figure 3.5- Jellyfish Graph $J(n,m)$

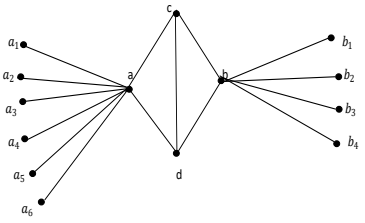

Figure 3.6- Jellyfish graph $J(6,4)$

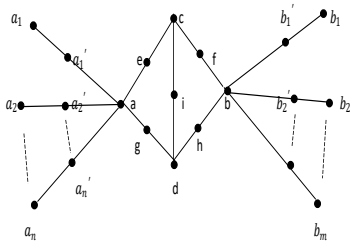

Figure 3.7- Subdivision of jellyfish graph $S(J(n.m))$

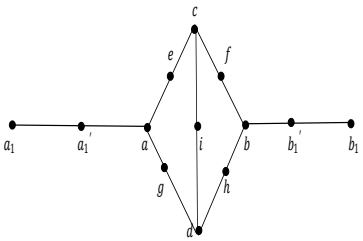

Figure 3.8. Subdivision of jellyfish graph $S(J(1.1))$

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REVIEW ARTICLE

A Review on Rotary Regenerators

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ABSTRACT

Energy recovery by using rotary regenerative heat exchanger commonly known as rotary regenerator has significant importance as it is economical and simple in construction. It is used as air preheater to preheat the air in thermal power plant, as a desiccant wheel for dehumidifying air and for heat recovery systems in buildings. Experimental and numerical works have been carried out by different researchers on rotary regenerators. Most of them have arrived at the conclusion that the performance of the rotary regenerative heat exchanger depends on various factors such as speed of rotor, period of rotation and combustion power. The factors which need to be considered for its numerical modelling are rotational speed, mass flow rate of fluids, geometrical size and shape, and pressure drop (Δp). In the present paper, discussion regarding the different numerical and experimental work on rotary regenerators in relation to heat transfer as well as their performance has been presented.

Keywords: Rotary regeneartor, heat transfer, fluid flow, matrix

INTRODUCTION

Heat exchanges are used extensively in thermal power plant which is one of the major sources of power generation in India. Besides this, it finds wide applications in air conditioning, chemical plants, and petrochemical industries. Different types of heat exchangers used in industries as a heat extraction medium. Among them regenerative heat exchanger or regenerator is most popular and worth mentioning. There are different designs of regenerative heat exchangers are used in industries. Out of them, the use of rotary regenerative heat exchanger has increased considerably due to its compactness, low cost, ease of maintenance and high efficiency.

Rotary regenerative heat exchangers or rotary regenerators consist of heat storage matrix with a lot of channels through which a fluid can flow and exchange heat energy. In one side of the matrix, the hot gas moves through, and

on the other side of the matrix, the cold gas. At a low speed, the matrix is constantly rotating. After switching side, the side of the matrix that has been heated up by the hot gas gives heat to the cold gas.

Rotary Regenerative Heat Exchanger Advancement

Alagic *et al.* [1] simulated a ljungstrom air preheater which is a rotary regenerative heat exchanger and carried out numerical analysis on heat transfer and fluid flow by using commercial software called "Comet" in Computational Continuum Mechanics (CCM) solver. The results of both one and three dimensional calculations were in good agreement with the field measurements. Mioralli and Ganzarolli [2] studied the heat transfer and fluid flow in a rotary regenerative heat exchanger with a constant pressure drop. They conducted scale analysis to determine the optimum porosity and maximum heat transfer.

Corsini *et al.* [3] created a virtual test rig of Ljungstrom air preheater using CFD based on the work of Molinari and Cantiano and used a series of metal plates as rotating matrix. They had got the results in the form of temperatures of primary and secondary air and pressure drop in a CFD environment using OpenFoam Library. The results were compared with the measured value of real power plant and found discrepancy of 3%.Cai*et al.* [4] carried out their work on minimizing leakage in rotary air preheater by using multiple seal technology both experimentally and numerically. They tested different seals starting from single to triple and found that triple seal was bettering in controlling leakage than double seal. The main parameters that affected air leakage were the flow expansion, inlet velocity at the seal gap entrance and the flow boundary conditions on the seal plate surface.

Ghodsipour and Sadrameli [5] numerically simulated a rotary regenerator and obtained results by solving mass, momentum and energy equations. The numerical results were compared with the experimental results obtained from a prototype and good agreement was observed. They concluded that the three important parameters that affected the regenerator performance were angular speed of rotor, hot air velocity and cold air velocity.

Ge *et al.* [6] developed a mathematical model for silica gel haloid compound desiccant wheel to predict the performance by considering the resistance of both solid and gas sides. The solutions of four governing equations including conservation of mass and energy in the air as well as in the desiccant material were numerically obtained. The important parameters which affect the performance of the desiccant wheel such as moisture removal and relative moisture removal efficiency were analysed for different values of flow rate and inlet temperature of process air. They had also simulated to obtain an optimal rotation speed to achieve the maximal moisture removal. The numerical results abstained were in good agreement with experimental results.

Narayanan *et al.* [7] designed a non-adiabatic desiccant wheel where the matrix consists of multiple channels that coated with desiccant material such as silica gel resulting in the simultaneous dehumidification and indirect cooling of air supply. The mass and energy conservation partial difference equations were solved numerically with the help of COMSOL Multiphysics version 3.5 to obtain results. They validated the results so obtained with the experimental results.

Zhang *et al.* [8] established a mathematical model of one-dimensional coupled heat and mass transfer to design and manufacture a honeycombed rotary desiccant wheel. They observed the existence of hump curve in the regeneration process which indicated a variation of air humidity ratio from duct entrance to duct exit inside the desiccant wheel. They also studied the effect of regeneration temperature and regeneration air velocity in order to determine the effectiveness of heat exchanger. The temperature and humidity profiles for both dehumidification and regeneration processes were verified with the experimental results and found good support.

Jonathan *et al.* [9] numerically optimized the thermal performance of rotary regenerative heat exchanger with a porous core. Finite volume method was used to maximize the heat transfer by taking both equilibrium and non-equilibrium model which was supported by scale analysis. It was found from numerical result that the efficiency of

rotary heat exchanger under local thermal equilibrium conditions was higher than non-local thermal equilibrium conditions. Two important design parameters of the porous core such as length and porosity had been optimized. The effects of the porosity distribution and differential periods between the hot and cold sides of rotary heat exchanger were also analysed.

Fu *et al.* [10] had made an investigation in the performance of honeycomb type rotary desiccant wheel by using different desiccant materials and found zeolite giving better performance than all others in terms of heat recovery. The effects of some crucial parameters like rotary speed, inlet velocity of fresh air as well as exhaust air on the performance of heat wheel were studied. Alhusseny and Turan [11] used porous media approach to analyse heat transfer and fluid flow in a rotary regenerator. They assumed local thermal equilibrium condition between fluid and solid phases for simulation. The values of two important input parameters of porous medium such as viscous resistance and inertial resistance were suitably selected. The impacts of different design parameters of the porous core on overall efficiency of the regenerator in terms of heat restored, pressure drop were investigated to improve the efficiency of regenerator. Stabat and Marchio [12] developed a numerical model of desiccant dehumidifiers to be used in building simulation tools. They described the model by Effectiveness-NTU method and compared the results to experimental as well as manufacturers' data for a wide range of operating conditions and found good agreement.

Sheer *et al.* [13] established a simulated model of rotary heat exchanger those which are used to preheat the inlet air to boiler in power plants. They proposed two types of model i.e rotating hood and rotating matrix that can be accommodated in simulation model. The input variables taken into account were rotational speed, leakage, blockage, and non-uniform inlet flow distribution. The heat transfer and pressure drop correlations were also determined experimentally for various plates of the heat exchanger. They also investigated the erosion caused by fly ash on thermal performance of heat exchanger and found little impact. Zheng and Worek [14] presented a simulation of combined heat and mass transfer process in a solid desiccant dehumidifier by using finite difference method. The numerical method used by them claimed to be of high-order accuracy, was numerically implicit and was unconditionally stable and took less time for doing performance simulation. They also investigated the effect of rotational speed on the performance of desiccant dehumidifier and obtained the optimum result. Frauhammer *et al.* [15] studied the effect of condensation and evaporation in a regenerative air-to-air heat exchanger by considering it as a moving boundary problem. They employed adaptive moving grid method to solve parabolic partial differential equations by using PDEX algorithm.Stiesch*et al.* [16] measured adsorption isotherms of a desiccant used as heat and mass exchanger in ventilated buildings. They used the program MOSHMX for their numerical analysis. The numerical results were found good agreement with the catalog information provided by the manufacturer.

Yilmaz and Buyukalaca [17] presented a mathematical model to calculate the effectiveness of rotary regenerators by considering different cell geometries and different speeds of revolutions of the rotary porous core. They used correction factor for rotational speed in their calculations which was not used earlier. The results were compared with the results obtained from experiment and found good agreement. However they did not taken into account the porosity of the rotary core which is an important parameter. Sanaye *et al.* [18] optimized the performance of a rotary air preheater in terms of effectiveness by using an optimization technique called genetic algorithm. The performance of the regenerator which was obtained by testing under optimized operating conditions was compared with the numerical results simulated by them and the results were within acceptable limit. Wang *et al.* [19] numerically simulated a tri-sectional air preheater which is used on most of the power plant in recent times. In order to solve the low temperature erosion problem, they determined the temperature distribution in the matrix and fluids of the regenerator. They used finite difference type semi analytical method for this purpose and the results were having good accuracy and better convergence.

Bu *et al.* [20] investigated the formation of Ammonium bisulfate (ABS) which could cause corrosion inside the rotary air preheater used in coal-fired power plant. They numerically simulated tri-sector air preheater of a 310 MW power plant in China by using porous media approach in FLUENT software. The effects of operating conditions such as

temperature difference between two fluids, mass flow rate of fluids and rotational speed of matrix on overall performance of the air preheater were studied. In addition, the temperature distribution inside the rotary air preheater was numerically obtained in order to investigate ABS deposition and corrosion.

Keydan *et al.* [21] simulated a three dimensional rotary air preheater using porous media approach. They used Moving Reference Method (MRF) to take into account the effect of rotational speed of the matrix. Local thermal equilibrium condition was taken for their simulation. The impact of several important parameters such as rotational speed of the matrix, mass flow rate of fluids, material of matrix and inlet air temperature on efficiency of the preheater were studied in detail. The effect of separator plate of the rotary core was also studied. Maharaj *et al.* [22] studied theoretically the leakage for an air preheater using an orifice flow analogy. They simulated a 2-D CFD model of air preheater having similar geometry with the one considered for theoretical approach to study the leakage numerically. A comparison was made between the two and it was found that theoretical calculated leakage was always lower than the CFD calculated leakage. Further they developed a CFD model of an actual air preheater to investigate leakage by introducing a correction factor.

Ozdemir and Serincan [23] used rotary regenerative heat exchanger in flue gas desulphurization system. They modelled using porous media approach in CFD using ANSYS-FLUENT. The heat transfer coefficient was obtained using a single channel model. The performance was analysed by taking heating cycle and cooling cycle for convenience. The matrix was composed of sinusoidal corrugated ducts which allowed the flow only in axial direction. The heat transfer coefficient and resistance coefficients of the porous media such as viscous and inertial were calculated from single channel analysis. The numerical results obtained were compared with the analytical results on effectiveness. The results obtained were presented as the effect of different operating parameters on the performance of regenerator. Smith and Svendsen [24] presented an experimental model of a plastic rotary heat exchanger which was used for single room heating application with polycarbonate honeycomb with small circular channels as matrix. The experimental set up was fabricated inside a guarded hot box to prevent leakage and temperature efficiency was more than 80 %. Zhang *et al.* [25] presented a computational fluid dynamics model of quad-sectional air preheater to control the wall temperature for 300 MW circulating fluidized bed (CFB) boiler. They studied the three dimensional temperature distribution, heat flux and heat transfer distribution of both working fluid and heating surface by using FLUENT software. They also investigated the formation of low temperature corrosion on heating surface of air preheater.

Akbari *et al.* [26] conducted experimental analysis on rotary heat exchanger for waste heat recovery for the air jet impingement food dryer. They used zigzag shape thin aluminium sheet as matrix. The results obtained revealed that increasing the rotational speed of the matrix and discharge flow result in decrease of both the outlet temperature of the hot fluid and the efficiency of the heat exchanger. Connor *et al.* [27] experimentally tested a rotary desiccant wheel consisting of radial blades coated with silica gel to reduce the pressure drop and regeneration temperature for desorption. They had observed that there was a reduction in pressure drop, regeneration temperature as well as relative humidity by using silica gel as desiccant material in comparison to powder coating. Nourozi *et al.* [28] used mechanical ventilation with heat recovery (MVHR) systems to recover heat from waste water for preheating cold supply air so as to reduce defrosting. The experimental results showed that there was a reduction in defrosting need. They had also simulated the performance by using TRNSYS software. Azamov and Bekimov [29] presented a mathematical model of rotary regenerative air preheater. They used nozzle to spray hot flue gas which was used to heat air inside the air preheater. Due to the complexity of heat exchange process in between nozzle, gas and air, the proposed model was based on averaging the quantities associated with heat exchange process in both spatial coordinates and time interval,

Wang *et al.* [30] carried out their experimental work on rotary air preheater with honeycomb ceramics and metal corrugated plates as matrix materials. They used a wind tunnel with a bi-directional switching valve to flow

alternately hot and cold fluid over the matrix and found that there was an increase in outlet air temperature as well as effectiveness while a reduction in pressure drop for metal heat transfer element.

Chen *et al.* [31] made an investigation on corrosion and ash deposition by taking samples from a coal fired power plant. They used X-ray fluorescence, X-ray diffraction and scanning electron microscope for testing the deposited samples and concluded that sulphuric acid had more impact both on the formation of corrosion and ash deposition rather than ammonium bisulphate. Nair *et al.* [32] presented a numerical model of rotary heat exchanger by using finite difference method to calculate heat exchanger effectiveness. They considered the dispersion of fluids in axial direction as well as longitudinal conduction of matrix for prediction of performance of heat exchanger. Butrymowicz *et al.* [33] presented a single blow technique for measurement of heat transfer coefficient of rotary regenerative heat exchanger. They obtained the average heat transfer coefficient by comparing the temperature profiles predicted from theoretical model with that of experimental results obtained by carrying out the experiment inside a wind tunnel.

Bogumił Bieniasz [34] conducted experimental investigation on mass transfer in rotary regenerator by using NaOH based electrolyte. They measured mass transfer coefficient in a rotor made of corrugated sheets consisting of number of ducts of different cross section and studied the effect of baffle shape on intensity of mass transfer. Jedlikowski *et al.* [35] investigated the formation of frost in rotary heat exchanger for high speed rotor conditions and stated that rotor speed had a significant effect on heat exchanger effectiveness as well as frost formation. They studied heat and mass transfer by taking dry and wet modes of heat exchange and three main zones of heat exchanger: 'dry', 'wet' and 'frost' described on the basis of temperature of matrix surface. The developed mathematical model based on ε-NTU method was validated experimentally.

CONCLUSION

Findings from literature review have shown that substantial numerical simulation work on regenerative rotary heat exchanger has been carried out by different researchers by applying different techniques. However not so much experimental work has been done due to the difficulty in fabricating experimental set up. The occurrence of practical problems like fouling, frosting and leakage needs more investigation. Throughout the literature, it is found that the applications of rotary regenerators are not limited to air preheater or gas turbines. It can be used for energy recovery applications in desiccant wheel, air conditioning and buildings.

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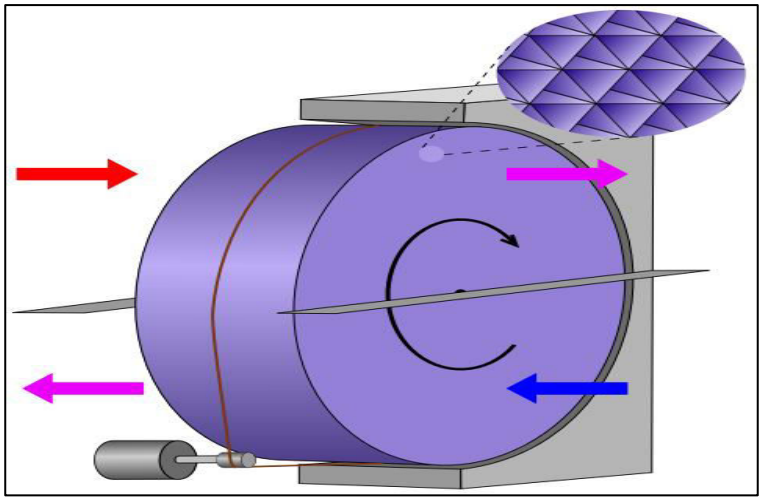

Fig 1: Rotary Regenerative Heat Exchanger

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RESEARCH ARTICLE

Studies on Germination and LD_{50} by Induced Chemical Mutagenesis in Tomato (*Lycopersicon esculentum* Mill.)

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ABSTRACT

Tomato (*Lycopersicon esculentum* Mill.) is one of the most commercial and nutritional important vegetable crops belongs to the night shade family Solanaceae cultivated in tropical and sub-tropical regions. Mutation breeding is an important tool to develop new varieties by using physical and chemical agents for crop improvement for cultivar. In addition, mutation breeding is one of the encourage options to increase the genetic diversity and achieve speedy crop development. In this present investigation, to assess the efficiency and effectiveness of chemical mutagens; Ethyl Methane Sulphonate (EMS), Diethyl Sulphate (DES) and Sodium Azide (SA) using different concentration. The LD_{50} value and germination percentage was noted to each group of treatment. According to results the LD_{50} was observed in 30mM of EMS, 20 mM of DES and 30 mM of SA.

Keywords: *Lycopersicon esculentum*, EMS, DES, Sodium Azide, Mutation Breeding, Seed germination and LD_{50} Value.

INTRODUCTION

Tomato (*Lycopersicon esculentum* Mill.) is one of the most commercial and nutritional important vegetable crops belongs to the night shade family Solanaceae, and it originate in South America [1,2] but first domesticated in Mexico and now widely cultivated in tropical and sub-tropical regions [3,4]. The tomato is an annual plant, commonly growing up to 100-200 cm height, with a weakly stem that usually struggles over other plants. The multiplication of good grade and viable tomato seedlings is the most extensive factor in the successful cultivation and yield of tomato

[5].Tomato is a protective food because it provides large amount of nutrients like β-carotene, lycopene, vitamin C and flavonoids. In addition to that tomato very familiar, because the presence of lycopene's and it have good anti-oxidative activities and anti-cancer functions [6].The comprehensive need for tomatoes increased excessively in recent years due to their diverse utilization in raw, cooked and processed food as well as their heavy nutritional values [7].Tomato has the richest source of vitamin A, B1 and C; and also the minerals like Fe, K, S, and P as well as flavonoids, carbohydrates and phenolic compounds [8,9].

Mutationis the great tool to study the function and nature of genes and thus producing raw materials for genetic improvement of economic crops [10]. A lot of mutagenic agents were used to induce favourable mutations at high prevalence; ionizing radiation, such as x-rays, gamma-rays as well as chemical mutagens for inducing variation is well established [11].Mutation-assisted development of crops has presently been enhanced by the doubled haploids and molecular markers. Tomato is a good illustration of the prosperous utilization of mutations affecting important genes for plant breeding [12]. Mutation breeding is an important tool to develop new varieties by using physical and chemical agents for crop improvement for cultivar [4].Induced mutagenesis as a breeding approach for the development of tomatoes had been explored through contrast studies [13].Mutation breeding is one of the advanced breeding methods in plant production. It is significant to different fields like Plant Morphology, Cytogenetic, Plant biotechnology and also Molecular biology, etc.

Mutation breeding has become increasingly widespread in advanced times as a powerful tool for crop development [14]. Induced mutagenesis as a breeding approach for the development of tomatoes had been explored through contrast studies [13]Mutation of many types can be clearly identified in tomato for their phenotype, because it functions like a basic diploid. More sufficient are alteration of form, size, colour and leaf venation also height and number of fruits per plant [15, 16].In India, Nearby 20 mutant varieties of tomatoes are introduced by through induced mutation [17]. Chemical mutagenesis is one of the most powerful and comfortable approaches used in distinct plant species. In tomatoes, EMS and Sodium azide has been used to chemical mutagens. The Ethyle Methane Sulphonate (EMS) is the maximum and universally used chemical mutagen in plants because of its immense capability at inducing point mutations and deletions in the chromosomal segments [18]. In tomato, EMS have been shown to production of both morphological differentiations and desired trait developments like disease resistance, fruit quality, and male sterility [19, 20]. In many cases, EMS mutagenesis initiated powerful where other conventional tomato breeding [5]. In this present investigation an attempt evaluation of LD_{50} values using chemical mutagenesis in tomato.

MATERIALS AND METHODS

Seed Collection and Mutagenic Treatments

The healthy seeds of *Lycopersicon esculentum* Mill. (PKM 1- variety) were taken from Tamil Nadu Agricultural Research Institute (TNAU) Coimbatore. Mutagens employed Chemical mutagens namely Ethyl Methane Sulphonate (EMS), Diethyl Sulphate (DES) and Sodium Azide (SA) were used at various concentrations to induced mutagenesis. The seeds were pre-soaked in distilled water for 6 hours in order to make then relatively more sensitive to mutagenic action. Pre-soaked seeds were treated with different concentration viz., 10, 20, 30, 40, and 50mM of Ethyl Methane Sulphonate (EMS), Diethyl sulphate (DES) and Sodium Azide (SA) solution for 4 hours with repeated stirring.After treatment, seeds were thoroughly washed in running tap water for 8-10 times to remove the residuals of the chemicals. Untreated seeds of *Lycopersicon esculentum* Mill.PKM1 variety was pre–soaked in distilled water for 4 hours and used as control. After pre-soaking, the seeds were sown in the petri plates.

LD_{50} values and Percentage Seed Germination

The LD_{50} is a measure of the lethal dose of chemicals. The LD_{50} was observed by the amount of material, given all at once, which caused the death of 50% of plants treated with chemical mutagen in seedlings.

Seed germination (%)

The seeds of each treatment along with control were placed on absorbent cotton- wet petridishes. For each treatment three replicates were studied and the number of seeds germinated on the 7th day was counted and the germination percentage was calculated. Based on the reduction of 50% seed germination, the LD_{50} value were fixed and the three treatments of EMS DES and SA around LD_{50} value for further studies.

$$\text{Germination (\%)} = \frac{\text{No. of seeds germinated}}{\text{No. of seeds sown}} \times 100$$

RESULTS AND DISCUSSION

Seed Germination

The plant that grows from seed was considered seed germination. The seed germination data on *Lycopersicon esculentum* Mill. PKM 1 Variety is given in the table. The present investigation focused on induced chemical mutagenesis on *Lycopersicon esculentum* Mill. Variety PKM 1 treated with three different mutagens in various concentrations for induction of mutation. The seed germination percentage of various mutagenic treatments under the laboratory in-vitro conditions exposed that, the seed germination percentage was decreased with increasing concentrations of EMS, DES and SA. The percentage of seed germination was high in EMS (30mM 40%), DES (20mM 55%) and (30mM 45%). Based on the seed germination percentage on the 7thDay, the LD50 values were fixed at 30mM of EMS, 20mM of DES and 30mM of SA.

While treatments with chemical mutagens EMS doses higher than 32mM were also proved to be lethal [21]. The results are similar to those of in *Capsicum annum* L. [22]. The result was supported by the previous work in cluster bean [23]. LD50 value for germination ranged between 51.3% and also in tomato and okra plant germination [24]. The results indicate that, percent of seed germination decreased with increasing concentration of EMS in chick pea [25]. The result was indicate that, seed germination percentage was decreased with increasing concentration of DES in Foxtail Millet [26]. EMS, DES and SA treatment reported in different crops such as soybean, Mung beans and LD 50 value was observed in 30mM of SA in Tomato [27].

CONCLUSION

The tomato seed germination was decreased by increasing the concentration of Ethyl Methane Sulphonate (EMS), Diethyl Sulphate (DES) and Sodium Azide (SA). From the present study, it is give up those lower concentrations of mutagens could be suitable for inducing genetic variability in the natural gene pool of this vegetable crop. Among the different concentration of chemical mutagen 30mM of EMS, 20mM of DES and 30mM of SA were founded as a threshold dose for further investigation.

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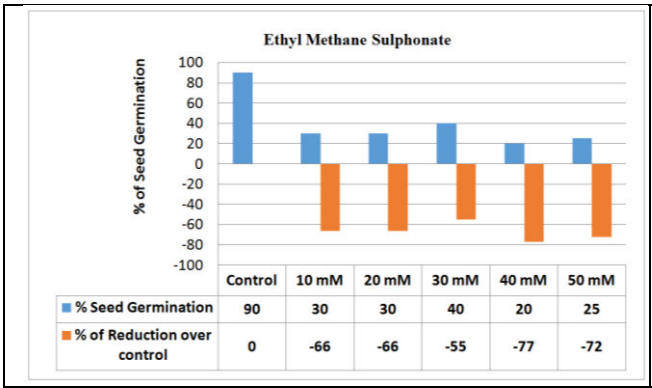
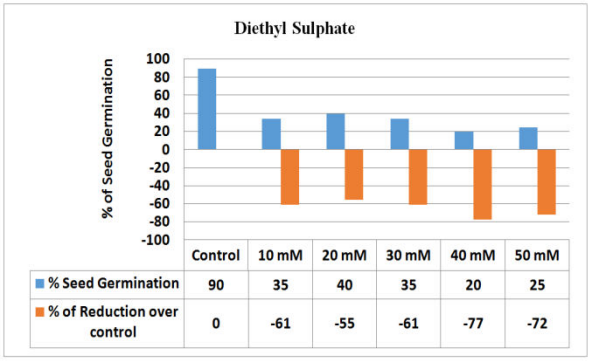
Table 1. Determination of LD_{50} for EMS, DES and SA on *Lycopersicon esculentum* Mill.

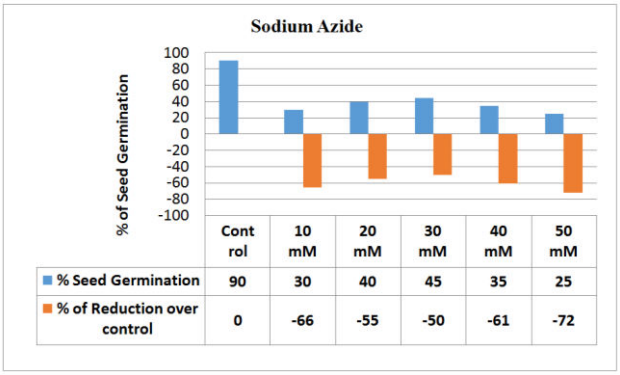
Mutagents	Treatments Con. (mM)	Number of Seed Sown	Number of Seed Germination	Percentage of Seed Germination	Percentage of Reduction over control
Control		20	18	90	00
EMS	10 mM	20	6	30	-66
	20 mM	20	6	30	-66
	30 mM	**20**	**8**	**40**	**-55**
	40 mM	20	4	20	-77
	50 mM	20	5	25	-72
DES	10 mM	20	7	35	-61
	20 mM	**20**	**8**	**40**	**-55**
	30 mM	20	7	35	-61
	40 mM	20	4	20	-77
	50 mM	20	5	25	-72
SA	10 mM	20	6	30	-66
	20 mM	20	8	40	-55
	30 mM	**20**	**9**	**45**	**-50**
	40 mM	20	7	35	-61
	50 mM	20	5	25	-72



Graph 1: Determination of LD_{50} for EMS on *Lycopersicon esculentum* Mill.



Graph 2: Determination of LD_{50} for DES on *Lycopersicon esculentum* Mill.



Graph 3: Determination of LD_{50} for SA on *Lycopersicon esculentum* Mill.

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REVIEW ARTICLE

Disintegrants: Understanding the Science behind Disintegration

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ABSTRACT

Disintegrating agents is a substance or mixture of substances added to tablets to facilitate its break up or disintegration. The active constituents must be released from the tablet as efficiently as possible to allow its rapid action. Hence the therapeutic action is based on the amount of drug released from the tablet, these disintegrants which allows rapid disaggregation of solid in to solution and followed by which absorption of the drug takes place. Most of the conventional and in novel preparation the impact of disintegrating agents had given a new dosage form such as rapid disintegrating tablets and mouth dissolving tablets. By fair choice of the disintegrating agents which has a greater impact in the final formulation to enhance the drug bioavailability.

Keywords: Disintegrants, Superdisintegrant, Disintegration, Mechanism, Natural.

INTRODUCTION

The solid dose forms, like tablets and capsules, swish match the foremost widespread technology to orally perform the active pharmaceutical ingredients (API) to the patient. at intervals this cluster disintegrating tablets establish out and away the majority of pharmaceutical merchandise. By selecting correct chemical and physical properties tablets are often developed to either modified release their API at once following oral administration (immediate modified release tablets) or to vary the drug modified release profile with the aim to realize or improved therapeutic effectuality, reduced toxicity, and improved patient compliance and convenience changed modified release tablets [1]. Immediate-release tablets area unit designed to completely disintegrate and dissolve upon exposure to physiological fluids at intervals at low amount of your time (2.5 to ten min) [2]. Such a quick disintegration is even additional vital for orally dispersible tablets, that area unit designed to disintegrate within the mouth in fewer than minutes before swallowing [3]. Such formulations area unit significantly vital wherever a fast onset of action is

desired, e.g. for analgesics or to change increased bioavailability of a poorly soluble drug substance [4]. In distinction, in changed modified release tablets the API modified release could also be designed to be steady so as to realize sluggish and sustained dissolution. Such modification of the drug modified release are often deliver the goods this one by embedding the API in a very chemical compound matrix that dissolves or swell at a gradual rate than the drug or by suggests that of a correct chemical compound coating that acts as a mass transfer limiting barrier. it's common follow to estimate the in-vivo performance of a drug product on its in-vitro drug modified release profile by establishing empirical in-vivo in-vitro correlations (IV, Ivc) throughout the pharmaceutical development. However, such empirical dissolution models have variety of inherent drawbacks, as well as that

i. The clarification of the underlying mass transport mechanisms isn't possible;
ii. Not one characteristic parameter of the dose type is comparable to the intrinsic dissolution rate of the drug;
iii. The generality of such experimental models is proscribed. Therefore, these studies do end in incomplete method and merchandise understanding [5].

In the majority of cases, the therapeutic dose of a drug is comparatively minute and thus the API has got to be mixed with correct excipients to realize a desired fill volume that permits for compression of the powder mixture into a fitly sized pill [6]. Properties of the API, like little particle size and needle like morphology will result in process limitations like poor flow ability difficulties with mixing additionally as undesirable adhesion to surfaces like pill punches or feeder walls [7]. These problems area unit addressed by choose associate degree applicable process route or by adding agents like glidants, lubricants or surfactants [8]. The admixture of such excipients is crucial to method most Apis and to assure a high product quality [9]. However, embedding the drug in a very advanced matrix usually reduces its bioavailability, and, within the case of immediate modified release tablets, it always delays the onset of dissolution. Disintegration agents area unit thus superimposed to the formulation, that promote the breakup of the pills into minute granules associate degreed their constituent particles and so change a faster liberation of the drug particles from the tablet matrix resulting in an raise in area for ulterior dissolution. the foremost wide used disintegrants area unit artificial polymers like crospovidone (XPVP), croscarmellose metal (CCS) and metal starch glycolate (SSG).

providing in immediate modified release tablets disintegration could be a necessary condition for dissolution, the disintegration performance has associate degree straight impact on the therapeutic impact of the medication and should be confirm, and ideally quantified, mistreatment above all designed disintegration tests. The disintegration processes is associate degree integral step in making certain, and so enlarge, the bioavailability of the API from the bulk of solid dose forms. With the exemption of diffusion controlled matrix system, in tablets the wetting and ulterior disintegration of the compact is that the opening towards the liberation of the API from the dose type. while not disintegration solely the API on the point of the surface of the pill would be ready to dissolve and therefore the consistent and full disintegration of the pill upon exposure to the dissolution medium is of important importance to realize a homogenous clinical performance of the dose type [10].

Ideal characteristics of disintegrants [11,12].

- Good association capability
- Good molding flow properties
- Poor solubility
- Poor gel formulation
- No tendency to make complexes with the medicine
- Good mouth feel

Method of addition of disintegrants [13,14].

Disintegrants area unit essentially superimposed to pill granulation for as a result of the compressed pill to separate or disintegrate once placed in binary compound surroundings. There area unit 2 ways of addition disintegrating agents into the pill • Internal Addition (Intra-granular) • External Addition (Extra-granular)

Internal Addition (Intra-granular)[15,16]

In wet granulation methodology, the disintegrants is superimposed to various excipients by wetting the powder with the granulating fluid. Thereby, the disintegrants is integrated at intervals the granules. In dry granulation methodology, the disintegrants is superimposed to various excipients by press the powder between the rollers. in a very pc optimized testing, the study show the impact of integrated a disintegrants, croscarmellose metal, intragranularly, further granularly or distributed equally between the 2 phases of a pill during which associate degree inadequately soluble drug ingrained a minimum of ninety two.5% of the formulation. The results analyze by suggests that of a typical quadratic response surface model recommend that, tablets with the similar total concentration of crosscarmellose metal dissolve at a quick rate once the super disintegrants is enclosed intragranularly. Pill crumbliness isn't have an effect on by the tactic of disintegrants incorporation.

External Addition (extra granular) [17, 18]

In each dry and wet granulation technique, the disintegrants is value-added to the granules throughout dry addition before compression. The impact of integrate of superdisintegrants (croscarmellose metallic element, metallic element starch glycolate and crospovidon) on dissolution of 3 model medicine with numerous binary compound solubility (carbamazepine, anodyne and cetrizine HCl) from their numerous pill formulations by wet granulation was studied. it's well-tried that crospovidone is effective in up the dissolution of the medicine in additional granular mode of addition looks to be the simplest mode of incorporation, moot of the solubility of the most pill part.

Mechanism of disintegration [19, 20]

The mechanism by that the tablets square measure broken into tiny items and so produces a unvaried suspension relies on

a) Porosity and surface tension
b) Swelling
c) Heat of wetting
d) Due to disintegrating particle/particle repulsive forces
e) Deformation recovery
f) Due to modified release of gas
g) Chemical reaction(acid base reaction)
h) By protien reaction

Porosity and surface tension (Wicking) [21, 22]

Effective disintegrants that don't swell square measure believed to impact their disintegrating action through consistence and surface tension. The pill consistence produces pathways for the penetration of fluid into tablets. after we place the pill into correct binary compound medium, the medium penetrates into the pill and replaces the air adsorbable on the particles, that weak the building block bond and breaks the pill into fine particles. Water uptake by pill depends upon hydrophilicity of the drug and excipients tableting conditions. For these styles of disintegrants maintenance of porous structure and tiny interfacial surface tension towards binary compound fluid is critical that helps in disintegration by making a hydrophilic system round the drug particles. It shows the disintegration of pill by swelling and wicking mechanism

Swelling [23, 24]

Although water penetration may be a needed initiative for disintegration, swelling is maybe the foremost wide accepted mechanism of action for pill disintegrants. Particles of disintegrants swell on forthcoming in touch with appropriate medium and a swelling force develops that ends up in cut of the matrix. Tablets with high consistence show poor disintegration because of lack of adequate swelling force. On the choice hand, comfortable swelling force is exerted within the pill with low consistence. it's worthy to notice that if the packing fraction is extremely elevated, fluid is unable to penetrate within the pill and disintegration is once more cut down

Heat of wetting [25, 26]

Ex alternative mic (heat generation) or end alternative mic (heat absorption) interactions square measure manifest by materials on interaction with water. Ex alternative mic properties square measure ascertained once disintegrants act with the binary compound medium. the warmth generated will cause localized stress connected with the enlargement of air preserved within the compact and this will in theory aid compact disintegration. Examined H changes for various disintegration

However, some researchers counseled that the quantity of warmth generated by wetting is very tiny and will not be significant to cause effective development of the entrapped air within the compact to bring on its cut. One analysis study conjointly opined that if heat generation was a crucial mechanism of pill disintegration, then cut would have occurred throughout compaction or ejection as significant heat was created throughout the compression cycle. but some researchers counsel that ascertained that the augmented temperature of the binary compound medium didn't essentially enhance the disintegration method in some pill formulations. Moreover, end alternative mic properties square measure exhibit by a number of the disintegrants. it's necessary to the study heat of interaction mechanism to determine the extent of its influence and if a thermodynamical model may well be developed to clarify its role within the pill disintegration method. To date, current literature and analysis work haven't considerably tried this mechanism of action.

Due to disintegrating particle/particle repulsive forces[27,28]

This is an alternative mechanism of disintegration that try and justify the swelling of pill created with non swellable disintegrants. in line with the particle repulsion theory, water penetrates into pill through hydrophilic pores and an everyday starch system is formed which will convey water from one particle to consecutive, impart a big hydrostatic pressure. The water that penetrates between starch grains thanks to its affinity for starch surface, thereby breaking atomic number 1 bonds and various forces holding the pill along. The electrical repulsive forces between particles square measure the mechanism of disintegration and water is needed for it. analysis found that particle repulsion force is secondary to wicking.

Deformation Recovery [29, 30]

It had well-tried that in pill compression, disintegrated particles get unshapely and these unshapely particles get into their traditional structure after they are available in contact with binary compound media or water. sometimes, the swelling capability of starch was improved once granules were extensively unshapely throughout compression. This increase in size of the unshapely particles produces a breakup of the pill. this might be a mechanism of starch and has solely recently begun to be studied. Starch grains square measure usually thought to be “elastic” in nature which means that grains that square measure unshapely harassed can come to their original form once that pressure is removed .But, with the compression forces concerned in tabulating, these grains square measure believed to be unshapely a lot of for good and square measure aforementioned to be “energy rich” with this energy being free upon exposure to water. In various words, the power for starch to swell is higher in “energy rich” starch grains than it's for starch grains that haven't been unshapely harassed.

Due to modified release of gases [31, 32]

Carbon dioxide free inside tablets on wetting because of interaction between Bicarbonate and carbonate with acid or hydroxyl acid. The pill disintegrates because of generation of pressure inside the pill. This effervescent mixture is employed once chemist must formulate terribly quickly dissolving pills or quick disintegrating tablet. As these disintegrants square measure sensitive to tiny changes in wetness level and temperature, strict management of atmosphere is needed throughout producing of the tablets. the bubbling mix is either value-added right away before compression or is value-added in to 2 separate fraction of formulation.

Chemical reaction (acid base reaction) [33, 34]

The pill is quickly broken apart by internal liberation of carbonic acid gas in water thanks to interaction between hydroxyl acid and acid (acids) with metallic element carbonates or bicarbonates (bases) in presence of water. The pill disintegrates thanks to generation of pressure at intervals the pill. thanks to liberation in carbonic acid gas gas, the dissolution of active pharmaceutical ingredients in water further as style masking result is increased. As these disintegrants are sensitive to tiny changes in wetness level and temperature, strict management of atmosphere is needed throughout preparation of the tablets. the bubbling mix is either superimposed right away before compression or is superimposed in 2 separate fraction of formulation. the bubbling mix is superimposed right away before compression or is superimposed into 2 separate fraction of formulation.

By protein reaction [35, 36, 37]

Here, enzymes presents within the body act as disintegrants. These enzymes Destroy the binding action of binder and helps in disintegration. it's believed that no single mechanism is accountable for the action of most disintegrants. But rather, it's additional probably the results of inter-relationships between these major mechanisms. The classical example of the earliest proverbial disintegrants is Starch. Corn Starch or Potato Starch was recognized as being the ingredient in pill formulations accountable for disintegration as early as 1906 (even though' pill disintegration was itself not given abundant importance in pill formulations till abundant later). Until fairly recently, starch was the sole excipient used as a disintegrants. To be effective, corn starch should be employed in concentrations of between 5-10%. Below 5%, there's insufficient “channels” accessible for wicking (and ulterior swelling) to require place. Above 10%, the hardness of starch makes it troublesome to compress tablets of adequate hardness. Though the association between bioavailability of drug and pill disintegration took it slow to become appreciated, it's currently accepted that the role of the disintegrants is extraordinarily necessary.

Method of Incorporation disintegrants [38, 39]

The incorporation of disintegrants within the indefinite quantity forms ar in the main of 2 types:

a) Direct compression
b) Wet Granulation

Direct compression [40]

Direct compression could be a widespread selection as a result of it provides the shortest, simplest and least advanced thanks to turn out tablets. The manufacturer will mix associate API with the excipient and therefore the material, followed by compression that makes the merchandise simple to method. No extra process steps are required needed. Moisture or heat sensitive ingredients, which might be contraindicated in wet granulation, may also be employed in this sort of method. However, it will need a awfully crucial choice of excipients as compared to granulation processes as a result of the raw materials should demonstrate sensible flowability and squeezability for no-hit operation. Both high and low doses of API gift a challenge during this respect. Most Apis tend to own poor squeezability, that affects the standard of tablets if the formulation needs an oversized proportion of API. At identical time, there may also be issues once low quantities of actives have to be compelled to be incorporated into tablets as a result of it's troublesome to accurately mix alittle amount of active in an exceedingly great amount of excipient to attain the specified uniformity and homogeneity. as an example, segregation of the various parts will occur. This implies there's not the same distribution of pill ingredients being fed to the press, and therefore batch to

batch consistency of the factory-made pill can't be assured. One of the principal risk factors for segregation is that the wide particle size distribution in direct compression formulations, during which active ingredients tend to be at the fine finish of the vary. Wherever there's a large vary of particle sizes, there's associate augmented probability of winnow, wherever the smaller particles 'slip through' the larger ones. Different bulk powder properties also are necessary for no-hit tabletting, like sensible flowability, and every one of those factors mix to put a high demand on the excipients used for direct compression.

Wet Granulation [41]

If a powder blend's properties don't suit direct compression tabletting, makers can communicate granulation processes to form the specified flowability and low dirt ability. These characteristics ar needed to minimise pill weight variations, and guarantee high density for top pill filling weight and high moldability for onerous pill manufacture. Granulation narrows the particle size distribution of a pill formulation's bulk powder, eliminating segregation issues. This successively ensures superior squeezability within the tabletting method, allowing higher quantities of API to be used and making certain sensible active distribution within the pill. However, granulation could be a additional long technique compared with direct compression and there's additionally a risk of product cross-contamination and products loss throughout the various process steps (granulation, drying, sieving). All of those factors will increase prices compared with direct compression. Dry granulation is additional versatile than direct compression. Compared with wet granulation, however, it's a shorter, more cost effective producing method. as a result of it doesn't entail heat or wetness, dry granulation is particularly appropriate for active ingredients that ar sensitive to solvents, or labile to wetness and elevated temperatures.

Factors poignant action of disintegrants [42, 43]

- Effect of filters
- Impact of binders
- Impact of lubricants

Effect of filters [44, 45]

The solubility and compression characteristics of fillers have an effect on each rate and mechanism of disintegration of pill. If soluble fillers square measure used then it's going to cause increase in viscousness of the penetrating fluid that tends to scale back effectiveness of powerfully swelling disintegrating agents and as they're water soluble, they're probably to dissolve instead of disintegrate. Insoluble diluents turn out speedy disintegration with adequate quantity of disintegrants. Tablets created with spray dried disaccharide (water soluble filler) disintegrate additional slowly because of its amorphous character and has no solid planes on that the disintegrating forces is exerted than the pill created with crystalline disaccharide hydrate.

Impact of binder [46]

As binding capability of the binder will increase, disintegrating time of pill will increase and this counteract the speedy disintegration. Even the concentration of the binder may have an effect on the disintegration time of pill.

Impact of lubricants [47, 48]

Largely lubricants square measure hydrophobic and that they square measure typically employed in smaller size than any different ingredient within the pill formulation. once the mixture is mixed, lubricating substance particles could adhere to the surface of the choice particles. This hydrophobic coating inhibits the wetting and consequently pill disintegration. Lubricating substance includes a robust negative impact on the water uptake if pill contains no disintegrants or maybe high concentration of slightly swelling disintegrants. On the contrary, the disintegration time is hardly affected if there's some powerfully swelling disintegrants square measure gift within the pill. however there's one exception like Na starch glycol ate whose impact remains unaffected within the presence of hydrophobic lubricating substance in contrast to different disintegrants.

Effect of surfactants[49,50]

Sodium lauryl salt inflated absorption of water by starch or had a variable impact on water penetration in tablets. Surfactants square measure solely effective among sure concentration ranges. Surfactants square measure counseled to decrease the property of the medicine as a result of the additional hydrophobic the pill the bigger the disintegration time. Disintegration time of granules of soluble medicine didn't appear to be greatly improved by the addition of nonionic wetting agent throughout granulation, however the specified impact of a wetting agent appeared once grain were manufactured from slightly soluble medicine. The speed of water penetration was inflated by the addition of a wetting agent.

TYPES OF DISINTEGRANTS

Starch [51, 52]

Starch is that the oldest and doubtless the foremost wide used disintegrants within the pharmaceutical trade. Regular starch USP has sure limitation and has been replaced to some extent by changed starches with specialised characteristics to serve specific functions. The mode of action of starch is that the disintegrants forms pathways throughout the pill matrix that alter water to draw into the structure by surface tension, therefore resulting in disruption of pill. Different construct relates to swelling of starch grains on exposure to water, a development that physically ruptures the particle bonding in pill matrix.

Na starch glycolate[53,54]

These square measure changed starches with dramatic disintegrating properties and square measure out there as explotab and primogel that square measure low substituted carboxy alkyl starches. Explotab consists of granules that absorb water speedily and swell. The mechanism by that this action takes place involves speedy absorption of water resulting in a colossal increase in volume of granules end in speedy and uniform disintegration. The natural dried starches swell in water to the extent of 10-20 % and also the changed starches increase in volume by 200-300 % in water. This changed starch is that the disintegration time is also freelance of compression force; the tablets developed by exploitation these disintegrants were disintegrated among 2 minutes. the upper dissolution rates discovered with super disintegrants is also because of speedy disintegration and fine dispersion of particles shaped when disintegration.

Alginates [55, 56]

Alginates square measure hydrophilic mixture substances extracted from sure species of brown algae. with chemicals they're out there as gum or salt of gum. gum could be a compound derived from seaweeds comprising D-mannuronic and L- glucoronic units. Its affinity for water absorption and high activity capability build it a wonderful disintegrants. It is with success used with vitamin C, multi vitamins formulation.

Cellulose [57, 58]

Cellulose like refined polyose, Methylcellulose, Cross-linked Na carboxy alkyl polyose (Ac-Di-Sol) and Carboxymethylcellulose square measure disintegrants to some extent counting on their ability to swell on contact with water. A cross coupled kind of Ac-Di-Sol has been accepted as pill disintegrants and it's basically water insoluble. it's high affinity for water, which ends in speedy pill disintegration.

Microcrystalline cellulose[59,60]

Microcrystalline polyose exhibits sensible disintegrants property at low as ten % concentration. It functions by permitting water to enter the pill matrix by means that of capillary pores, that break the chemical element bonding between adjacent bundles of polyose microcrystal's. Tablets with excess crystalline polyose have an inclination to stay to the tongue because of speedy capillary absorption and dehydrating the foremost surface. crystalline polyose includes a quick wicking rate for water, thus this and starch makes a wonderful combination for effective and speedy disintegration in pill formulation. To develop a speedily disintegrating pill, a combination of MCC (microcrystalline

cellulose) and L-HPC (Low-Substituted Hydroxypropyl Cellulose) was within the vary of 8:2 – 9:1 shown shortest disintegration time. MCC was used as disintegrating agent within the formulation of quick emotional compressed propranol complex suppositories. The concentration of MCC Shows quicker drug unleash from medicament and evaluated their materia medica and pharmacodynamics performance and .

Ambrelite Ipr88 (ion exchange resins)[61]

Activity rosin has ability to swell within the presence of water. once used as a disintegrants care should be taken that several resins have the power to soak up drug particles. Anionic and ion resins are wont to absorb substances and unleash them once the charge changes.

Chitin and chitosan[62,63]

Chitin and chitosan obtained from marine sources. polysaccharide a structural constituent within the sheels of crutacean and bug has associate degree acylated polyamine, that is perishable and non-toxic. it's the foremost easy natural chemical compound once polyose . Polysaccharide and Chitosan as disintegrants in paracetamol tablets were evaluated and compared with four usually used disintegrants like corn starch, Na starch glycolate, and alkyl group polyose and croscarmellose Na. Tablets containing Chitosan shows quicker disintegration, bigger dissolution and area unit slightly softer than those containing polysaccharide. Associate degree increment in concentration of those polymers causes significantly quicker disintegration and higher dissolution. pill containing seven % Chitosan disintegrate among one minute that was abundant quicker than those containing Na starch glycolate and croscarmellose Na. wetness activity and water uptake was found the main mechanism of disintegration whereas dissolution associated with swelling capability.

Smecta[64]

Smecta is associate degree clay largely composed of smectile, a non fibrous attapulgite (magnesium aluminum phylosilicate), happiness to the family montomorillonite. Its bedded leaf like structure consists of aluminium and octahedral layers sandwiched between 2 tetrahedral silicon dioxide layers. Smecta incorporates a large specific space and high affinity for water. Smecta was found a lot of adsorbent than various anti-diarrheal clays, as fibrous attapulgite and kaoline. Smecta is value as disintegrants in pill created by compression and by wet granulation victimization disaccharide, Dicalcium phosphate as water soluble and water insoluble fillers. Inorganic clay, metallic element aluminium salt (Veegum), changed starch, Ac-di-sol and cross coupled PVP (Poly vinyl pyrrolidone) as a disintegrants. Smecta perform moreover as a disintegrants in pill superior Veegum and starch, however inferior to Ac-di-sol and cross coupled PVP.

Gellan gum [65, 66]

It's a linear anionic saccharine, perishable chemical compound obtained from Pseudomonos monocot genus consisting of a linear tetra-saccharine repeat structure and use as a artificial additive. Marcus Antonius (1997) studied the Gellan gum as a disintegrants and also the potency of gum was compared with various standard disintegrants like dried corn starch, explotab, crystalline polyose and Ac-di-sol. The disintegration of pill can be thanks to the fast swelling characteristics of gellan gum once it comes into contact with water and as a result of its high deliquescent nature. the whole disintegration of pill was ascertained among four minutes with gellan gum concentration of 4%w/w and ninetieth of drug dissolved among twenty three min.

Isapghula husk[67,68]

It's a natural substance as disintegrants. It consists of dried seeds of the plant referred to as dicot genus ovate. It contains mucilage that is gift within the stratum of the seeds. The mucilage is employed as binding agent within the granulation of fabric for compressed tablets. dicot genus ovata seeds husk has high swellability and provides uniform and slightly viscous answer thus it's used as thickening and suspending agent. The disintegrating property of the isapghula husk, sicklepod and cassia nodosa and also the formulations were evaluated for the quality of dispersible tablets.

Polacrillin metal (tulsion) [69]

Tulsion (339) may be a rosin consisting of extremely refined cross-linked polacrillin polymer in metal type. it's used as a pill disintegrants and as a style masking agent for numerous medication. once tulsion-339 is employed as disintegrants, it swells up at in no time rate upon contact with water or gastro internal organ fluid and act as an efficient pill disintegrants. it's to be intercalary \in a dry type within the proportion of zero.5 five |to five} of the whole weight of pill; quantity might vary relying upon nature of tablet. polacrillin metal is high relative molecular mass chemical compound therefore cannot be absorbed by body tissues & is safe for human consumption. it's no any physiological action at counseled dose & it's non-toxic. Specific options of tulsion-339 as a disintegrants

Agar [70, 71]

Agar is that the dried jellylike substance obtained from Gelidium Amansii (Gelidanceae and a number of other various species of alga like, Gracilaria (Gracilariaceae) and Pterocadia (Gelidaceae). Agar is xanthous grey or white to just about colorless, inodorous with sticky style and is obtainable within the sort of strips, sheet flakes or coarse powder. Agar consists of 2 polysaccharides as agarose and agar pectin. Agarose is liable for gel strength and Agaropectin is liable for the consistence of agar solutions. High gel strength of agar makes it a possible candidate as a disintegrants. Investigated the employment of agar powder as a disintegrating agent for the event of speedily disintegrating oral tablets. Agar was chosen as a result of it absorbs water and swells considerably however don't become jellylike in water at physiological temperature.

Gas–evolving disintegrants [72, 73]

Another approach for the disintegration of pill is inclusion of acid and hydroxy acid in conjunction with the saleratus, sal soda, potassium acid carbonate or carbonate. These react connected with water to liberate dioxide that disrupts the pill. the method of constructing speedily disintegrating tablets. The tablets consisting of malic acid or effervescence base, carbonate as a full of life ingredient (antacid) and cornflour as a bulking agent and disintegrating agent. The tablets ready from these ingredients disintegrated among twenty second.

Superdisintegrants[74,75]

Disintegrating agents ar substances habitually enclosed within the pill formulations to assist within the break-up of the compacted mass into the first particles to facilitate the dissolution or modified release of the active ingredients once it's place into a fluid surroundings. They endorse wet penetration and dispersion of the pill matrix. the foremost perform of disintegrants is to oppose the potency of the pill binder and physical forces that act underneath compression to structure the pill.Recently new materials termed as “superdisintegrants” are developed to enhance the disintegration processes. Superdisintegrants an alternative version of super-absorbing materials with tailored swelling properties. These materials don't seem to be planned to soak up important amounts of water or binary compound fluids, however planned to swell in no time. Superdisintegrants ar used as a structural agent for the meltable solid dose forms. they're physically spread among the matrix of the dose type and can expand once the dose type is exposed to the wet surroundings. These newer substances ar more practical at lower concentrations with bigger disintegrating potency and mechanical strength.

Superdisintegrants ar usually used at an occasional level within the solid dose type, generally one - ten you interested by weight relative to the entire weight of the dose unit. Their particles ar usually tiny and porous, which permit for fast pill disintegration within the mouth while not AN objectionable mouth-feel from either giant particles or gelling. The particles also are compressible that improves pill hardness and its breakableness. Effective superdisintegrants offer improved sponginess, compatibility and haven't any negative impact on the mechanical strength of formulations containing high-dose medication. Generally, one gram of superdisintegrant absorbs 10-40 g of water or binary compound medium. Once absorption, swelling pressure and isotropic swelling of the superdisintegrants particles produce stress targeted areas wherever a gradient of mechanical properties can exist because of that whole structure can break apart.

Type of Superdisintegrant and their example

Two styles of Superdisintegrant:

a. Synthetic superdisintegrant
b. Natural superdisintegrant

Natural superdisintegrant [76,77,78]

These superdisintegranting agents ar natural in origin and ar most well-liked over artificial substances as a result of they're relatively cheaper, copiously obtainable, non-irritating and nontoxic in nature. The natural materials like gums and mucilage's are extensively utilized in the sphere of drug delivery for his or her straightforward handiness, value effectiveness, Eco friendliness, emollient and non-irritant nature, and non toxicity, capable of multitude of chemical modifications, doubtless degradable and compatible because of natural origin. There ar many gums and mucilage's ar obtainable that have super disintegrating activity.

Mucilages as Superdisintegrants[79,80]

Plantago ovata Seed Mucilage (Isapgula)

Isapghula consists of dried seeds of the plant dicot genus ovata and it contains mucilage that is gift within the cuticle of the seeds. The seeds of dicot genus ovata were soaked in water for forty eight hrs so stewed for jiffy for complete modified release of mucilage into water. the fabric was squeezed through textile fabric for filtering and separating out the brandy. Then, AN equal volume of dimethyl ketone was additional to the filtrate thus on precipitate the mucilage. The separated mucilage was dried in kitchen appliance at temperature but 60°C [79]. The mucilage of dicot genus ovata could be a recent innovation for its superdisintegration property in comparison with Crosspovidone. It shows quicker disintegration time than the superdisintegrant, Crosspovidone.

***Lepidium sativum* Mucilage[81]**

Lepidium sativum(family: Cruciferae) is thought as easily and is wide used as flavorer medication in Asian country. it's wide obtainable in market and has terribly low value. elements used ar leaves, root, oil, seeds etc. Seeds contain higher quantity of mucilage, dimeric iminazole alkaloids lepidine B, C, D, E and F and 2 new monomeric iminazole alkaloids semilepidinoside A and B. Mucilage of cress has varied characteristic like binding, disintegrating, gelling etc .

Gum Karaya[82]

Gum Karaya could be a negative mixture and a posh saccharide of high mass. On reaction it yields saccharose, rhamnose and galacturonic acid. Gum Karaya happens as a partly acetylated spinoff. it's a dried exudation of angiospermous tree Uren tree (Family Sterculiaceae). Its synonyms ar *Karaya, sterculia*, *Indian gum*, *Bassora gum, kadaya, Kadira,katila*. Gum Karaya is compatible with different plant hydrocolloids still as proteins and carbohydrates.

Fanugreek Seed Mucilage [83,84]

Trigonella Foenum graceum, commonly called Fenugreek, is AN vascular plant of the herbaceous plant family. it's found wide applications as a food, a additive, and as a conventional medication. The leaves and each the ripe and unripe seeds of *Trigonella Foenum graceum* are used as vegetables. Fenugreek has been utilized in treating intestinal colic flatulence, dysentery, diarrhea, indigestion with loss of craving, chronic cough, dropsy, enlargement of liver and spleen, rickets, gout, and polygenic disorder. it's additionally used as gastro protecting, antiurolithiatic, diuretic, antidandruff agent, Anti- inflammatory agent and as inhibitor. The seed is declared to be a tonic. It is also utilized in post-natal care and to extend lactation in nursing malternatives. Fenugreek seeds contain a high share of mucilage (a natural pasty substance gift within the coatings of the many seeds). though it doesn't dissolve in water, mucilage forms a viscous tacky mass once exposed to fluids. Like different mucilage containing substances, fenugreek seeds expand and become slick once they are exposed to fluids. The ensuing soft mass isn't absorbed by the body, however instead passes through the intestines and triggers viscus muscle contractions.

Guar gum[85,86]

Guar gum may be a galactomannan, unremarkably employed in cosmetics, food product and in pharmaceutical formulations. gum is especially consisting of the high mass (approximately (50,000 8,000,000) polysaccharides composed of galactomannans and is obtained from the reproductive structure of the seed of the cluster bean plant, genus *Cyanosis tetragonaloba* (L) Taub (Cyamopsispsoraloides). it's used as thickening, stabilizer and wetter, and approved in most areas of the globe (e.g. EU, USA, Japan, and Australia). Its synonyms ar Galactosol; *cluster bean* flour; cat gum; meprogat; meyprodor. it's additionally been investigated within the preparation of sustained modified release matrix tablets within the place of polysaccharide derivatives like methylcellulose. In prescription drugs, gum is employed in solid indefinite quantity forms as a binder and disintegrants, and in oral and topical product as a suspending, thickening, and helpful agent, and additionally as a controlled modified release carrier. gum has additionally been examined to be used in colonic drug delivery.

***Cassia fistula* gum[87,88]**

Seeds of pudding pipe tree gum obtained from pudding pipe tree tree. Gum obtained from the seeds of pudding pipe tree comprisesβ- (1→4) joined d-mannopyranose units with random distribution of α (1→6) joined d-galactopyranose units as facet chain. Carboxymethylation additionally as carbamoylethylation of Cassia gum is reportable to enhance cold water solubility, improve viscousness and increase microbic resistance as compared to native gum thus, a trial was created to include metal or Na salts of carboxymethylated or carbamoylethylated.Fistula gum as superdisint-egrant within the formulation development of FDT.

***Locust Bean* gum[89,90]**

Locust bean gum is extracted from the reproductive structure of the seeds of the carob bean tree *Ceretonia siliqua* that grows in Mediterranean countries. it's additionally referred to as *algarroba bean* gum. Some different acquainted polysaccharides starch and polysaccharide, that ar manufactured from long chains of the sugar aldohexose. In algarroba bean gum, the quantitative relation of mannose to brain sugar is above in gum, giving it slightly completely different properties, and permitting the 2 gums to act synergistically in order that along they create a thicker gel than either one alone. It shows as a binder and as a disintegrants property at completely different concentration. Pharmaceutical applications of algarroba bean gum ar applied in nearly each novel drug delivery systems. algarroba bean gum has been wide employed in food business as a thickening and gelling agent algarroba bean gum has additionally been delineated to possess bio-adhesive and solubility improvement properties. There ar varied reports that algarroba bean gum will be employed in pharmaceutical and biotechnological purpose.

***Hibiscus rosa-sinensis* Linn. Mucilage[91]**

Hibiscus rosa-sinensis Linn of the Malvaceae family is additionally called called plant, China rose, and shoe black. The plant is offered in Republic of India in giant quantities and its mucilage has been found to act as a super-disintegrant. The plant contains cyclopropanoids, alkyl radical sterculate, alkyl radical a pair of hydroxysterculate, a pair of hydroxysterculate malvate and β-rosasterol. The leaves contain carotene (7.34 mg/100 g of recent material) wet, protein, fat, sugar, fibers, calcium, and phosphorus. Mucilage of Hibiscus rosa-sinensis Hibiscus rosa-sinensis, D-galactose, D--galactouronic acid, and D-glucuronicacid.

Mango Peel cellulose [92,93]

Dried mango peel powder is use for extracting cellulose. Rather mango peel cellulose cannot be used for promising the behavior of super disintegrants, however because of its sensible swelling index and sensible. Solubility in biological fluids it will be wont to prepare quick dispersible tablets. varied Natural Super-disintegrant at the side of completely different medicine and methodology adopted for his or her preparation .

Synthetic Superdisintegrants [94]

Synthetic super disintegrants ar often employed in pill formulations to enhance the speed and extent of pill disintegration thereby increasing the speed of drug dissolution. Particles ar used to get speedy disintegration. Larger

particles give a quicker disintegration than smaller particles. Crospovidone disintegrants ar extremely compressible materials as a results of their distinctive particle morphology. Crospovidone also can be used as solubility attention. it's offered in 2 particle sizes within the type of Polyplasdone XL and Polyplasdone XL-10.

Advantages of artificial Superdisintegrants [95]

- Effective in lower concentrations than starch.
- Less result on squeeze ability and flow properties.
- More effective intra-granularly. However, there ar variety of limitations that superdisintegrants much impose in pharmaceutical applications. for instance additional absorptive (may be a haul with wet sensitive drugs)
- Some ar anionic and will cause some slight in-vitro binding with cationic medicine (not a haul in-vivo). Associate in Nursing acidic medium considerably reduces the liquid uptake rate and capability of Na starch glycolate and croscarmellose Na, however not crospovidone. The degree of swelling of Primojel1 (sodium starch glycolate) and Polyplasdone XL101 (crospovidone) is reduced following wet granulation formulation. Finally, the medium ionic strength was found to possess Associate in Nursing adverse result on the swelling capability of croscarmellose. Therefore, natural superdisintegrants serve.

Limitations of artificial Superdisintegrants [96,97]

1. Additional absorptive (may be a haul with wet sensitive drugs)
2. Some ar anionic and will cause some slight in-vitro binding with cationic medicine (not a haul in-vivo).
3. Associate in Nursing acidic medium considerably reduces the liquid uptake rate and capability of Na starch glycolate and croscarmellose Na, however not crospovidone.
4. The degree of swelling of Primogel (sodium starch glycolate) and Polyplasdone XL101 (crospovidone) is reduced following wet granulation formulation. Finally, the medium ionic strength was found to possess Associate in Nursing adverse result on the swelling capability of croscarmellose.

Croscarmellose Sodium[98]

It is Associate in Nursing internally cross joined chemical compound of cellulose Na. it's high swelling capability with bottom gelling leading to speedy disintegration. because of fibrous structure, croscarmellose particles additionally show wicking action. In pill formulations, croscarmellose Na could also be employed in each direct compression and wet-granulation processes. once employed in wet-granulation, the croscarmellose Na ought to be additional in each the wet and dry stages of the method (intra- and extra-granularly) in order that the wicking and swelling ability of the disintegrant is bestutilized.

Cross-linked polyvinyl Pyrrolidone (Crospovidone)[99,100]

Unlike various superdisintegrants, that trust primarily on swelling for disintegration, crospovidone use a mixture of swelling and wicking. because of its high crosslink density, crospovidone swells apace in water while not gelling. Crospovidone particles area unit found to be granular and extremely porous that facilitates wicking of liquid into the pill and created by crosslinking of potato starch because it provides the merchandise with the simplest disintegrating properties. The degree of cross-linking and substitution area unit vital factors in determinant the effectiveness of those materials as superdisintegrants . The result of the crosslinking is to scale back each the water soluble fraction of the chemical compound and also the consistency of dispersion in water. The natural predried starches swell in water to the extent of 10-20 % and also the changed starches increase in volume by 200-300 % in water.

The mechanism by that this action takes place involves fast absorption of water resulting in a massive increase in volume of granules that lead to fast and uniform disintegration. This area unit offered as explotab and primogel that area unit low substituted carboxy methyl group starches. The result of introduction of the massive deliquescent carboxymethyl teams is to disrupt the atomic number 1 bonding at intervals the chemical compound structure. This permits water to penetrate the molecule and also the chemical compound becomes cold water soluble.

CONCLUSION

Selecting appropriate formulation excipients and manufacturing technology can obtain the design feature of fast disintegrating tablet. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet. The stronger the binder, the more effective must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared. Disintegrants prepared by intra and extra granulation method was found to be the most effective as they disintegrate rapidly when compared to alternative disintegrants, and the percentage drug release also shows a higher dissolution profile.

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REVIEW ARTICLE

A Mini Review on Techno-Feasibility Assessment of Low-Cost Adsorbents for Wastewater Treatment

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ABSTRACT

Low-cost adsorbents from agricultural and industrial by-products have been identified as an alternative for the wastewater treatment process. These enable us to treat the pollutant from wastewater and contribute to the waste minimization, and subsequent reuse of the treated water. To summarize a lot of work had been under taken, particularly during the last decade, to develop cheaper alternate adsorbents. Most of these works concentrate on flyash, silica, peat, chitin, and agro-wastes like rice husk, bagasse pith, banana pith etc. Owing to their porous structure and their surface charge, they appear to be potential candidates for the indented application.

Keywords: Adsorbents, Low-cost adsorbents, Techno-feasibility, Wastewater treatment, adsorption process

INTRODUCTION

Careful analysis of the strengths and weakness of all the options available for the treatment of various industrial effluent shad clearly shown that adsorption is one of the most promising technologies. With this backdrop, it can be clearly understood that search for an effective low cost alternate for the expensive conventional adsorbents as if activated carbon is eminent in developing countries like India.

Figueiredo *et al.,*(2000) in their studies, investigated the materials containing chitin and Anodonta shells for color removal from textile wastewaters was studied and showed promising adsorption capacities. Gonzalo V'azquez *et al.,* (1994) investigated pre-treated *Pinus pinaster* bark as adsorbent for uptake of phenol (the breakthrough curves have been satisfactorily described using different models) from aqueous solution. The potential to remove Cr (VI) from aqueous solutions using the husk of Bengal gram was investigated and the results showed removal of 99.9% chromium solution (Ahalya *et al.,* 2003). The potentialities of castor seed shell (CSS), a waste agricultural by-product, in the remediation of water, contaminated with Methylene Blue (MB), a basic dye, were investigated. The sorption capacity of the CSS, as obtained from the Langmuir plot was 158 mg/g (Oladoja *et al.,* 2008). In some other studies, the adsorption of two basic dyes, namely, Malachite Green and Methylene Blue onto both agricultural by-products (i.e. rice bran and wheat bran) has been investigated(Xue *et al.,* 2009). Of late, there has been increasing interest in evaluating the use of practically every possible natural adsorbent for adsorption resulting in various degrees of successes.

METHODOLOGY

The utilization of waste materials that are available in nature that have very limited or of no use, available naturally as agricultural or industrial by-products as low-cost adsorbents for the treatment of waste water. This review gives an overview to wastewater treatment, particularly using the low-cost alternative adsorbents.

Agro-Residue as Adsorbent

In fact, there had been extensive studies on use of agro-residue as adsorbent. Nawar and Doma (1989) studied the adsorptive capacities of rice hulls for two industrial textile dyes and found much encouraging results as well as successful an application of the Freundlich Model. A Kenaf (lignocellulosic fibers) found to be effective for adsorption of several toxic heavy metals (namely, nickel, copper, zinc, and cadmium) from storm water. The adsorption potential of these Kenaf were found to be related to their sugar content, extractives composition, lignin content, and physical property. It was also found that a decrease in the lignin and cellulose content in Kenaf contributed to a lower density and easy accessibility of ions to the reactive sites on Kenaf's surface, thus increasing the adsorptive capacity (Han, 1999). Brown *et al.,* (2000) in his studies, demonstrated the relatively lower capacity of raw peanut hulls (and peanut hull pellets) than that of the ion-exchange resin; yet the substantial low-cost of production of the formers, in comparison to the latter, would probably compensate their deficiency more than adequately for their use in treatment of low-strength metals contaminated waste streams.

Besides naturally available soils and agro-residue (biomass), several workers have attempted several chemically synthetic and non-biodegradable wastes as adsorbents. The Langmuir and Freundlich adsorption models were used to express the sorption phenomenon of the sorbate. Although non-biodegradable wastes are naturally of low-adsorption capacity than the naturally available soils and agro-reside-based adsorbents, yet due to their increased magnitude and resultant solid-waste disposal problems, attempts have been made for at least some use of them, even in the field of adsorption. Zhang and Chuang (2001) reported that in their study that activated carbon removed colour effluents from a Kraft pulp mill at high pH. It was also observed that adsorption capacity of activated carbon is twice that of fly ash. Rengaraj *et al.,* (2002) in their studies, further investigated activated carbon prepared from rubber seed coat (RSCC), an agricultural waste by-product, for removing from aqueous solution. They found RSCC is 2.25 times more efficient than CAC. Tanthapanichakoon *et al.,* (2005) investigated in their studies the liquid-phase adsorption–desorption characteristics of phenol. Some of the low cost adsorbents that are tested for the dye sorption process are rice husk (Manoj kumar, 2013), wood dust (Garg *et al.,* 2004), tree bark powder (Paul Egwuonwu, 2013), peat (Fernandes *et al.,* 2006), lignin (Cotoruelo *et al.,* 2010), Groundut shell (Malik *et al.,* 2007), Lentil Shell (Aydin *et al.,* 2008), Sugarcane baggase (Tsai *et al.,* 2001, Khoramzadeh *et al.,* 2013), Corn cob (Juang *et al.,* 2002), Potato peel (Aman *et al.,* 2008), cotton and gingelly seed shell (Thinakaran *et al.,* 2008), pomegranate peel (Moghadam *et al.,* 2013), Cane pith (Juang *et al.,* 2001) and so on.

Rationale of Deoiled Cake- As Adsorbent

Biodiesel has been considered to be one of the most safe and reliable non-conventional energy options for future years, by virtue of its renewability, close semblance to conventional fuel technology, possibly, lower pollution potential, as well. Some of the edible oil (essentially, soy, rapeseed and palm oil), known as the first-generation feedstock, had got wider usage in production of biodiesel in earlier days; yet, with increase demand of energy and advancement of technology, over years there have been progressive transition of biodiesel feedstock market to the second generation low-cost & non edible feedstock (Naik, *et al.*, 2010). Of all the oil seeds used in second generation, *Jatropha curcas* (physic nut) and *Millettia pinnata* (Karanja) are considered to be the best candidates for future production of biofuels (Goldman Sachs, 2010; Paul *et al.*, 2008). *Jatropha* is grown widely in southern Asia, Africa, Brazil and, of late, China (Emerging market online, 2008) Karanja is naturally distributed in tropical and temperate Asia, from India to Japan to Thailand to Malaysia to north and north- eastern Australia to some Pacific islands. It is is a fast-growing leguminous tree with the potential for high oil seed production and the added benefit of the ability to grow on marginal land, the exclusive properties that support the suitability of this plant for large-scale vegetable oil production required by a sustainable biodiesel industry (Paul *et al.*, 2008). With regard to India, with more than 20% of its geographical area classified as wasteland, all endeavors are in the way, as per the National Policy on Biofuels, to promote the use of wasteland for growing non-edible oilseeds (to an area of 0.4 million hectare in 26 states) so as to bring about a blend of about 20% of the fuel by *Jatropha*-derived-biodiesel to the fuel market by the year 2017 (MoRD & NRSC, 2010; MNRE, 2009; TERI, 2005).

The deoiled cakes of first generation biofuels, being edible, were priced cattle feed, and sometimes, even a source of protein substitute for human diet (Das *et al.*, 2012). However, the deoiled cakes for second generation biofuels, although production of residue is often quite high. *Jatropha*, for example, generates about 3 tons of deoiled cake per hectare of oil yield (@ 65% oil recovery). For the massive *Jatropha*-cultivation project as enumerated in preceding paragraph, the generation of deoiled cake would be significantly high (about 0.68 million tonnes of deoiled cake). *Jatropha* deoiled cake cannot be used as animal feed because of the presence of phorbol esters, which is a proven potential toxic compound to animals (viz. goat, sheep, mice, rats, fish, etc.) leading to reduction in blood glucose level, lack of appetite, diarrhea, dehydration and hemorrhagic effects (in different organs) ((Makkar and Becker, 1999). Pongamia, on the other hand, although contains 30-40% oil content and is a good source of proteins (33.2%). is non-edible, due to the presence of anti-nutritional constituents, such as phytates, tannins and protease inhibitors, glabrin and karanjin (a furano-flavonoid), creating a formidable constraint (Vinay and Kanya, 2008).

DISCUSSIONS

Conventionally, there have been isolated studies revealing the feasibility of usage of many non- edible deoiled cakes as biofertilizer& composting or as pesticide & insecticide (Wiesenhutter, 2003). However, recent studies explore its other uses- as lubricant, bio-pesticide, extraction of enzymes (protease & lipase), and alternative medicine and in detergent and tanning industries. (Sangeetha, *et al.*, 2011). However, the usage of these low cost alternatives as adsorbents of pollutants has been rather lesser explored.The Freundlich isotherm model showed good fit to the equilibrium adsorption data. The adsorption kinetics followed the pseudo-second-order modeland suggested that J. curcas deoiled cake can be used as an efficient bio sorbent (Garg *et al.*, 2007; Rawat and Rawat, 2013). *Jatropha* deoiled cake was also found to be effective in removing Ni(II) upto 62-63 %, at pH 6.2 both in its natural as well as immobilized form, within 60-90 minutes (Mahajan *et al.*, 2013). With regard to evaluating the potential of deoiled cake as an adsorbent for the treatment of dye wastewaters, an equilibrium time of 3.5 hr, 90% adsorption at 400-ppm initial concentration through batch studies was observed. Sip and Redlich-Peterson isotherm models are found to be best suited to the adsorption process (Subramanyam, 2016). Besides, as studied in authors' laboratory, adsorption studies carried out at varying initial dye concentrations, pH and contact times showed maximum adsorption capacity at neutral pH, for optimized adsorption period of 6 hrs. When comparing various equilibrium isotherms,

Redlich–Peterson and Sip isotherms were found to be the best representatives for reactive red dye sorption on the deoiled cake adsorbent studied (Das *et al.,* 2015).

CONCLUSION

The present review has been formulated to carry out an in-depth exhaustive investigations of adsorption capacities of agricultural and industrial by-products (with or without blend with agro-waste, which have already studied to be potential in laboratory of investigators) for treatment of wastewater. Based on the extensive literature reviewed, agriculture and industrial by-products, showed good results for the removal of dyes, heavy metals and other pollutants. Still, among some industrial by-products, they can be utilized partially with other technologies that may pave a way to replace the commercial activated carbon used widely, which is very expensive when compared to these naturally available low cost adsorbents. Furthermore, most of the studies focused on synthetic wastewater rather than using the actual industrial effluents or wastewater. The regeneration of the spent adsorbents and their disposal should be evaluated taken into account the new frontiers of research on these naturally available alternate low cost adsorbents.

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REVIEW ARTICLE

A Review of Scintillators

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ABSTRACT

In the present day when anyone visits a medical for checkup, doctors immediately refer him/her for diagnosis. Out of many diagnosis medical imaging like X-Ray, CT, PET and MRI are the important ones. In one line the quality of photograph is important which depends on the associated Scintillators including the electronics driver. In the present paper a reviews of properties of a Scintillators has been discussed.

Keywords: CT,PET, MRI.

INTRODUCTION

A scintillator crystal has the property of emitting photons, when hit by a gamma photon, a number of photons in the visible/UV range depending on the energy of the incoming gamma ray: this phenomenon takes the name of *scintillation* [1-2]. The most important features that must be taken into account when choosing a crystal scintillator for a determined application are discussed bellow.

Properties

(High stopping power) : To better understand how this parameter should be chosen, a brief overview of the main physics interaction types which may occur inside a crystal is presented. The main interaction modalities which lead to a partial or total energy transfer from the photon to the crystal in the energy range of our interest (which varies between 10 keV and 10 MeV) can be of three types: Photoelectric Absorption, Compton Scattering and Pair Production. In Fig.1, as example, is shown the variation of the Total Attenuation Coefficient in the CsI crystal with highlighted the various phenomena which take places. Moreover, the Total Attenuation Coefficient is defined as the ratio between the absorption coefficient and the material density and it is therefore possible to obtain from it the

absorption length in the specific crystal at the various energies. [3-5]. Materials with an high Z allow then to maximize the probability of photoelectric effect compared to the Compton scattering. There are different types of materials with high atomic number and density used as scintillators: some are organic (plastic scintillators or liquid), other inorganic (NaI, CsI, BGO, LaBr3, etc...), but all have an absorption coefficient and a density such as to allow, for low energies (lower than the 150-200keV), the complete absorption of the gamma photon in a few mm of thickness. Instead, materials such as Silicon, characterized by a low Z value, are almost transparent to gamma photons at those energies. Therefore, to absorb a gamma photon to do a direct conversion would be necessary to use very thick layers, which is not advisable, both from the economic point of view and also because increasing the volume would cause a corresponding increase in leakage currents, limiting the performance of the system.

High scintillation speed : This specification is required mainly because it allows the formation of signals which, properly processed, are of short duration: this results in a low system dead time and therefore in good performances both in terms of counting frequency and temporal resolution. Furthermore, a measurement requires the acquisition of a high number of events, so it is necessary to have a rapid scintillation time to obtain a high statistic in a short time. The photons emission takes place through two secondary phenomena internal to the material: the fluorescence and the phosphorescence. In conclusion, in order to be a good scintillator, the material must convert the major fraction of the incident radiation in instantaneous fluorescence and minimize unwanted contributions due to the phosphorescence. This latter is in fact characterized by lower energies which may not be completely absorbed depending on the photo detector type and moreover, being delayed, cause a slowdown of the detection system.

High scintillation efficiency: A high scintillation efficiency or light yield simplifies the discrimination between the real signal and the background noise. It is usually expressed in number of photons per MeV or keV and it represents how many photons in the visible/UV range can be obtained per unit of energy of the interacting gamma ray. The problem is solved by adding small amounts of impurities called activators, which create states in the band gap of the crystal through which the electron can return from the conduction band in the valence band making a lower energy jump; this causes that the emitted photon has a wavelength belonging to the visible region. Obviously, in order to obtain this result, the activator must be chosen in function of the crystal material: two examples of materials widely used as activators are the Thallium (NaI(Tl) and CsI(Tl)) and Sodium (CsI(Na)).

Refractive index of the material & the optical grease: The light produced in the scintillator must be efficiently transmitted to the photo detector avoiding that a part of it remains trapped in the crystal due to effects of internal total reflection. This requires an adaptation between the refractive index of the crystal and either the photodete ctor window material or the optical grease in-between. One of the weaknesses in the indirect conversion method is indeed the way in which all the light generated is collected by the photo detectors: in their random motion, the photons can interact with different surfaces and consequently undergo reflections and transmissions depending on the correspondent refractive indices. If, for example, a photon interacts with a crystal surface which is not in contact with the photo detectors, it can exit from the crystal if the angle of incidence is not greater than the angle limit of total internal reflection and, moreover, the opposite can occur at the contact surface between the crystal and the photo detectors where the difference in the refractive index between the two can produce an undesired reflection. To minimize these effects, usually an optical grease is inserted in-between the crystal and the photo detectors, which reduces the difference between the refractive indices and therefore the unwanted reflections; the problem of photons leakage can instead be solved by covering the crystal either with a layer of a material which acts as a diffuser (e.g. Teflon) or simply reflects back the photons (e.g. Aluminum), or with a layer of black paint which prevents the backscattering of the photons and works as a total absorber.

Wavelength of the emission and photo detector : The scintillation light must be efficiently detected by the photo detectors. To this purpose, from the datasheet of each photo detector is possible to obtain the wavelength at which corresponds the maximum efficiency and the range in which it functions properly. Therefore a scintillator with a wavelength of peak emission included in that range should be selected.

Stability at different temperatures The mean value of the Poisson curve which represents the statistical distribution of the secondary photons emitted by the crystal is not constant with the temperature. Therefore, gradients inside the crystal may change the photon production and using appropriate cooling systems to reduce the temperature variation may be important to avoid unwanted behaviors [6-7].

SUMMARY AND CONCLUSION

A review has been done for scintillators properties as the scintillators are very important for the diagnostics and detection purpose. Many important points has been discussed which need to keep in mind during the scintillators study.

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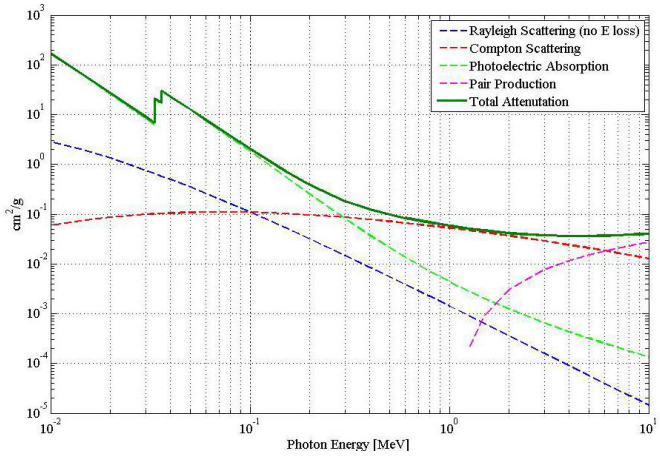

Fig.1: Total Attenuation Coefficient in a CsI crystal with highlighted the contributions of the different physical phenomena

REVIEW ARTICLE

Nanoerythrosomes: An Overview

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ABSTRACT

Nanotechnology is a field that is constantly increasing in its vitality and importance in various fields such as biology, pharmacy, chemistry & physics, etc. Nanoerythrosomes are prepared from erythrocytes of mammal especially human. However, based on the average diameter, we can include in the category 'Microspheres'. Non-pyrogenicity, easy manufacture, non-immunogenicity, bio-degradable nature due to natural origin are considered as some of the important merits. There are 3 types of Nanoerythrosomes on the basis of resealing capacity.It is prepared by various techniques like hypotonic lysis & resealing method, dialysis, lipid fusion, chemical perturbation, etc. Characterization of prepared Nanoerythrosomes (NER) can be subjected to osmotic studies, physical properties including shape and surface morphology, in-vitro drug studies, spectroscopic and chromatographic studies, etc. Microbiological studies are considered essential like cell viability test, Erythrocyte Sedimentation rate, etc. It has various developments in this field. Rigidity of NER can be improved by protein scaffolding. Co-ordination of cascades of signal transduction can be achieved by Protein scaffolding process. High yield of Nanoerythrosomes can be achieved by fabrication process. NER has applications in medical field. Enhanced cancer immunotherapy for antigen delivery, drug carrier, combination with protein and peptide Drug Delivery System, tumor targeted delivery, etc. are considered as some of the major applications.

Keywords: Nano-technology, Nanoerythrosomes, chemical perturbation, osmotic studies, protein scaffolding.

INTRODUCTION [1,3]

Nanotechnology is a field that is constantly increasing in its vitality and importance in various fields such as biology, pharmacy, chemistry & physics, etc. Nanotechnology is defined as the branch of science to work in the nano levels .i.e. the atomic (or) nuclear level to produce higher grade products in utilization and performance. 'Nano' is a term which is usually referring to range of about 10^{-9} to 10^{-7} meter. Foreign particles have two major limitations:

a. High rate of tolerance is produced on frequent administration.
b. In some cases, due to certain posological factors, severe Adverse Drug Reactions (ADR) can be produced. Sometimes, such ADR may be fatal raising the risk of mortality.

However, if the bio-availability of a drug is low, i.e. when the concentration of drug has not reached the minimal effective dose at the site of receptor (or) action, nanotechnology can be applied.

ERYTHROCYTES [1-5, 8, 10, 20, 38, 40]

Nanoerythrosomes are prepared from erythrocytes of mammal especially human[1,3,4,5,20]. However, it can be prepared from other animal sources [15]. 'Erythro' is usually a prefix which denotes to something red in color. Erythrocytes are also known as Red Blood Cells (RBC). These are the type of cells which are produced by bone marrow along with White Blood Cells (WBC) & platelets. An erythrocyte is formed from its precursor, which is pleuri-potent stem cell via Erythroblast and Reticulocyte [2,5]. This constitutes about 99% of the blood cell volume in the plasma. A mature mammalian Red Blood Cell (RBC) lacks nucleus and the diameter is around 7-8 μm. A Red Blood Cell is actually biconcave in shape, which makes it suitable for binding to maximum number of oxygen molecules as possible [2,38,40]. Erythrocytes are produced by a process known as erythropoiesis. In this process, erythropoietin secreted by the renal region plays a crucial role. Erythrocyte has an average life of 3-4 months (120 days) [2,5].

CHEMICAL NATURE OF ERYTHROCYTE MEMBRANE[1,3,4,13]:

The phospholipid concentration in the outer leaflet equals that of inner leaflet. The membrane removed RBC are called 'ghosts'. This is due to absence of structural unit. Erythrocytic membrane (Outer leaflet) possess enormous amount of sphingomyelin & phosphatidylcholine when compared with inner part of RBC. These two phospholipids together constitute about 40% of the total phospholipid content of erythrocytes. The content of human erythrocyte membrane is normally determined by electrophoresis by using Sodium Dodecyl Sulphate (SDS) Polyacrylamidegel. The graph obtained from the process of electrophoresis is called electrophoretogram. When the membrane is stained with Periodic Acid Schiff's (PAS) reagent, 4 bands conforming to polypeptides can be seen distinctively. This reagent is used to stain carbohydrates. The contents in these bands can be extracted by changing ionic strength (or) pH. These contents are referredto as peripheral proteins. Such extraction is not possible by using dyes like Coomasssie brilliant blue (or) Congo red.

NANOERYTHROSOMES

Nanoerythrosomes are also known as nano-erythrocytes, which play a vital as well as crucial role in drug carrier system. These may be defined as the small vesicular cellular carriers which possess an average diameter of 100 nm (0.1 μm)[3,4,9,13,20]. Based on the average diameter, we can include in the category 'Microspheres'. Nanoparticles contain therapeutic molecule which could camouflaged them with erythrocyte membrane to reduce toxicity.

ADVANTAGES

- ✓ They don't elicit an immunological response easily, since it is prepared from component of human blood [4,5,9,13,20].
- ✓ They don't cause fever (or) increase in body temperature. I.e. Nano-erythrocytes are non-pyrogenic[9].

- ✓ Drug is entirely bound to protein of the membrane of nano-erythrocyte, thereby increasing the drug bio-availability[7,26].
- ✓ These are readily available in huge amounts[1,3,20,26].
- ✓ The source of the nano-erythrocyte is natural. I.e. Human erythrocyte, bovine erythrocyte (Cow)[15].
- ✓ These are bio-degradable in nature, which reduces carrier induced ADR to the patients[9, 10,12].
- ✓ Route of administrations of nano-erythrosomes are multiple. I.e. Intra-venous, intra-muscular, subcutaneous, intra-peritoneal, etc. [11]
- ✓ It has optical exceptionality as well as magnetic exceptionality[20].
- ✓ Nanoerythrosomes possess high degree of versatility [9].

TYPES OF NANO-ERYTHROSOMES[20,37]

There are 3 types of nano-erythrosomesbased on the resealing capacity:

Type-1: These are the type of NER which reseal immediately.

Type-2: These are the type of ghosts, which reseal at a slower rate than type-1 NER. Such NER are partially leaky in nature.

Type-3: These ghosts are leaky in various investigational processes.

The ghosts which are prepared by hypotonic dilution of RBC are called hypotonic ghosts. This can be classified into two types, namely:

a. **White ghosts:** This class of ghosts can be characterized by absence of intra-cellular toxins. White ghosts are prepared under freezing point of water (0℃) using only CO_2 free water only wherever needed.
b. **Resealed ghosts:** By the modulation of cation composition medium, membrane shells of lysed Red Blood Cells. This type of ghosts is mostly not permeable. However, it is observed to be of more permeability than original membrane of RBC.

MECHANISM OF RELEASE OF DRUG [1-4, 6]

Red Blood Cells have an average lifespan of 120 days. There are various stages to become mature RBC (or) erythrocyte. It all begins in the bone marrow where pleuripotent stem cells are formed. Part of the population of stem cells converts into erythroblast via pro-erythroblast. Erythroblast is considered to be an immature erythrocyte possessing a nucleus. Integrins play an essential role in erythroblasts. As the process of ageing occurs, it loses its actin cytoskeleton. The change in transferrin receptor and erythropoietin receptor show the progress of maturation in erythroblasts.

It begins a complete erythrocyte after the conversion of erythroblast into reticulocyte. Mature RBC lose its physical integrity, capacity of oxygen binding as well as the flexibility as it nears the mark of 113-120 days. The old cells are lysed in the spleen. Sometimes, it can be destroyed by macrophages of Reticulo-Endothelial system. These macrophages recognize the old RBC, bind on its surface and destroy the Red Blood Cell. Owing to the high penetrability and retention effect, Nano Erythrosomes, unlike RBC, can specifically bind to tumor regions. NER can effectively cross the outer layer (Endothelium)of tumor by a process of extravasation. Within the tumor, NER releases the drug concealed within it. This provides more drug concentration at the specific site. NER, however, cannot permeate into normal vasculature of organs such as liver, spleen, etc. This factor reduces the toxicity to the barest minimum.

PREPARATION OF NANO-ERYTHROSOMES

Step-I: preparation of erythrocyte ghosts (general)

Erythrocyte ghosts are formed as a result of hemolysis of RBC [37]. Blood samples are taken from the volunteer using a hypo-dermicneedle syringe. The specific volume of blood is centrifuged so as to separate the blood cells from liquid plasma. Blood cells settle at the bottom by the process known as sedimentation. Settled red blood cells are separated, cleaned and refrigerated to preserve the originality. Erythrocyte ghosts are the type erythrocytes which

lack (or) possess hemoglobin (Hb). The blood vessels in which the RBC with less hemoglobin runs do not really get enough O_2. Such blood vessels are called ghost blood vessels. This problem is more common in old age people of about more than 60 years [2, 18].It shouldbe noted although there are several hemolytic methods, noticeable change in the protein compositions in the so formed erythrocyte ghosts. Such erythrocyte ghosts are prepared by usually subjecting the Red Blood Corpuscles (RBC) to a process known as osmotic lysis. It involves the following steps:

- Transfer the blood with anti-coagulant mix (Heparin, etc.) into a conical tube.
- Centrifuge the conical tube for 1 minute. Leave the yellow plasma, which is the supernatant liquid. Red cell pellet is present in the bottom of the tube.
- Vortex and re-suspend the RBC after filling the conical tube completely to the 1.5 ml level with 0.15 M Sodium Chloride (NaCl) solution maintained at pH 7.4. Stable pH of the solution is required.
- Remove the supernatant liquid obtained during the centrifugation process.
- Repeat the centrifugation & removal of supernatant liquid with deionized water for 2 more times.

The first two times of centrifugation was meant for complete isolation of RBC from other cells and plasma. But, the last two times of centrifugation using de-ionized water involves in the lysis of RBC (Hemolysis). After the last step mentioned above, erythrocyte membrane is completely in all RBC. As a result, Hemoglobin is lost and formation of erythrocyte ghosts is achieved.

METHODS FOR PRODUCTION OF ERYTHROCYTE GHOST

Hypotonic lysis & resealing method: In this method, the erythrocytes are immersed in a hypotonic solution. IT results in any one of the three types of ghosts mentioned earlier. Hemolysis of erythrocytes is performed by incubation at 37°Cin a hypotonic solution[7,10,17,37]. The hypotonic solution can be produced from isotonic saline solution, which can be approximately 300 mOSm. The osmotic pressure of such prepared hypotonic solution must be in the range of 30 mOsm to 50 mOsm[17]. In case of lesser tonicity than required is formed, hypertonic buffer is added to increase the solution tonicity. 1-8% of drug loading can be done by this method [40].

Dialysis[20,23,40]: In this process, free flow of ions is passed efficiently for the formation of erythrocyte ghost from RBC. This process ensures that anything which is larger than the pore size to be retained successfully. Semi-permeable Cellophane & bovine bladder are used in this process. The pore size is in the microns level. Lysis of erythrocytes followed resealing of erythrocytes can be observed. Intra-cellular: Extracellular volume ratio is exploited followed by resealing of RBC ghosts. Phosphate buffer is widely used at a pH of 7.4. Sealing of RBC occurs in such a way that the RBC suspension fills merely 75% of the dialysis bag of semi-permeable membrane. Concentration of the ionic solution which produces ion must be within the optimal range. I.e. Sodium Chloride solution must be in the concentration of 125-150 mM (millimoles). The advantage of dialysis is that it has better entrapment efficiency than the first method.

Isotonic osmotic lysis: Isotonic solution is used in this process. An isotonic solution need not be isotonic at all times. The tonicity may change in increase in time. This process is also known as osmotic pulse method, which can be performed by physical (or) chemical means. Diffusion of solute into the RBC occurs, when the erythrocytes are in incubation with a solution of higher membrane permeability. Maintenance of osmotic balance is made with incursionof water molecules. Resealing of erythrocytes is done by incubating at 37°C. Even though the process is time consuming, it has improved in-vivo survival. Anti-malarial drugs like Bulaquine, Amodiaquine and anti-neoplastic drug like vincristine, Daunorubicin can be loaded into erythrocytes during this process[4,11, 16]. The isotonic solutions which are used are Ammonium chloride, Polyethylene glycol (PEG), Urea, etc. However, Dimethyl Sulfoxide (DMSO) is considered effective, which was developed in 1987.

Presswelldilutional hemolysis: Initial controlled swelling of erythrocytes is considered as the basic principle in the process by the aid of hypotonic buffered solution without lysis. The resultant mixture obtained using the principle

the previous method is centrifuged in low 'g' values. Supernatant liquid formed during the process of centrifugation is discarded. Lysis point is detected by the presence of distinct boundary between supernatant liquid and the cell fraction. At this point, tonicity is restored to normalcy by addition of hypertonic buffer in calculated quantities. Recovery of cells is done by gentle centrifugation post 5 minutes of incubation at 37℃[8,12,13,20]. The efficiency of this procedure is observed in the range of 30-90%[40].

Loading by red cell loader: In this procedure, the red blood cells are washed with 2 sequential & precise hypotonic dilutions. Then, the resultant is concentrated by hemo-filter. Hemofiltration is a process in which convection (Solute and solvent moves along the pressure gradient) is the main principle. Hemofiltration differs from the hemo-diafiltration. This is because hemo-diafiltration (HDF) is based on the combination of convection and diffusion[19]. 35-50% recovery of cell is achieved by subsequent isotonic resealing of erythrocytes. Normal in-vivo survival of cells is observed in processed Red Blood Corpuscles (RBC). The range of drugs which can be encapsulated by employing this technique is as follows:

S.NO	NAME OF DRUG	CATEGORY
1	Propanolol	β- antagonist, anti-hypertensive
2	Methotrexate	Anti-carcinogenic
3	L-asparaginase	Enzyme, Anti-carcinogenic
4	Insulin	Anti-diabetic, endocrinal hormone
5	Metronidazole	Anti-fungal

Chemicalperturbance of membrane[40]**:**This method is also known as membrane perturbation method. It is performed by employing chemical to which permeability of the erythrocyte membrane escalates in specific period of exposure time with the chemical. Halothane, Amphotericin-B, etc. It had been used to entrap the anti-neoplastic drugs such as Daunomycin, Daunorubicin, etc. But, this method usage has sharply diminished due to the irreversible destructive changes in the cell membrane. Chances of mutation still exist. It also showed poor in-vivo survival rates.

Lipid fusion method [12, 40]: Very low encapsulation efficiency is observed by this technique. Exchange of lipid entrapped drug molecule is observed when lipid vesicle containing bio-active molecule is fused with human erythrocytes. Tyrosine kinase enzyme has been resealed human erythrocytes b employing quick freeze & thawing in liquid.

Electrical method[11, 12]: In this method, permeability changes are achieved by applying potential differences at high membrane. Potential difference is applied by two approaches:

- **Direct:**By applying electrodes intra-cellular (or) inter-cellular
- **Indirect:**Attain the Donnan membrane by applying internal field to the electric cell post perforation of membrane.

Membrane is polarized for few microseconds to produced electrical breakdown. Varied voltage required for this process is around 2kV/cm for 20μ sec.

Extrusionmethod[11]: This procedure is performed in room temperature (37℃) under nitrogen pressure. This process involves Uranyl acetate for microscopic staining of erythrocyte ghosts. The end-products are stored and preserved at refrigerator at 4℃.

Characterization of nanoerythrosomes

Osmotic studies: Osmosis is defined as the phenomenon in which solute particles (or) solvent transports from lower concentration to a higher concentration via semi-permeable membrane [21]. This property is useful in the determination of drug within the NER. It is also essential in transport of O2 in the blood vessels effectively. In the osmotic studies, there are 2 two parameters:

Osmotic fragility [13,17]: It plays a vital role in in-vitro studies. Osmotic fragility provides a close relationship with shelf life, in vivo survival and effect of encapsulated substances. Osmotic fragility can be mentioned as a degree of resistance of RBC membrane against the environmental changes in osmotic pressure. The test for osmotic fragility can be performed by incubation of the NER at 37±2℃ in a hypotonic solution of sodium chloride solution. The given process of incubation is continued up to 10 minutes. It should be noted that the concentration of saline solution must be 0.9-1% w/v. After 10 minutes, the resultant is made to undergo a 15 minute centrifugation at a revolutionary speed of 2000-5000 rpm changes. The process of centrifugation is done so as to efficiently determine the drug release from NER. Using dilution method, 540 nm peak obtained for the sample is checked for its absorbance. A graph is plotted between concentration Vs. absorbance.

Osmotic shock [11,17]: This parameter is determined so as to estimate the maximum stability under sudden harsh environmental exposure. Here, harsh environment usually refers to a condition in which tonicity level is far from the isotonic state. In short, the given test furnishes the maximum tonicity stability of NER. In this experimental procedure, the suspension of NER is collected and is subjected to incubation with distilled water for 15-20 minutes. Then, centrifugation is done at a speed of 2500-3000 rpm. The supernatant liquid formed during the process is sent for spectrophotometric studies like UV, IR, etc. to estimate the drug content released by the NER. These studies are done on a half-hourly basis to provide the maximum accuracy possible.

Viscosity

Viscosity is a qualitative parameter and is defined as resistance to liquid flow due to internal friction between different layers of liquid during the flow. The unit of viscosity is expressed in poises. It is denoted as η[22]. The viscosity of NER is determined using a rotator Brookfield viscometer.

$$\boldsymbol{F = v_u \div v_0}$$

F=sedimentation volume;
V_u= Ultimate volume of sediment;
V_0= Original volume of formulation
Sedimentation volume of the formulation was obtained by measuring the height of sediment in a graduated measuring cylinder[11, 13].

Centrifugal studies

Variation in sedimentation volume in presence of centrifugal force is studied to determine centrifugal stress. Process of Centrifugation is set at variable rpm[10,13]. Higher the variability rate; more accurate the centrifugal stress will be. It should be noted that only refrigerated centrifuge is used since this experiment must be performed at low temperature (4±1℃). The supernatant liquid coming during the process undergoes High Performance Liquid Chromatography (HPLC) for drug content[10]. This helps in indirect determination of drug release by the nanoerythrosomes (NER). Duration taken for this experimental procedure is about 15 minutes[10,13].

Deformability

Deformability is considered as an indirect parameter in estimating the life span. It is used to determine the comfort level of circulation of NER in narrow capillaries as well as through Reticulo Endothelial System (RES). The unit is obtained in terms of passage time. The experiment to obtain the deformability is performed by passing a definite

volume of cells through a filter which has diameter ranging to 4-45 mm. It has made of polycarbonate[10, 13]. There are 2 important types of deformation that needs to be evaluated:

- **Elastic deformation:**It is considered as the type of deformation in which the work is recovered in a reversible manner, as soon as the work is removed.
- **Plastic deformation:** In this deformation, dissipation occurs in the form of heat thereby, altering the shape of the body enduringly[22].

This rheological property is proportional to [13]:

- Viscosity
- Viscoelasticity
- Cellular surface-to-volume ratio

Turbulence shock

Turbulence studies are performed on the basis of turbulence theories, simulation and modeling. 3 types of simulation approaches are available, they are:

- Direct numerical simulation
- Large Eddy simulation
- Reynolds averaged Navier-Stokes approach

These approaches may tend to reduce the onset of Reynolds stresses, which are considered as unapparent stresses[24, 25].*Silvis et.al* has proposed about the sensitivity of critical velocity in respect to turbulence before entering the tube. This experiment involves the use 23-gauge hypodermic needle. The flow rate of formulation is adjusted to 10 ml/min. This flow rate is comparable to flow rate of blood. The number of successful passings is calculated as a utility of turbulence. After every pass, withdrawal of aliquot of the suspension is done and centrifuged at 300 rpm for 15 min. Leakage of drug content is valued using High Performance Liquid Chromatography (HPLC)[10,11,13, 43].

***In-vitro* drug studies:**

As per *Dissanayake et.al.*,there are three important classes under which In-vitro drug takes place:

- Sample and separate
- Dialysis membrane
- Continuous flow

Out of these approaches, dialysis membrane method involves the use a semi-permeable membrane. Similarly, Continuous flow method employs a pump to circulate the buffer at a constant rate throughout the apparatus. In sample & separate method, introduction of nano-particulate dosage system into the release media is done. In this method, mode of agitation is influenced by the container size [26,27].

Jaya Agnihotri.et.al suggests the use of dialysis membrane method to provide in-vitro drug release effectively. The molecular cut-off of the semi-permeable membrane was adjusted to 1000 Da (Daltons).The formulation is centrifuged at 18000 rpm for 20 minutes to remove the drug present in it using a refrigerated centrifuge. The temperature is maintained at 4±1℃ at this stage of process. Introduction of 1 ml of formulation is established post removal of free drug. Magnetic stirrer is switched on by placing it in a beaker containing 100 ml of 0.1 N HCl and ethanol mixtures. It should be noted that the temperature is to be maintained at 37±2℃ throughout this second step of this process [7,10]. 37±2℃ is actually the normal human body temperature range[2].

For Nano Erythrosomes (NER), *Sagar R. Paygude.et.al* however suggests that the in-vitro studies can be performed by incubation of both normal & loaded NER at 37±2℃ using phosphate buffer (pH =7.4).0.8µ spectropore membrane filter is attached to a sterile hypodermic needle. With this filter attached hypodermic needle, samples are withdrawn at regular periodic intervals. Determination of hemoglobin (or) drug can be done using Laser Light Scattering (or) spectrophotometrically at 540 nm. *Ravikant Gupta et.al.*has a procedure somewhat similar to *Sagar R. Paygude.et.al.*However, *Ravikant Gupta et.al.*suggested proteination by employing solvents like methanol after

drawing the sample through syringe containing hypodermic needle. The filter involved in this methodology is about the size of 45 µm. It also suggests the storage conditions for the suspension to be used for these studies [20]. *Dong et.al* has proposed a method similar to *Jaya Agnihotri.et.al* with a change in molecular cut-off of semi-permeable membrane (3500 Da). The width of the dialysis tube is reported to be 10 mm, into which the NER is introduced. The volume of sample taken for analysis of drug content is replaced with Phosphate Buffer Saline (pH =7.4)[10]. *Nangareet.al.* which employs a metabolic rotating wheel incubator bath [13], is similar to the procedure discussed under *Sagar R. Paygude.et.al. Raut Deepikaet.al.* describes the methodology for determination of in-vitro drug stability. The NER can be checked for its stability by incubating the cells in autologous plasma (or) iso-osmotic buffer. Temperature is maintained at 4℃ and 37℃. Hematocrit is adjusted between 0.5-5%[12].

In-vitro storage must be done at 40℃. Acid-citrate solution and Hank's balanced solution are considered as some of the in-vitro storage media. Lyophilization post exposure to membrane stabilizing agents can help in enhancing stability. Examples of membrane stabilizing agents include Glutaraldehyde, Toluene-2,4-diisopropionate, etc[13].

Erythrocyte sedimentation rate

Erythrocyte Sedimentation Rate is defined as parameter through which stability of suspension of RBC is measured under specified test conditions. It is considered as a parameter for detection of inflammatory process and infections [28, 29]. However, *Dissanayake et.al* does not approve this point. It proposes with various methods for measurement of ESR. Westergren method and Wintrobe method are considered as the two most significant methods. *RautDeepika et.al* postulates the determination of NER using a standard tube. When the value of ESR is higher than 15 mm/hr, the possibility of obscure and active disease is evident [12].
Ravikant Gupta et.al suggests the methodology [20] which is same to *Raut Deepika et.al.*

Shape and surface morphology

Shape and morphology is considered as an essential factor for nano-erythrosomes. It is considered that biconcave and circular structure of such particles is highly considered. This is due to less toxicity [2, 14]. Scanning Electron Microscopy (SEM), Transmission Scanning Microscopy (TEM) can be used for determination of erythrocytes before the conversion to NER. Occasionally, it can be applied to NER as well [10,12,41]. *Jaya Agnihotri.et.al* discusses the methodology in detail. It employs a double sided tape to stick the drug loaded NER. It is placed under desired microscopy and studied. The tape is stuck to metallic stand, which is coated with a reedy layer of Gold (Au) under Argon atmosphere. Dynamic Light Scattering (DLS) technique is employed to study the vesicular size [10]. *Kavita et.al* furnishes data to study hematological indices such as Mean Hemoglobin Concentration (MHC), mean corpuscular volume (MCV), etc. It also employs Scanning Electron Microscopy (SEM)[17].

The permeability in erythrocyte ghosts is tested using 2 different fluorescent dyes: DiD (Red) & FITC Dextran (Green). FITC Dextran is used at a higher concentration (100µg) than Red fluorescent dye (10µg). Structure of Nano-RBC is then analyzed under Transmission Electron Microscopy (TEM). Beckman Coulter is used to determine the particle size [7, 39]. Along with the shape & structure, size must also be investigated, since it plays a key role in determination of precarious & therapeutic aspects of the Nano-RBC [14]. Confocal Laser Scanning Microscopy (CLSM) is considered to be microscopy of choice and NER can be viewed post staining with some suitable solvents containing functional groups like perchlorate [52].

Cell viability

Cell viability can be defined as number of live (or) healthy cells in total sample [31]. Viable counts are determined using Spread plate & Pour plate methods. Miles-Misra method and membrane filtration are also considered [36]. Tetrazolium reduction assays are being conducted for detecting viable cells. MTT, MTS, XTT, WST-1 are some of the compounds which are used in this type of assays [32,33]. Bio-compatibility can be diagnosed by performing MTT type of assay. Dimethyl Sulfoxide (DMSO), Trypan Blue, MTT-Tetrazolium are the reagents required in this process.

These reagents are required in very low concentrations & dilutions. Along with a micro-plate reader, absorbance of culture medium is checked at 570 nm[7, 33].

***In-vivo* studies**

The type of studies, which are conducted in a live organism in order to monitor the toxicity & metabolism of a drug is called In-vivo studies [34].In-vivo studies can be performed if in-vitro studies show good result [10]. In-vivo studies require labeling of the drug, which can be done using Bio-markers (or) Radio isotopes [35]. The studies are conducted in SD rats. Ethyl p-hydroxybenzoate and acetonitrile was used in this experiment. The drug is injected at tail vein of rats. Pharmacokinetic parameters like half-life ($T_{1/2}$), Maximum plasma concentration, Area Under Curve (AUC), etc. are calculated using a software. Tissue distribution is also estimated in this fashion[7]. CDF_1 mice can be also employed. In such cases, intra-peritoneal route of administration is preferred. Phosphate Buffer Saline is considered as placebo.Lethal dose (LD_{50}) as well as effective dose (ED_{50}) must be determined for drug safety[4]. Albino rats can be used for in-vivo studies as well.Caudal vein is chosen for injection of drug in Albino rats. HPLC is used for drug content determination. However, rats are sacrificed in latter half of the experiment[10].

Applications

- It can be used as drug carrier for various drugs such as Artesunate, Pyrimethamine, etc[4, 10, 39, 41].
- It is used in enhanced cancer immunotherapy for antigen delivery in the form of Nano-Ag@Nanoerythrosome[39].
- Long time circulation on the localized tumor can be achieved by Nano-RBC [38,39].
- It is applied in the treatment of disease using enzymes [12, 42].
- Nanoerythrosomes play an essential role in enhancement of targeted drug delivery by encapsulating drug safely [42, 43].
- Encapsulation of drug loaded hydrogel substances by Nano-RBC is done to produce a Novel Drug Delivery System (NDDS)[43].

Nanoerythrosomes tailoring[44,45]

Recently in 2019, a technique has been found by which the size of nano-RBC can be adjusted. Size of Nanoerythrosomes produced by this technique can vary from 30-200 nm. By changing the lipid type and ratio, size modulation of NER can be effected. Rigidity of NER can be improvedby protein scaffolding. Co-ordination of cascades of signal transduction can be achieved by Protein scaffolding process.

Fabrication process of NER[46-48]

Nano-fabrication is considered as a downscaling process by which physical aspects of a constituent is reduced to required level. High yield of Nanoerythrosomes can be achieved by fabrication process. Recent technology has been invented in which ion beam to produce micro-ripples. Nano-machining employing ultrasonic vibration has also been developed for the purpose of nano-fabrication. Nanoerythrosomes are considered as drug delivery systems of choice for monoclonal antibodies.

Combination with peptide delivery system[49-51]:

The application of Nanoerythrosomes as carrier is extensive in Cancer therapy, delivery of other drugs like peptides. Pulmonary vasodilation can be enhanced in duration of action, thereby, using peptide having good cell permeability. These NER are produced by extrusion and hypotonic dilution method. Drug release by NER occurs for about 48 hours; meanwhile, the physical stability of such formulations is as high upto 21-25 days.Rho kinase inhibitor like Fasudilis used in preparation of such NER.IT has been observed that the drug conjugated delivery system must be smaller than threshold size limit of 250 nm. Staying below the threshold limit of 250 nm provides the drug to cross the natural defense mechanism of pulmonary system, thus, increasing the contact time with lungs resulting prolonged duration of action. Due to drug concentration within the therapeutic window for longer time, therapeutic

effects are attained at a higher magnitude. Besides in conjugation with other drug delivery system, Nano-erythrosomes itself acts as bioactive carrier.

CONCLUSION

It can be concluded by saying that nano-erythrosomes is one of the novel drug delivery systems, which has the least possible Adverse drug reactions (ADR). Since, nano-technology is one of the most prolific fields of science, advances in this type of drug delivery system also briskly arrives on passing course of time. When taken from the humans, there is almost no immunological issuewhen administered in intensive care of a patient suffering from chronic (or) lethal disease or disorder. This Drug delivery system owing to nano-size, targeting to the tumors can be done thereby maximizing the drug effect on the site of infection (or) problem.

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RESEARCH ARTICLE

Social Media and Depression during COVID-19: Developing a Logistic Regression Model

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ABSTRACT

COVID-19 has forced masses to take refuge in the digital world due to self-isolation and quarantine. The over dependency on the digital medium for communicating with peers and others has led to array of new problems especially among the adolescents. The well-being of the adolescents is negatively affected by the use of social media primarily depression which is associated somewhat with increased morbidity and mortality. Therefore, the purpose of this study was to determine the prevalence and the factors associated with depression due to excess social media use among under graduate students during COVID-19 pandemic. This cross-sectional study was conducted among one hundred and two randomly selected undergraduate subjects aged between 16 to 23 years of Manipal University Jaipur. Depression among subjects had been diagnosed through the scale made by Aaron T. Beck. The data of age, gender, source of accessing social media, usage of social media in a day and average length of each visit to social media were used as independent variables. The dichotomous dependent variable was whether the subjects were depressed or not-depressed. Chi-square results revealed that depression was significantly associated with usage of social media in a day and average length of each visit. However, logistic regression results revealed the higher depression rates in the subjects with average length of each visit to social media. The study suggests appropriate use social media with proper schedule and self-regulation to prevent or manage depression.

Keywords: Social Media, Usage, Depression, Chi Square, Logistic Regression.

INTRODUCTION

Social Media has brought a paradigm shift in the human communication process. The exceptional rise in the use of social media by youth is a part of normal life today which has a great impact on their life. The COVID-19 pandemic

has equally transformed the routine of citizens across the globe. The pandemic has brought about revolutionary changes especially with reference to digital communication. Strict implementation of lockdowns and quarantine precautions have forced masses to take refuge in the digital world for communication, entertainment, profession and other requirements. This has opened new avenues and lots of opportunities but there are many concerns as well which need to be addressed immediately. One of the serious concerns is the rise in the cases of depression among youth with many opting for terminal steps. As depression is ranked as the single largest contributor to global disability (7.5% of all years lived with disability in 2015). More than 300 million people are now living with depression, an increase of more than 18% between 2005 and 2015 (WHO, 2019) and in the United States, current estimates suggested a lifetime incidence of between 13.3% and 17.1% and a yearly cross-sectional prevalence ranging from 2.3%-4.9% (Fava & Cassano, 2008).

Shapiro (1999), argued that the "emergence of new, digital technologies signals a potentially radical shift of who is in control of information, experience and resources". According to Neuman, (1991) "We are witnessing the evolution of a universal interconnected network of audio, video and electronic text communications that will blur the distinction between interpersonal and mass communication and between public and private communication". As predicted by Neuman the new media will escalate the opportunities, speed and volume of communication and integrate all forms of communication. According to National Mental Health Survey 2015-16 of India, nearly 15% Indian adults need active intervention for one or more mental health issues and one in 20 Indians suffer from depression. It is estimated that in 2012, India had over 258,000 suicides, with the age-group of 15-49 years being most affected (WHO, 2019).Social media are web-based sites like Facebook, Instagram, Twitter, Snapchat, WhatsAppetc. that allow people to interact with each other and are very popular among adolescents (Rideout, Foehr& Roberts, 2010). Some studies highlight that among these social media sites, Facebook was used by more than70% of adolescents (Lenhart, Purcell, Smith & Zickuhr, 2010).

Different cognitive behavioural theorists have developed their own unique twist on the cognitive way of thinking. According to Dr. Aaron Beck, negative thoughts, generated by dysfunctional beliefs, are typically the primary cause of depressive symptoms. A direct relationship occurs between the amount and severity of someone's negative thoughts and the severity of their depressive symptoms. In other words, the more negative thoughts you experience, the more depressed you will become. Beck also believes that there are three main dysfunctional belief themes (or "schemas") that dominate a person with depression's thinking: I am defective or inadequate, all of my experiences result in defeats or failures and the future is hopeless. Together, these three themes are described as the negative cognitive triad. When these beliefs are present in someone's thoughts, depression is very likely to occur (if it has not already occurred). (Nemade, R., 2019).

The attraction of social media is the instantaneous action-reaction that is gratifying for the users but opens up door for other problems. The social media, in some sense, is connected to the machine and acceleration seems to be the operating principle behind the machine. Hence a peculiar method of life is originating with this perception and leading to different levels of anxiety as the leading factor behind depression. The term 'Facebook depression', has been gaining popularity with youngsters exhibiting the signs of depression due to over engagement with social media platforms. It is known 'Facebook depression' only because Facebook phenomena is fore runner for the social media platforms. Amassing 'likes' and commenting on others posts has become the central activity for the youngsters. To keep up with the popularity of peers post youngsters are going extra mile and risking lives. But even after such efforts if they fail to gain likes there is a huge vacuum and sense of failure. This needs continuous engagement and creates a sense of self-awareness which stimulates depression. Furthermore this may give rise to seclusion or other self-destructive habits. The problem with digital world is once you post anything it cannot be deleted easily, it may be traced with someone this maybe another cause of depression and anxiety.

In addition social media promotes the projection of a perfect self, which leads to depression anxiety. Social media promotes superficial connections that can end up causing long-term emotional and psychological problems. Social media also fosters false intimacy both intentionally false and unintentionally false, as seen in the selfie photo and catfish examples. Without acknowledging these negative personal impacts of social media, the harms, both psychological and emotional will continue to grow. Several research studies were conducted to evaluate the association between social networking sites and depression out of which some researches revealed that there is an association between social media and depression. In several recent studies, teenage and young adult users who spend more time on Instagram, Facebook and other platforms had substantial (from 13 to 66 percent) higher rate of reported depression than those who spent less time (Miller, 2019) while on the other hand there are studies that found no association among the said variables (Selfhout et. al., 2009, Ohannessian, 2009, Primack et. al., 2011 & Jelenchick et. al., 2013).The study is important because the social communication integrates the diverse people and directly intersects with lives of users that have multidimensional perspectives. Therefore, the purpose of the present study is to determine the prevalence and risk factors of depression during COVID-19in context of social media usage among undergraduate students.

Objectives of the Study

- To understand the social media and its association with depression
- To investigate the association of usage of social media and with depression among youth
- To examine the average length of each visit to social media with depression among youth
- To develop the logistic model based on age, gender, social media usage, average length, Access of Social media and Social Media Platform

Hypotheses of the Study

- It was hypothesized that there is a significant association between usage of social media and depression among youth
- It was further hypothesized that there is a significant association between the average length of each visit to social media and depression
- It was further hypothesized that the logistic model so developed on the basis of age, gender, social media usage, average length, access of social media and social media platform is having significant impact for being depressed and not-depressed.

REVIEW OF LITERATURE

Orleans and Laney (2000) tried to study the approach of children and youth towards the latest technologies whereas Hughes and Hans (2001) and others tried to identify the trends in internet usage and the amount of time spent during this engagement.

A study in "Journal of Epidemiology and Community Health (2013)", states, "the wellbeing of men and women, especially in midlife, depends on having a wide circle of friends, and lack of friends is associated with significantly lower levels of psychological wellbeing. Living in the era of hyper connectivity, with hundreds of 'friends' on our social network, it is but logical to expect our mental wellbeing to be the best ever in the history of humanity". The book Social Networks in Youth and Adolescence by Cotterell (2007) focuses on youth and adolescence between 12-25 years of age and their use of social media. The author highlights the methods adopted by youth and analyses the thinking behind networking in societal relationships. The author has discussed key topics such as, "youth transitions, network analysis, peer victimization, youth citizenship etc."The unique characteristic of online community forums is that "[n]o one knows everything, everyone knows something, [and] all knowledge resides in

humanity". Keles, McCrae, & Grealish (2019) done the systematic review to synthesize the evidence on the influence of social media use on depression, anxiety and psychological distress in adolescents. Their findings revealed that all domains (time spent, activity, investment and addiction.) correlated with depression, anxiety and psychological distress. Shimoga, Erlyana, &Rebello (2019), examined the "associations between the frequency of social media use and physical activity and sleep adequacy among middle and high school students and found that an optimal level of social media use that was beneficial to a variety of health behaviors would be most beneficial to adolescents who were in the middle of the health behavior spectrum.

Kelly et. al. (2018) conducted a study to assess whether social media use is associated with adolescents' depressive symptoms, and also tried to investigate multiple potential explanatory pathways via online harassment, sleep, self-esteem and body image. The result of this study revealed that the association between social media usage and depressive symptoms was larger for girls than for boys and also found that greater social media usage related to online harassment, poor sleep, low self-esteem and poor body image; associated to higher depressive symptom scores. Shensaet. al. (2018) done a study, to identify distinct patterns (time, frequency, multiple platform use, problematic social media use, and social media intensity) of social media use (SMU) and to assess associations between those patterns and depression and anxiety symptoms. Multivariable logistic regression models were used to assess associations between cluster membership and depression and anxiety. They concluded that SMU patterns are associated with risk for depression and anxiety.

Ali, Al Harbi& Rahman (2018), undertaken a cross-sectional study to find out the association between social media users and depression in female teenagers in Buraydah city QassimReigon, K.S.A. Result of the study revealed that people, who spend a lot of time using social media, do not necessary to have depression. Hardy &Castonguay(2018), highlighted the "relationship between social media and mental well-being moderated by age and suggested that young adults, unlike middle-aged adults, are using social media in the way it was intended; to come together and garner social support". Huntet. al.(2018) undertook an "experimental study to investigate the potential causal role that social media plays in the relationship between social media use to worse well-being and came to a conclusion that limiting social media use to approximately 30 minutes per day may lead to significant improvement in well-being

McCrae, Gettings, &Purssell (2017) done a systematic review of 11 studies measuring social media use and depressive symptoms among children and adolescents and results showed a small but statistically significant relationship between social media use and depression. Another meta-analysis of 23 studies conducted by Marino, Gini, Vieno, &Spada (2018), result of the study showed the correlation of problematic Facebook use and psychological distress among adolescent and young adults.Selfhoutet. al. (2009) examined the "longitudinal associations of time spent on Internet activities for communication purposes (i.e., IM-ing) versus time spent on Internet activities for non-communication purposes (i.e., surfing) with depression and social anxiety, as well as the moderating role of perceived friendship quality in these associations and their results supported social compensation effects of IM-ing on depression and poor-get-poorer effects of surfing on depression and social anxiety, respectively". Early research by Kraut et. al. (1998) and Nie&Ebring (2000), found that, "internet usage leads to an increase in depression, loneliness, and neglect of existing close relationships."The social media updates and awaiting the feedbacks from the peers has increased undue stress on the users. A research undertaken on 7,000 mothers, discovered, "42% of mothers using the photo-sharing site Pinterest, reported occasionally suffering from Pinterest Stress (Dube, 2013)."The constant search for self-recognition and remaining alert for the same has increased stress hormones. The users try to project the perfect self on social media platforms, which is an unending struggle giving rise to depression.

According to Koerner and Fitzpatrick (2000), communication plays a central role in the family hence it was important to study the impact of social media usage as decrease in communication among the members of family and mental health of students.Turow and Nir (2000) and Varghese and Nivedhitha (2014) in their study have noted that the

students avoid discussing personal problems with family members which leads to lack of moral support which is important for mental stability. The result was similar to McAndrew and Jeong (2012) which suggests that social comparison is quite common on social networking sites. The study at Stony Brook University by Davila & Starr, (2010) revealed, "in a sample group of teenage girls, excessive Facebook usage caused the sample group to be at a higher risk for depression and anxiety. A year later, the researchers re-valuated the group for any signs of depression or anxiety. The study findings proved that users who frequently discussed their problems with friends, through social media, experienced higher levels of anxiety than those who did not. Texting, instant messaging and social networking make it very easy for adolescents to become even more anxious, which can lead to depression. Clearly social media is inadvertently leaving youth susceptible to become overly self-conscious, anxious and ultimately depressed".Davila et. al (2010) found that there is a link between depression and social media as students felt that the lives of others are better as compared to their, only going by the social media pages of their friend. The findings of O'Keefe & Clarke-Pearson (2011), that conceptual and technical gaps may create relational gaps between parents and their children which again leads to loneliness and other mental disorders.

METHODOLOGY

Social media is a collection of online platforms and tools that people use to share content, profiles, opinions, insights, experiences, perspectives and media itself, facilitating conversations and interactions online between groups of people. The term new media and Social Media have been used interchangeably during the research (Boyd & Ellison, 2007). According to World Health Organisation, Depression is a common mental disorder affecting more than 264 million people worldwide. It is characterized by persistent sadness and a lack of interest or pleasure. The causes of depression include complex interactions between social, psychological and biological factors. Jaipur is the capital and the largest city of the Indian state of Rajasthan in Northern India. It was founded on 18 November 1727 by Jai Singh II, the ruler of Amer, and after whom the city is named. As of 2011, the city had a population of 3.1 million, making it the tenth most populous city in the country. Jaipur is also known as the Pink City, due to the dominant color scheme of its buildings. It is located 268 km (167 miles) from the national capital New Delhi.

Sampling is a process of selecting certain number of units from the population of research. To fulfil the purpose of the present study, random sampling method was used which is a type of probability sampling method in which participants that represent the population included in the sample. The survey was sent to randomly selected 150undergraduate students of Manipal University Jaipur, out of which only 107 participants (71%) completed the survey. Among the 107 participants who completed the survey a meagre 4% of students denied using social media. These subjects were excluded from the investigation since they did not qualify for the hypothesis testing. Hence this cross-sectional study was conducted on 102 undergraduate students aged between 16 to 23 years. The Depression among the subjects was diagnosed through the Beck's Depression inventory made by Aaron T. Beck (1961) through online survey form. The independent variables for the study were age, gender, source of accessing social media, usage of social media in a day and average length of each visit to social media. The dichotomous dependent variable was whether the subjects were depressed or not-depressed. A score of seventeen or higher was accepted as presence of depression, while rest of the subjects who scored less than seventeen fell under the non-depression category.

The subject's demographic information were determined by frequency and percentage, whereas the Chi-square test was used to find out the association between social media, average length at each visit and depression. It is a test of significance generally used to test that the two variables are statistically associated or not. On the other hand, logistic regression was employed using Statistical Package for Social Sciences (SPSS) version 20.0 to determine whether social media usage, average length, gender, age is responsible for being depressed and not-depressed. Logistic regression is a predictive analysis which is used to describe data and to explain the relationship between one dependent binary variable and one or more nominal, ordinal, interval or ratio-level independent variables.

RESULTS

Demographic information of 102 subjects (male=56 and female=46) are described in **Table-1**with the help of frequency and percentage. Subjects percentage of age among 16-18 yrs. was 41.2%, the 19-21 yrs. was 54.9% whereas 22 and above were 3.9% respectively. The percentage of access of social media only by computer, only by mobile and by both computer and mobile phone were 02%, 15.7% and 82.4 5 respectively; the social media platform most used among Facebook, Instagram, WhatsApp, Snapchat or any other were 13.7%, 19.6%, 49% and 17.6% respectively. The frequency of social media usage less than 06 times and more than 06 times were 45.1% and 54.9% respectively whereas the average length of each visit less than 30 minutes and more than 30 minutes were 70.6% and 29.4% respectively. The total depressed male and female were 42.9% and 57.1% respectively, while the percentage of not-depressed male and female were 59.5% and 40.5% respectively.

Table-2 shows that the subjects who were in depressed category, 71.4% % of were using social media more than six times, whilst of all subjects in not-depressed category, 51.4% of them were using social media less than six times. In table-3SPSS highlighted that "0 cells have expected count less than 5 and the minimum expected count is 12.63" which satisfied the sample size requirement for the chi-square test of independence and also revealed that usage of social media is associated with depression as the p-value is less than 0.05 (Chi-square: 4.257; $p<0.039$). Table-4 shows that the subjects who were in depressed category, 78.6% their average length of each visit was more than 30 minutes, whilst the subjects in not-depressed category, 89.2% the average length of each visit was less than 30 minutes. Table-5 highlighted that "0 cells have expected count less than 5 and the minimum expected count is 8.24" which satisfied the sample size requirement for the chi-square test of independence and also revealed that average length of each visit is associated with depression as the p-value is less than 0.05 (Chi-square: 44.925; $p<0.000$).

Table-6highlightedthe Omnibus Tests of Model Co-efficients which gives the result of the Likelihood Ratio (LR) which indicates whether the inclusion of this block of variables contributes significantly to model fit. Also the statistics for the Step, Model and Block are the same because we have not used stepwise logistic regression or blocking. In this case, the model is statistically significant because the p-value is less than 0.000 ($p<0.000$), that indicates the accuracy of the model improves when we add our explanatory variables.Table-7 provides the -2 log likelihood and pseudo R^2 values for the model. The Cox & Snell R Square and Nagelkerke R Square values reveal how much variation in the outcome is explained by the model. This model explained variation ranges from 38.0% to 55.0%, respectively in the dependent variable i.e., Depression. Table-8 explains the Hosmer and Leme show Test, which tests the goodness of fit. Results revealed that the model is a good fit to the data as the p-value for the given chi-square value (9.756) is less than 0.05 ($p>0.283$).Table-9 displayedin the classification matrix that 86.3 % of the cases are correctly classified the outcomes. Table-10 explains the Wald test results which show the contribution of each independent variable to the model and its statistical significance. From these results only average length of each visit added significantly to the model as the p-value is less than 0.05 ($p<0.05$), which is having more power of predicting the probability of an individual to be in depression category.

DISCUSSION AND CONCLUSION

COVID-19 has drastically changes the way we communicate; perform our professional work and other social activities. The dynamic Indian society has been abruptly brought to halt and left us unprepared for the challenges we are encountering. The new lifestyle post COVID-19 has lead to isolation and susceptible to depression even in the young generation. According to World Health Organisation (WHO), Depression is a significant contributor to the global burden of disease and affects people in all communities across the world. The report of WHO and other organisations reflects that the consequences are worse that even lead to suicide. Almost 1 million lives are lost annually due to suicide, which counts to 3000 suicide deaths every day. When every person who commits a suicide,

20 or more may attempt to end his or her life as per the WHO report, 2012 (WHO, 2012 & Marina, 2012) and both male and female are equally affected by the depression. Researcher has taken this study with a consideration that the generally bustling Indian students in campus are deprived of real social life and hence the digital communication platforms (social media) has engrossed the students and has dominant influence on the understanding of day today life. The study explores, the social media habits of undergraduate who are busy communicating those people who are not actually there at the cost of those who are with them. Considering the rising amount of individuals who are engaged with social media for a long time, it is of great importance to examine the potential impact it has on the mental health of the users and hence develop preventive mechanisms which will equip those at risk as early as possible. The most vulnerable aspects of social media usage on mental health are yet to be determined. Therefore, the main purpose of this study post COVID-19 was to examine the depression issue that needs to be addressed first and to know whether the frequency of social media usage by individuals is related to the deteriorating effect on mental health. The results of this study suggest that during COVID-19, depression among undergraduate students is greatly influenced by social media usage.

The present study was undertaken to examine the association between social media usage and depression among adolescents. The results of the study revealed that, female are more depressed as compared to male in the category which is supported by the study done by WHO (2008), which highlights that the burden of depression is 50% higher for females than males. In fact, depression is the leading cause of disease burden for women in both high-income and low-and middle-income countries. Also, Van Ordenet..al. (2010) study recommended that women might probably experience many risks that highlight the presence of thwarted belongingness and perceived burdensomeness and Yaka (2014) also concluded in their paper that depression was significantly associated with female gender, being single or divorced, lower educational status, low income, unemployment, and lack of health insurance. Likewise, those who have spent more time on social media are likely to have depression in their later life. These results are in partial consonant of the study done by Woods et.al. (2016), as mentioned in their study that using night-time social media and emotional investment can affect the sleep quality and levels of depression in adolescents. Their findings also concluded that the use of social media is a major factor that affects adolescence sleep quality, and levels of anxiety which results in poor sleep quality and increased depression.

Hypothesis taken earlier that there is a significant association between usage of social media and depression among the undergraduate students was accepted and conforms to results from previous studies done by Khanet. al. (2018) which concluded that the usage pattern of social media users reflects the mood of the user which can be used to analyse the mental state of the users and predicting depression. These results are also supported by the studies conducted by Aldar wish and Ahmad (2017), De Choudhury et. al. (2013) and Saravia et. al. (2016). Likewise there was also a significant association between average length of social media at each visit and depression; these results are in a partial consonant of the study done by Linet. al. (2016)which concluded that social media use was significantly associated with increased depression. The study compared those in the lowest quartile with individuals in the highest quartile of social media site visits per week which revealed that there is significantly increased chances of depression among highest quartile of social media visit per week. Robinsonet. al. (2019) concluded in their research that higher participation in social media usage behaviour is associated with a higher likelihood of having Major Depressive Disorder (MDD).

Lastly the hypothesis also reflected that average length at each visit on social media is the most contributing factor leading to depression which is supported by the study done by Hu et. al. (2015)who predicted that the depression in users by building a classification model using Logistic Regression method and concluded that it is practical to predict whether a user is depressed or not with respect to Social media usage. Feinstein et al. (2013) also found that social comparisons on social media were associated with an increase in depressive symptoms. Steers et. al. (2014) have suggested that the amount of time spent on social media is related to the likelihood of making social comparisons, which is associated with an increase in depressive symptoms. Likewise, Grieve et. al., 2013; Mota, 2014; Wright et. al., 2013 in their respective studies have shown that individuals who use Facebook as a means to enable

perceived social support and connection also reported some depressive symptoms. The overall findings of this study highlight the strong association between social media usage during COVID-19, and depression among the undergraduate students. In the present study WhatsApp was the most preferred social media platform followed by Instagram and Facebook. The increased average length at every visit to social media is the important contributing factor leading to depression. The female participants were found to be more prone to depression in comparison to male counterparts using social media. The participants using social media for more than 30 minutes during their visit to social media platforms are also susceptible to depression. The social media has enabled us to socialize and coordinate public life, form opinion and create movement and build consensus. Social media has allowed youth to explore and create their own language and assert their own identities and has facilitated a new type environment which has transformed the conventional modes of communication but at the same time it poses threat to the psychological aspects of the undergraduate students.

The current study is strengthened by both the rigor of the data collection design and the established validity of the measurement tool used. However, as a single study cannot prove or disprove an association, replication of our findings across diverse demographic groups is necessary. The current study is limited to undergraduate students in a single university setting and a moderate sample size. It is also important to note that we assessed the association between social media use and depression symptoms measured with the data collected at a single time point, due to time and resource considerations. Longitudinal studies are necessary to elucidate more clearly the association of social media and depression that would be useful in formulating policies to improve depression risk factors among undergraduate students. Nonetheless, our findings will have important implications for youth counsellors and the model may further moulded as per requirement. Hopefully in changing times post COVID-19 when we are glued to our gadgets for communication, with early intervention and successful prevention in childhood and adolescence we can reduce the occurrence of depression in future.

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Table 1. Demographic Information

Demographics		**N (%)**
Age	16-18 Yrs	42 (41.2)
	19-21 Yrs	56 (54.9)
	22 Yrsand Above	04 (3.9)
Gender	Male	56 (54.9)
	Female	46 (45.1)
Access of Social Media	Only by Computer	02 (02)
	Only by Mobile Phone	16 (15.7)
	By both Computer and Mobile Phone	84 (82.4)
Social Media Platform Most Used	Facebook	14 (13.7)
	Instagram	20 (19.6)
	What's App	50 (49)
	Snapchat or Any other	18 (17.6)

Social Media Usage	Less than 06 Times	46 (45.1)
	More than 06 Times	56 (54.9)
Average Length of each Visit	Less than 30 Minutes	72 (70.6)
	More than 30 Minutes	30 (29.4)
Depressed	Male	12 (42.9)
	Female	16 (57.1)
Not-Depressed	Male	44 (59.5)
	Female	30 (40.5)

Table 2. Association among Social Media Usage and Depression

			Category		Total
			Not Depressed	Depressed	
Social Media Usage	Less than 6 times	Observed Count	38	8	46
		Expected Count	33.4	12.6	46.0
		% within Depression Score	51.4%	28.6%	45.1%
	More than 6 times	Observed Count	36	20	56
		Expected Count	40.6	15.4	56.0
		% within Depression Score	48.6%	71.4%	54.9%
Total		Observed Count	74	28	102
		Expected Count	74.0	28.0	102.0
		% within Depression Score	100.0%	100.0%	100.0%

Table 3. Chi-Square Test

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.257[a]	1	**.039**		
Continuity Correction[b]	3.387	1	.066		
Likelihood Ratio	4.385	1	.036		
Fisher's Exact Test				.047	.032
Linear-by-Linear Association	4.216	1	.040		
N of Valid Cases	102				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 12.63.					
b. Computed only for a 2x2 table					

Table 4. Association among Average Length of each Visit and Depression

			Depression Score for Logistic		Total
			Not Depressed	Depressed	
Average Length of each visit	Less than 30 minutes	Observed Count	66	6	72
		Expected Count	52.2	19.8	72.0
		% within Depression Score	89.2%	21.4%	70.6%
	More than 30 minutes	Observed Count	8	22	30
		Expected Count	21.8	8.2	30.0
		% within Depression Score	10.8%	78.6%	29.4%
Total		Observed Count	74	28	102
		Expected Count	74.0	28.0	102.0
		% within Depression Score	100.0%	100.0%	100.0%

Table 5. Chi-Square Test

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	44.925[a]	1	.000		
Continuity Correction[b]	41.721	1	.000		
Likelihood Ratio	43.790	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	44.485	1	.000		
N of Valid Cases	102				
a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 8.24.					
b. Computed only for a 2x2 table					

Table 6. Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	48.833	6	.000
	Block	48.833	6	.000
	Model	48.833	6	.000

Table 7.Logistic Model Summery

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	71.056[a]	.380	.550
a.Estimation terminated at iteration number 6 because parameter estimates changed by less than .001.			

Table 8. Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	9.756	8	.283

Table 9. Classification Matrix

	Observed		Predicted		
			Depression Score for Logistic		Percentage Correct
			Not Depressed	Depressed	
Step 1	Depression Score	Not Depressed	66	8	89.2
		Depressed	6	22	78.6
	Overall Percentage				86.3
a. The cut value is .500					

Table 10.Variables in the Equation

	B	S.E.	Wald	df	Sig.	Exp(B)
Usage of Social Media	-.999	.853	1.372	1	.242	.368
Average Length of Each Visit	4.472	1.014	19.439	1	.000	87.488
Gender	-.144	.722	.040	1	.842	.866
Age	-.191	.662	.083	1	.773	.826
Access of Social media	.417	.820	.258	1	.611	1.517
Social Media Platform	-.595	.350	2.895	1	.089	.552
Constant	-5.029	2.198	5.234	1	.022	.007

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REVIEW ARTICLE

Potential Drugs & Therapies for CoVID-19 – A Literature Review

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ABSTRACT

Ever since the start of this century, the world has been witnessing pandemics, the Severe Acute Respiratory Syndrome (SARS) in 2003, the H1N1 influenza in 2009, the Middle East Respiratory Syndrome (MERS) in 2012, and now Corona Virus Disease (CoViD-19) have caused havoc around the globe. CoViD-19 caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) formerly known as Novel Corona Virus, originated in Wuhan but has widely spread to many countries in the world. Mutation and adaption are the survival instincts for the microbial world. The world needs to be prepared to combat this invisible enemy. Even with advanced therapies and treatments, viruses have found a way to bring the world to its knees. Starting with a mere cold, it exceeds to pneumonia within a fortnight, having a high transmission rate through small droplets from the nose or mouth of an infected person. Even though the mortality rate of CoViD-19 is not as much as SARS and MERS, its transmission rate is much higher, as a result of which the World Health Organization (WHO) has declared this disease as a pandemic on March 11, 2020. Its resistance to drugs and therapies has put the researchers in a dilemma as to how to curb this deadly battle against CoViD-19. Most countries across the world have been following strict surveillance systems, movement restrictions and social distancing measures according to the Centre for Disease Control and Prevention (CDC) and WHO guidelines to restrict the transmission of this disease. This narrative review was conducted to summarize the origin, virology, transmission, clinical presentation, management and effectiveness of pharmaco therapies, immune therapies and psychological therapies for COVID-19.

Keywords: Coronavirus disease (CoViD-19), Severe Acute Respiratory Syndrome-2 (SARS-CoV-2), Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), World Health Organization (WHO), Centre for Disease Control and Prevention (CDC), pharmaco therapies, immune therapies, psychological therapies.

INTRODUCTION

History of Outbreak

In December 2019, while the people of China were heading home to celebrate spring festival with their families, they were encountered with cases of pneumonia caused by an unknown etiology detected in Wuhan, China [1]. A novel corona virus, the causative agent for the outbreak, was tentatively named 2019–nCoV by the WHO [2]. The patients presented an array of symptoms such as fever, dyspnea, dry cough and radiological findings showed bilateral lung opacities [3]. Furthermore, the public health office traced 27 cases to Huanan Seafood Wholesale Market which trades live species of bats, snakes, pangolins and badgers [4]. During the Spring Festival travel rush, Wuhan witnessed thousands of people leave the city potentially carrying the virus with them. [1] On 25th January 2020, a total of 1320 cases were confirmed globally, while 1965 cases were suspected nationwide [5]. Eventually the WHO issued a public health emergency of international concern (PHEIC) alarm on January 30, 2020. As a result of the rapid spread of this infection across the globe, the WHO declared a change in its status from an epidemic to a pandemic disease on March 11, 2020 [6].

Origin of SARS-CoV–2

Zoonotic viruses often jump from an initial animal carrier to an intermediate host species, which then transmits the virus to humans; such is seen in the case of the SARS outbreak and the MERS outbreak [7,8,9]. Table 1. Understanding intermediates helps the public health authorities to control risks as well as help scientists understand the evolution and pathogenesis of the disease. Similar to the case for SARS-CoV& MERS-CoV, the bat is still a probable species of origin for SARS-CoV-2 as it shares 96% whole-genome identity with a bat CoV, BatCoV RaTG13, from Rhinolophus affinis from Yunnan Province. Although there is only 4 % of divergence, it is another piece of evidence that suggest that SARS-CoV-2 could have passed to people through an intermediate species as its spike diverges in the RBD, which suggests that it may not bind efficiently to human ACE2 [8]. There is evidence of SARS-CoV-like CoV from lung samples of two dead Malayan pangolins and this fact was discovered close to when the COVID-19 outbreak occurred [9]. A compilation of all these findings portrays that pangolins are the possible intermediate hosts while bats are the possible initial host for SARS-CoV-2 [7, 8, 9].

Mode of Transmission

The SARS CoV-2 has 4 stages of transmission: Stage 1- first appearance of the disease through people with a travel history Stage 2- local transmission Stage 3- community transmission Stage 4- disease becomes epidemic. Many areas are seeing a steady growth in cases, and a cluster containment strategy has now been drawn up for large local outbreaks [12]. As SARS-CoV-2 virions are shed throughout the clinical course, patients with COVID-19 can spread the infection prior to symptom presentation, during the symptomatic course and also during the clinical recovery period [13]. 3 major routes of transmission have been known. *Respiratory transmission*, when the virus is mainly transmitted between people through "respiratory droplets" (>5-10 μm in diameter) when symptomatic people sneeze or cough. These are larger droplets with viral content deposit close to the emission point. *Aerosol transmission*, when the virus is mainly transmitted between people through "aerosols" (<5μm in diameter), these are smaller and can travel meters or tens of meters long distances through the air current. 3. *Contact transmission*, when the viral particles emitted from the respiratory tract of an infected individual land on a surface. Another person touches that object, and then touches their nose, mouth or eyes. The virus then sneaks into the body via the mucous membranes, infecting the second person [14]. Additionally, transmission through the fecal-oral route, [15] conjunctiva [16] and intrauterine vertical transmission [17] are still under study.

Clinical presentation of COVID-19

The World Health Organization (WHO) and the Center for Disease Control and Prevention (CDC) issued guidelines concerning the symptoms of CoViD-19.

Clinical presentation

- Presenting signs and symptoms of COVID-19 vary.
- Most persons experience fever (83-99%), cough (59-82%), fatigue (44-70%), anorexia (40-84%), shortness of breath (31-40%), myalgias (11-35%). Other non-specific symptoms, such as sore throat, nasal congestion, headache, diarrhea, nausea, and vomiting have also been reported. Loss of smell (anosmia), loss of taste (ageusia) preceding the onset of respiratory symptoms has also been reported.
- Older people and immunosuppressed patients in particular may present with atypical symptoms such as fatigue, reduced alertness, reduced mobility, diarrhea, loss of appetite, delirium and absence of fever.
- Symptoms such as dyspnea, fever, gastrointestinal (GI) symptoms or fatigue due to physiological adaptations in pregnant women, adverse pregnancy events, or other diseases such as malaria, may overlap with symptoms of COVID-19. [18, 19]

Risk factors for severe disease

- Age more than 60 years (increasing with age).
- Underlying non-communicable diseases (NCDs): diabetes, hypertension, cardiac disease, chronic lung disease, cerebrovascular disease, chronic kidney disease, immunosuppression and cancer have been associated with high mortality. Smoking [18, 19].
- CoViD-19 is classified as four levels based on the severity of symptoms: mild, moderate, severe, and critical. [20, 21].

Mild disease

Symptomatic patients (above table) meeting the case definition for CoViD-19 without evidence of viral pneumonia or hypoxia.

Moderate disease

Clinical signs of pneumonia (fever, dry cough, dyspnea, fast breathing) but no signs of severe pneumonia.

Severe disease

Severe pneumonia with hypoxemia SpO_2 < 90%.

Critical disease

Acute respiratory distress syndrome (ARDS), or respiratory failure and may present shock, encephalopathy, myocardial injury or heartfailure, coagulopathy, acute kidney injury and multiple organ dysfunctions. [20, 21]

Virology

On 7th January 2020, the China CDC discovered the novel corona virus (nCoV-19), informally known as 'Wuhan virus' or 'China virus', as the causative virus for the pneumonic outbreak. [22] On 11th February 2020, the WHO renamed the virus as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) as the virus is genetically related to the coronavirus responsible for the SARS outbreak of 2003 and to destigmatize the association of the virus with any geographic location [23]. Although RNA viruses are more likely to be zoonotic than DNA viruses, advantageous genetic mutations and adequate cellular environment provided by the animal reservoir enables the virus to become more infectious to cross-species, infect and multiply within human hosts effectively [24].

Structure

SARS-CoV-2, a novel β-corona virus, is an enveloped, non-segmented, positive sense RNA virus. SARS-CoV-2 can be contracted from animals and fellow humans. Corona viruses are roughly spherical (diameter about 65-125nm) &moderately pleiomorphic in structure. Enclosed in the membrane protein are single strands of RNA. Structurally, SARS-CoV-2 has four main structural proteins including spike (S) glycoprotein, small envelope (E) glycoprotein, membrane (M) glycoprotein, and nucleocapsid (N) protein. The S glycoprotein is a transmembrane protein that assembles into homotrimers protruding in the viral surface to form the distinctive spikes and facilitates binding of envelope viruses to host cells by attraction with Angiotensin-Converting Enzyme 2 (ACE2). ACE2 are largely expressed in lower respiratory tract cells. S glycoprotein is cleaved by the host cell furin-like protease into 2 sub units namely S1 and S2. The S1 subunit consists of an amino-terminal domain and a receptor-binding domain (RBD). The S2 subunit consists of a fusion peptide (FP) region and two heptad repeat regions: HR1 and HR2. S1 is responsible for the determination of the host virus range and cellular tropism with the RBD make-up while S2 functions to mediate virus fusion in transmitting host cells. The N protein is the structural component of CoV localizing in the endoplasmic reticulum-Golgi region is thought to bind the genomic RNA in a beads-on-a-string fashion. The protein is involved in processes related to the viral genome, the viral replication cycle, and the cellular response of host cells to viral infections. N protein is also heavily phosphorylated and suggested to lead to structural changes enhancing the affinity for viral RNA. The M glycoprotein is the most structurally structured protein and the most abundant constituent of corona viruses. It plays a major role in determining the shape of the virus envelope. This protein can bind to all other structural proteins and also helps to stabilize nucleocapsids or N proteins by promoting the completion of viral assembly by stabilizing N protein-RNA complex, inside the internal virion. The smallest protein in the SARS-CoV-2 structure is the E protein. It plays a role in the production and maturation of this virus. These special structures of the SARS-CoV-2 help it to invade the host cell and cause severe health problems [25, 26, 27, 28, 29].

Pathogenesis

- **Receptor recognition**

  SARS CoV-2 can enter the human body through its receptors, ACE2 which are found in various organs such as heart, lungs, and gastrointestinal tract, thus facilitating viral entry into target cells [30]. Nasal epithelial cells, specifically goblet/secretory cells and ciliated cells display the highest ACE2 expression throughout the respiratory tract [30, 34, 36].

- **Attachment**

  The S glycoprotein on the outer surface is responsible for the attachment and entry of the virus to host cells [30, 31, 36]. This attachment occurs in the binding domain of S protein of SARS-CoV-2 receptors and can bind strongly to human ACE2 [31].

- **Endocytosis**

  RBD binding to ACE2 triggers endocytosis of the SARS-CoV-2 virion and exposes it to endosomal proteases [32]. Within the endosome, the S1 subunit is cleaved away, exposing the FP, which inserts into the host membrane [32]. The S2 region then folds in on itself to bring the HR1 and HR2 regions together. This leads to membrane fusion [32]. After fusion occurs, the type II transmembrane serine protease (TMPRSS2) that is present on the surface of the host cell will clear the ACE2 and activate the receptor-attached spike-like, S proteins [30].

- **Replication**

  After the virus enters the cells, the viral RNA genome is released into the cytoplasm [30, 32, 33]. Genome RNA is translated into viral replicase polyproteins pp1a and 1ab, which are then cleaved into small products by viral proteinases [33]. The polymerase produces a series of subgenomic mRNAs by discontinuous transcription and finally translated into relevant viral proteins [33]. Viral proteins and genome RNA are subsequently assembled into the membrane of the endoplasmic reticulum or Golgi [32, 33]. The nucleocapsid is formed by the

combination of genomic RNA and nucleocapsid protein. Then, viral particles germinate into the endoplasmic reticulum-Golgi intermediate compartment (ERGIC) [33]. At last, the vesicles containing the virus particles then fuse with the plasma membrane to release the virus through exocytosis [30, 32, 33,35].

Immune response

The effective antiviral responses of the host innate and adaptive immunity are essential for controlling the viral replication, limiting the spread of virus, inflammation and removing the infected cells [37, 42]. The host innate immune system detects viral infections by using pattern recognition receptors (PRRs) to recognize pathogen-associated molecular patterns (PAMPs) [38]. When SARS-CoV-2 infects the cell representing ACE2 and TMPRSS2, the active replication and release of the virus cause the host cell to undergo pryoptosis and release damage associated molecular patterns, including ATP, nucleic acids, etc [39]. This abnormality in the host cell is recognized by its neighboring epithelial cells, endothelial cells and alveolar macrophages, which triggers a cascade of events [39]. Later, when SARS-CoV-2 infects macrophages, it present CoV antigens to T cells [40]. This leads to T cell activation and differentiation which includes the production of cytokines associated with the different T cell subsets [40]. The tissue injury caused by the virus could induce the exaggerated production of proinflammatory cytokines, the recruitment of proinflammatory macrophages and granulocytes [37,39,40]. This results in the cytokine storm (CS) termed as a macrophage activation syndrome (MAS) or secondary hemophagocytic lymphohistiocytosis (sHLH), thus leading to further tissue damage [37,41]. COVID-19 possesses different levels of various cytokines and chemokines through the mild to severe stage of the disease [41]. When there is a negative (defective) immune response it may further lead to accumulation of immune cells in the lungs, which causes overproduction of pro-inflammatory cytokines [39,42]. This eventually damages the lung infrastructure. If not taken care the resulting cytokine storm circulates to other organs, leading to multi-organ failure [37,39]. In case of positive (healthy) immune response, the initial inflammation will attract virus-specific T cells to the site of infection, where they can eliminate the infected cells before the virus spreads [39]. Viral infection in these individuals can be blocked by neutralizing antibodies [39, 42]. Neutralized viruses are recognized by macrophages and apoptotic cells clear them by phagocytosis [39].

Altogether, these processes lead to clearance of the virus and minimal lung damage, resulting in recovery [39]. Similar to common acute viral infections, the antibody profile against SARS-CoV virus has a typical pattern of IgM and IgG production [43]. The SARS-specific IgM antibodies disappear at the end of week 12, while the IgG antibody can last for a long time, which indicates IgG antibody may mainly play a protective role [43]. Excessive inflammatory response with features of cytokine storm cause severe disease course such as septic shock or even multi-organ failure and worsens the prognosis in COVID-19 [37]. Based on the accumulated data it shows that innate immune response plays a crucial role in protective or destructive responses [42].

Diagnostic Tools

The primary goal of the CoViD-19 pandemic containment is to reduce the infection transmission in the population by reducing the number of susceptible persons by identifying and isolating infected patients [44]. The deployment of CoViD-19diagnostic testing has varied widely across the globe [45]. Many diagnostic tests for CoViD-19are available so far, with more gaining emergency approval every day [44,45].

Specimen collection

Samples are isolated from two major sources: the lower respiratory tract (LRT) and the upper respiratory tract (URT). A nasopharyngeal swab or the oropharyngeal swab, will be collected from URT and the bronchoalveolar lavage, tracheal aspirate, or sputum will be collected from the LRT[46].

Nucleic acid amplification test (NAAT) Detects nucleic acid of pathogen by amplifying RNA/DNA using Real-Time Reverse Transcription-Polymerase Chain Reaction (rRT-PCR)/ Loop- mediated isothermal amplification(RT-LAM[44,45,46].

rRT-PCR Amplifies target sequence using reverse transcriptase & PCR
Advantages: Provides information at the initial stages of infection.
Disadvantages: Long turnaround time, labor-intensive, complex, costly, technically intricate & easily contaminated[44,45,47,48].

RT-LAMP- Amplifies the target sequence in a single reaction & is extremely specific.
Advantages: Amount of DNA produced is high, it is simple, cheap, rapid and specific.
Disadvantages: No large background of literature [44,45,47,48].

Point of care (POC)
Molecular diagnostic testing from labs to POC to efficiently detect positive cases. Helps in effective use of quarantine resources, infection control measures, and patient recruitment into clinical trials of treatments. Gained Conformité Européenne (CE) marking / Food and Drug Administration (FDA) approval. Utilizes isothermal nucleic acid amplification techniques, PCR technology & lateral flow technology [44, 47].
Advantages: Easy to perform and produce rapid results to guide clinician care.
Disadvantages: Performs on specific instruments & amplifies a single genomic target of SARS-CoV-2, reducing their sensitivity and specificity [44,47].

Serological testing

Serological tests are blood-based tests that measure antibodies or antigens present in the blood when the body is responding to a particular infection [44,50]. According to FDA, IgM antibodies to SARS-CoV-2 are detectable in the blood just a few days after initial infection whereas IgG becomes detectable three days from symptom onset or at least 7–10 days after infection. 20–80% of SARS-CoV-2-positive cases are asymptomatic [44,50].
Advantages: Could identify previous exposure to a particular pathogen, used on a large scale to assess the overall immune response in a population.
Disadvantages: Less than 40% of infected individuals are seropositive (IgM/IgA) in the first seven days, making it unreliable for the detection of acutely infected individuals. Also, those with mild cases of CoViD-19do not produce antibodies as their innate immune system (cell-mediated immunity) wiped out the virus before the adaptive immune system (antibodies) had to produce antibodies [44,47,49].

Enzyme-Linked Immunosorbent Assay (ELISA)
It detects the presence of antibodies (i.e, IgM, IgG, or IgA) by binding of predetermined specific viral antigen to antibodies present in patient serum [47,49,50].
Lateral Flow Immunoassay (LFIA)
It will detect antibodies by binding it to tagged viral antigen, and then binding them to immobilized capture antibodies, which can be visualized as a line by the conjugated chromatographic tag[47,49,50].
Microsphere Immunoassay (MIA): It is a combination of chemiluminescence technique with immunochemical reactions to detect IgM and IgG antibodies that are specific to a specific pathogen [47,49,50].
Fluorescence immunoassay
It that can be performed on multi-test cover slides or be based on fluorescence immunochromatography which is rapid, but both need analyzers to read the results[47,49,50].

Imaging

X-ray examination

Shows bilateral multifocal alveolar opacities, which tend to confluence up to the complete opacity of the lung during advance stages of infection. Pleural effusion can be associated [45,51].

CT Scan

Sensitive to detecting early infection, assessing the nature &extent of lesions, & discovering subtlechanges thatare often not visible on chestradiography [45,51].

Epidemiology

An analysis of CoViD-19 active cases and mortality (fig. 4)

Clinical management

Strategies for preventing the spread of CoViD-19 include 1. Applying standard precautions for all patients at all times. 2. Ensuring triage, early recognition and source control. 3. Implementing empiric additional precautions for suspected cases of COVID-19 infection. 4. Implementing administrative controls. 5. Implementing environmental and engineering controls. Standard precautions consist of 1.Hand hygiene 2. Respiratory hygiene (cough etiquette).3. PPE according to the risk.4. Safe injection practices, sharps management and injury prevention 5. Safe handling, cleaning and disinfection of patient care equipment 6. Environmental cleaning 7. Safe handling and cleaning of soiled linen 8. Waste management. For patients with mild and severe disease, early supportive therapy and monitoring, Intravenous (IV) Fluid Administration, Oxygen Therapy and Corticosteroids should be provided according to the WHO guidelines [18].

Discharge criteria & quarantine discontinuation

COVID-19 patients may be discharged from hospital and moved to home care (or other types of non-hospital care and isolation) based on:

- Clinical criteria (e.g. no fever for > 3 days, improved respiratory symptoms, pulmonary imaging showing obvious absorption of inflammation, no hospital care needed for other pathology, clinician assessment)
- Laboratory evidence of SARS-CoV-2 clearance in respiratory samples; 2 to 4 negative RT-PCR tests for respiratory tract samples (nasopharynx and throat swabs with sampling interval ≥ 24 hours). Testing at a minimum of 7 days after the first positive RT-PCR test is recommended for patients that clinically improve earlier.
- **Serology:** appearance of specific IgG when an appropriate serological test is available.
- The discharge from hospital of mild cases – if clinically appropriate – may be considered, provided that they are placed into home care or another type of community care. After discharge, 14 days of further isolation with regular health monitoring (e.g. follow-up visits, phone calls) can be considered, provided the patient's home is equipped for patient isolation and the patients takes all necessary precautions in order to protect family members and the community from infection and further spread of SARS-CoV-2. Due to increasing evidence of virus shedding through faeces by convalescent patients, particularly children, recommendations for careful personal hygiene precautions after de-isolation are warranted [57,58].

DRUGS & THERAPIES

Pharmacologic therapies

Pharmacologic therapies against SARS-CoV-2 target its viral structure and genome. These therapies/drugs act as an inhibitor of ACE2 receptor or works by inhibiting the replication, membrane fusion and assembly of the RNA virus or either work as immunomodulators. The basic aim of pharmacologic therapy is to inhibit the viral replication process and hence reducing the transmission [59].

Inhibitors of replication, membrane fusion and assembly

Remdesivir

Antiviral drug (formally known as GS-5734), Mono-phosphate prodrug, Adenosine analog [60,61].

Mechanism of action: Remdesivir is metabolized in cells to form an active nucleoside triphosphate (NTP), it competes with ATP; for incorporation into the nascent RNA strand. It appears as adenosine to the enzyme, which results in inhibition of RdRP, halting the growth of the RNA strand. It also outpace the viral proofreading activity, thus maintaining antiviral activity [61, 62, 66].

Previous Use: It has broad-spectrum activity against a wide array of RNA viruses: Ebola, SARS-CoV and MERS-CoV, Treatment of Ebola virus disease and Marburg virus infections [66, 64].

Favipiravir

Favipiravir (T-705; 6-fluoro-3-hydroxy-2-pyrazinecarboxamide) is a prodrug of a purine nucleotide [61,62].

Mechanism of action: Targets RdRP (an important enzyme used in the viral replication process). It is transformed to an active form, which is recognized as a substrate by RdRP and inhibits the RNA polymerase activity. This leads to inhibition of viral replication [61, 65, 66].

Previous Use: It inhibits replication of a large number of RNA viruses, including influenza A virus, Ebola virus, noroviruses, Lassa virus, etc [64].

Lopinavir/ ritonavir

Lopinavir is an aspartic protease inhibitor with ritonavir as a booster which increases lopinavir plasma concentration through inhibition of cyt-P450 [65, 66, 67].

Mechanism of action: They inhibit the coronavirus polyprotein processing via inhibition of 3-chymotrypsin-like protease [65, 66, 67].

Previous Use: Developed for treatment of HIV which provides potent and sustained viral load reduction for patients with HIV [66, 67].

Umifenovir

Umifenovir (Arbidol) is a small indole-derivative molecule [61].

Mechanism of action: It targets and blocks the S protein-ACE2 interaction as well as virus-endosome fusion through incorporation into cell membranes and interferes with the hydrogen bonding network of phospholipids [61,67,68].

Previous Use: It has a broad spectrum activity against Ebola virus, human herpesvirus 8, hepatitis C virus, & Tacaribe arenavirus [67,68].

Ribavirin

Ribavirin is a guanosine analogue with activity against RNA and DNA viruses [69,70].

Mechanism of action: It metabolizes and mimics guanosine that enhances its incorporation into RNA thus halting the synthesis of RNA [69,70].

Previous Use: It has antiviral properties against hepatitis B, C and respiratory syncytial virus [69, 70].

Azithromycin

A therapeutic drug which belongs to the class of antibiotics known as macrolide and can act as a prophylaxis for declining the infection rate [67,71,72,79].

Mechanism of action: It leads to an increase in the pH of host cell and potentially block endocytosis and/or viral shedding from lysosomes, thereby limiting viral replication. It also reduces levels of the enzyme furin in host cells, and therefore interfere with viral entry [67,71,72,79]
Previous Use: Used to treat bronchitis, pneumonia & MAC infection &prevent replication of H1N1 & Zika virus [67,71,72,79].

Camostat & Nafamostatmesilate

They are serine protease inhibitor and used as a potential antiviral drug [61,65,73,74].
Mechanism of action: It inhibits TMPSSR2-mediated glycoprotein activation of MERS-CoV and SARS-CoV and hence inhibits cell entry in SARS-CoV-2 also. [61,65,73,74].
Previous Use: Used for the treatment of chronic pancreatitis, against viral infection& in certain bleeding complications.

Inhibitor of ACE2 receptor

Chloroquine (CQ) & Hydroxychloroquine (HCQ)

Aminoquinolines categorized as anti-viral drug. HCQ has a hydroxyl group, which makes it less toxic while maintaining similar activity [62,64,72,75].
Mechanism of action: CQ diffuses in the cell passively, becomes protonated and increases intravascular pH which leads to degradation of proteins and glycosaminoglycan. It also prevents virus-cell fusion by interfering with glycosylation of ACE2 receptor and its binding with spike protein. [62,64,72,75].
Previous Use: Used to treat malaria and other autoimmune conditions such as systemic lupus erythematosus, rheumatoid arthritis. [62,64,72,75].

Immunomodulators

Ivermectin

A potent anthelmintic drug, which has the potential to prevent viral replication in a broad spectrum of viruses [66,76,77,78].
Mechanism of action: It binds to the Impα/β1 heterodimer, leading to its destabilization and prevention of Impα / β1 binding to the viral proteins. This prevents viral proteins from entering the nucleus, thereby leading to an efficient antiviral response [66,76,77,78].
Previous Use: Has antiviral effect on RNA viruses such as Zika, dengue, yellow fever, HIV-1, SARS-CoV-2, etc [66,76,77,78].

Nitazoxanide

An orally active nitrothiazoly-salicylamide, antiparasitic and antiviral drug [66,69,79].
Mechanism of action: It is metabolized to tizoxanide and its conjugates, amplifying cytoplasmic RNA sensing and type I IFN pathways. It potentiates IFN α and β production and exhibits activity against MERS-CoV and other coronaviruses [66,69,79].
Previous Use: Indication for its antiprotozoal activity to treat diarrhea [66,69,79].

Corticosteroids

Dexamethasone

Is a potent glucocorticoid used as an anti-inflammatory drug[80].
Mechanism of action: It inhibits inflammatory cells and suppresses the expression of inflammatory mediators, thus avoiding lung damage in patients who develop ARDS [80,81].

Previous Use: It is used in the prevention and treatment of altitude sickness, chemotherapy-induced nausea and vomiting, etc.

Ulinastatin

It is a serine protease inhibitor that reduces the pro-inflammatory response [82].
Mechanism of action: It protects the vascular endothelium by inhibiting the cytokine storm and increasing the level anti-inflammatory factor IL-10[82].
Previous Use: Previously used as a treatment for severe sepsis [82].

Anticoagulants

Heparin

It is used to treat pulmonary coagulopathy in severe CoViD patients [83,84,85,87].
Mechanism of action: Heparin sulfate (HS) proteoglycan binds to the S protein thereby inhibiting initial infection or spread of disease [67,83,84,85,87].
Anticoagulant therapy mainly with low molecular weight heparin appears to be associated with better prognosis in severe COVID-19 patients meeting SIC criteria or with markedly
elevated D-dimer.[101]
Previous Use: Used as an antithrombotic to prevent blood clots.

Non-steroid anti-inflammatory drugs (NSAIDS)

Ibuprofen

It is a nonselective cyclooxygenase (COX1) inhibitor [64,86].
Mechanism of action: It works by reducing the production of fever-causing prostaglandins (PGs) via the inhibition of cyclooxygenase. They can also inhibit the release of anti-inflammatory prostaglandin [64,86].
Previous Use: Used to treat muscle pain, headache, arthritis, etc.Ibuprofen demonstrates superior efficacy in fever reduction compared to acetaminophen. [102]

Inhaled Nitric Oxide

Inhaled nitric oxide (iNO)

iNO is a naturally occurring prostaglandin, common pulmonary vasodilator [88,89].
Mechanism of action:NO induces vasodilatory &bronchodilatory effect & inactivates viruses by modifying proteins and nucleic acids that are essential for viral replication. NO showed inhibitory effects on SARS-CoV replication& inhaled iNO therapy may prevent cytokine storms[88,89].
Previous Use: NO produces antimicrobial effects against a broad range of microbes including bacteria & viruses, which may help prevent pulmonary infections.Inhaled NO, which is relatively of low cost and readily available, may be a promising interventional therapy for patients with severe
COVID-19 ARDS. [103]

Immunotherapy

Immunotherapy entails the administration of agents (e.g., cellular components or complexes combined with another immune agent, etc.) that activate the immune system or act to induce a desired endogenous immune response in the recipient. Virus replication and inflammatory responses may result to tissue damage. Individuals whose immune system cannot defend against the virus quickly, or who overly respond to the virus with inflammation, are at highest risk of serious disease consequences, in addition to other "at risk" groups. Hence different treatments are provided to curtail the infection caused by SARS CoV-2 [104].

CoViD-19 Convalescent Plasma (CP) / SARS CoV-2 Immune Globulins:

Antibodies from plasma, is collected from donors, who have recovered from COVID-19, through a process called apheresis. It works best for patients earlier in the disease course.[105]

Mechanism of Action: CP provides immunomodulatory effects via the infusion of anti-inflammatory cytokines & antibodies i.e. IgG, IgM & IgA. The humoral immune response is mainly directed towards the S protein.[105].

Intravenous Immune Globulin (IVIg)

Immunotherapy using IVIg, IgG antibodies (collected from patients recovered from CoViD-19), in combination with antiviral drugs could be used to treat or prevent CoViD-19 by neutralizing the virus and strengthen immune response [107]

Mechanism of Action: IgG antibodies include $F(ab)_2$ & (Fc), which is responsible for antigen recognition & for activation of the immune response. Octagam, an IVIg, may block proinflammatory cytokines, Fc-gamma receptors (FcγRs) & leukocyte adhesion molecules, suppressing pathogenic Th1 and Th17 subsets and neutralizing pathogenic auto antibodies [107].

Interferon (IFN)

Interferons are signalling proteins (first line of defence) that target different stages of a virus's life cycle, inhibiting them from multiplying & also boost immune response by activating different immune cells to help clear an infection [109].

Mechanism of Action*:* IFN-1is recognized by the IFNAR present at the plasma membrane & induces the phosphorylation of transcriptional factors such as STAT1 & activates interferon-stimulated genes (ISG). Most ISGs are involved in inflammation, signaling & immunomodulation. They interfere with viral replication & slowdown cell metabolism or secretion of cytokines which activates adaptive immunity [109].

Janus Kinases (JAK) & Numb Associated Kinase (NAK) inhibitors

JAKs are cytoplasmic tyrosine kinases that link cytokine signaling from membrane receptors to signal transducers and activators of transcription (STAT) factors. NAK are linked to broad cellular functions. Drugs that target NAK may mitigate systemic and alveolar inflammation by inhibiting cytokine signaling involved in immune-mediated inflammatory response [111].

Mechanism of Action: A known regulator of endocytosis is the AP2-associated protein kinase-1 (AAK1). The ability to disrupt AAK1 may interrupt intracellular entry of the virus. Baricitinib, JAK inhibitor, is also a NAK inhibitor with a particularly high affinity for AAK1 [111].

INTERLEUKIN (IL) INHIBITORS

IL -1 inhibitors

IL-1 is a regulator of inflammation. It has a wide range of biological functions, Endogenous IL-1 levels are elevated in individuals with COVID-19 [113].

Mechanism of Action*:* Anakinra, a recombinant human IL-1 receptor antagonist, blocks the IL-1 receptor and its downstream signaling pathways [113].

IL -6 inhibitors

IL-6 is a proinflammatory cytokine. CoViD-19 induces a dose-dependent production of IL-6 from bronchial epithelial cells [115].

Mechanism of Action: Tocilizumab, IL-6 inhibitor is a humanized, IgG1- IL-6 receptor monoclonal antibody. The binding to ILR inhibits its dimerization preventing signalling [115].

CELL THERAPIES

Mesenchymal Stem Cells (MSC)

MSC can be isolated from different adult tissues, including preferably bone marrow, peripheral blood, adipose tissues and neonatal birth-associated tissues, including placenta, umbilical cord, Warton jelly, amniotic fluid and cord blood, and then stored for future possible applications [117].

Mechanism of Action: There are two main mechanisms of MSCs therapy for COVID-19.1-MSCs could lodge in the pulmonary vascular bed after injection, release anti-inflammatory mediators and reduce the cytokine storm. 2-MSCs could secrete angiopoietin-1 and keratinocyte growth factor, which are pivotal in the restoration of alveolar capillary barriers disrupted by COVID-19 [117].

Human Monoclonal Antibodies

Monoclonal antibodies are used to bind to one specific substance in the body. This binding is very versatile and can mimic, block, or cause changes to enact precise mechanisms, and provide an effective therapeutic intervention with a very specific treatment for diseases [119].

Mechanism of Action: Most monoclonal antibodies can identify the S1 fragment of SARS-CoV and RBD in subunit S1 and can block the interaction of RBD and its ACE2 receptor [119].

Psychological therapies

Psychological intervention is being considered as adjuvant therapy to provide more help for CoViD-19 patients. Psychotherapy uses psychological methods to educate and treat patients. It can eliminate physical symptoms and improve mental health. Some CoViD-19 patients feel anxious and difficult to reintegrate into society. In addition, the quarantine has caused negative emotions such as fear, public panic, mental stress, depression, boredom, etc. Using psychological intervention will reduce psychological stress, patient's anxiety, prevent immunity decline and help to integrate CoViD-19 patients into society [124].

CONCLUSION

This literature review comprehensively summarizes the origin, virology, transmission, clinical presentation, management and the drugs & therapies used to treat CoViD-19. CoViD-19, the pandemic, caused by SARS-CoV-2, emerged in Wuhan, China and has widespread to 213 countries as of July 1, 2020. It has a high transmission rate but a low fatality rate as compared to SARS & MERS. Due to its high transmission rate, most countries around the world have implemented strict movement restrictions, social distancing and quarantined patients who are highly suspected to have CoViD-19. Originating from reservoir of bats and pangolins, SARS-CoV-2 binds to ACE2 with high affinity as a virus receptor to infect humans. Although the immune system plays an important role in fighting COVID-19, paradoxically it could also be harmful causing ARDS as a result of the cytokine storm. With symptoms similar to common cold and flu, several diagnostic tools are used to aid in the treatment of this disease. Scientists are working extensively on the therapies and vaccines against the virus. So far, a combination of pharmacotherapies, immunotherapies, cell therapies and psychological therapies have been conducted with definite effect on treat COVID-19 patients, while solid data from more clinical trials are needed. Studies are needed to explore the evolution, transmission, pathogenesis and immune response to SARS CoV-2, which would provide the basis of future research on developing targeted drugs and therapies.

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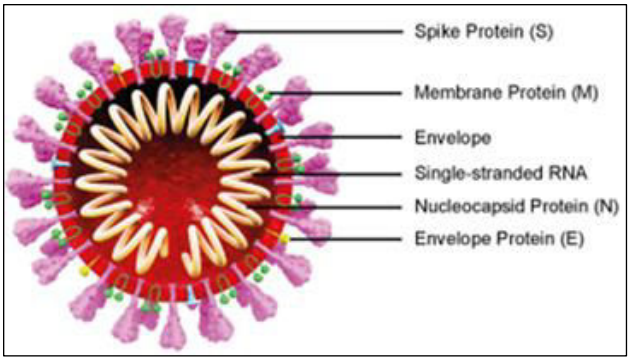
Table 1: Comparison of SARS, MERS and CoViD-19 [10, 11]

	SARS	**MERS**	**CoViD -19**
Place & Year	Guangdong, China November 2002	Jeddah, Saudi Arabia June 2012	Wuhan, China December 2019
Causative Agent	SARS CoV	MERS CoV	SARS CoV– 2
Possible Natural Reservoir	Bat	Bat	Bat
Possible Intermediate Host	Civet cats	Camel	Pangolins
Predominant Cellular Receptor	ACE2 (Angiotensin - converting enzyme2)	Dipeptidyl peptidase 4 (DPP4, also known as CD26)	ACE2 (Angiotensin - converting enzyme2)
Mean Incubation Period	5 days	5 days	5 days
Mode of Transmission	Droplets produced by coughing, sneezing, talking, or breathing	Droplets from person to person, unclear from camels to humans.	Droplets produced by coughing, sneezing, or talking, limited evidence of other routes
Reproduction number(Ro)	3	<1.0	1.4 to 2.5 (median of 1.95)
Case Fatality Rate	9.6%	34.3%	1.38% - 3.4%
Key Symptoms	A cough (dry at first), a fever and diarrhea in the first or second week of illness, or both.	A fever, a cough, shortness of breath	A fever, a dry cough, shortness of breath.
At Risk Group	People with underlying medical conditions	Men above the age of 60, particularly those with underlying medical conditions	Adults aged 65 and over, a people of all ages with underlying medical conditions.
Confirmed Cases	8,096.	2499	>65 million cases till 4thDec 2020.

Table 2. Immune Enhancers

Vitamin C	Vitamin D	Zinc
Vitamin C has a pleiotropic physiological role, there is evidence supporting the protective effect of intravenous vitamin C during sepsis-induced ARDS. It affects the immune system, for example the function of phagocytes, transformation of T lymphocytes and production of interferon. [121]	Vitamin D has been found to modulate macrophages response, preventing them from releasing too many inflammatory cytokines and chemokines. Vitamin D agonist, calcitriol, exhibited protective effects against acute lung injury. [122]	It has a potential to enhance antiviral immunity also act in a synergistic manner when co-administered with the standard antiviral therapy. Effectiveness of Zn against a number of viral species is mainly realized through the physical processes, such as virus attachment, infection, and uncoating.[123]



Source: https://images.app.goo.gl/wWd81PkcMN7utgAU9

Fig.1. SARS-CoV-2 Structure

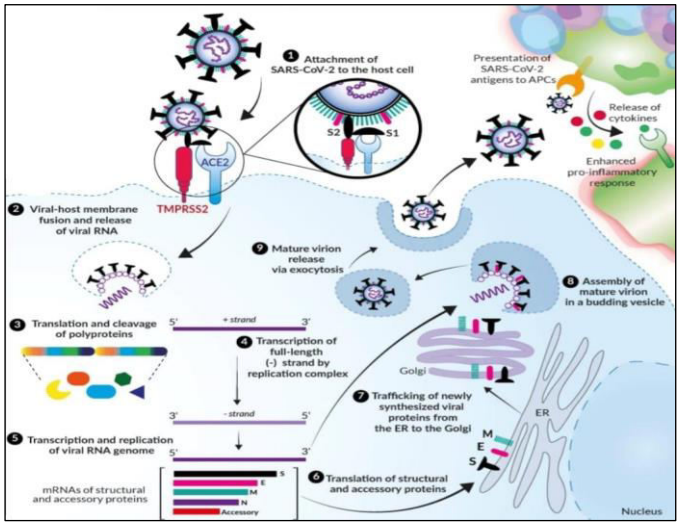


Fig.2. Pathogenesis of SARS-CoV-2

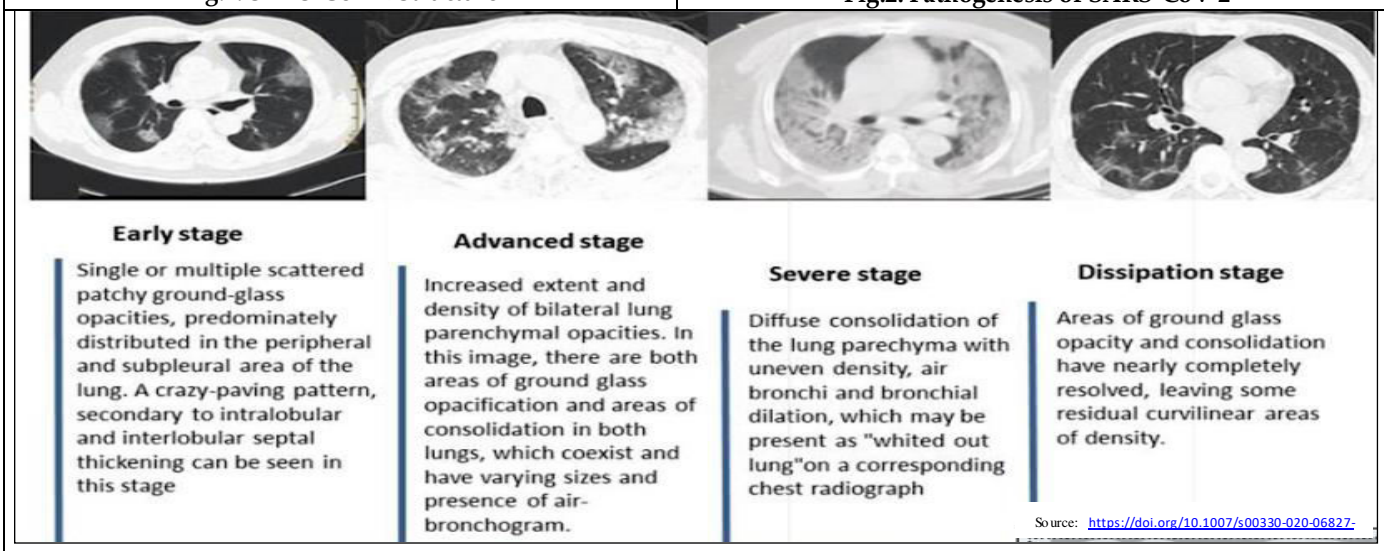
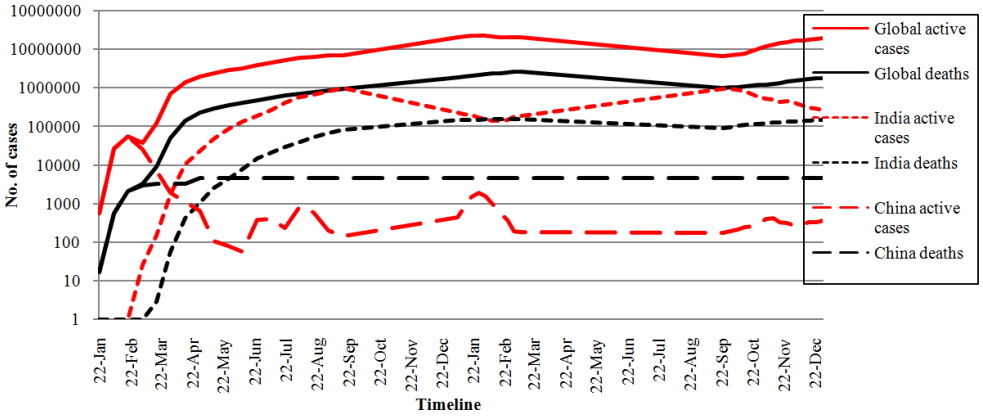


Fig.3.CT manifestations of different stages of COVID-19.

An analysis of CoViD-19 active cases and mortality. [52]



Global graph analysis

After globally witnessing the first wave of the pandemic, it is now receding due to climate changes. The virus may also have infected a huge population of people in many areas. Giving them immunity from re-infection. This possibly may create a so-called herd immunity, which protects those who haven't been infected by curtailing the circulation of virus. Many countries adopted movement restrictions on an unprecedented scale with social-distancing measures. Variable factors may contribute to a second wave – increasing economic crisis, probable mutation of the virus and onset of a cooler climate [54].

- Dec 8 2019- 1st patient develops symptoms for Wuhan coronavirus.
- Dec 31 2019- The public health office traced 27 cases to Huanan Seafood Wholesale Market.
- Jan 1 2020- Huanan Seafood Wholesale Market was closed.
- Jan 8 2020- The unknown etiology was confirmed as novel corona virus (nCoV) by the China CDC.
- Jan 11 2020- 1st confirmed death in China.
- Jan 13 2020- 1st case outside China in Thailand.
- Jan 20 2020- Human – Human transmission officially reported.
- Jan 23 2020- Wuhan goes into lockdown.
- Jan 30 2020- WHO declared PHEIC & 1st confirmed case in India.
- Feb 11 2020- WHO officially named the disease CoViD-19 and renamed nCoV as SARS CoV-2.
- Mar 11 2020- WHO declared CoViD-19 as a pandemic.
- Mar 22 2020- 1 day Janta curfew in India.
  - 1st confirmed death in India
- Mar 25 2020- Nationwide lockdown in India [53]
- May 252020- Domestic Flight services resume
- June 8 2020- Unlock 1.0 due to economic crisis in India
- July 1 2030- Unlock 2.0 with relaxation in night curfew in India
- July 15 2020- Phase1 clinical trails of India's first Covid19 vaccine Covaxin started
- Aug 01 2020- Phase 3.0 unlock allowing gym in India
- Aug 11 2020- Russia grant regulatory approval of "Suputnik V" covid19 vaccine for civilian use
- Aug 04 2020- Unlock 4.0 allowing metro services to start, large gathering with 100 people were allowed in India
- Sept 16 2020- Confirmed cases in India crossed 5 million mark.
- Oct 19 2020- Globally, confirmed cases surpass 40 million.
- Nov 16 2020- Moderna announces its Covid-19 vaccine candidate has shown 94.5% efficacy
- Dec 02 2020- UK approves Pfizer's Covid-19 vaccine.

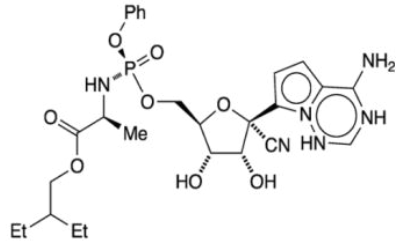
India graph analysis

India is at a greater risk because of its very large population density, limited infrastructure and healthcare systems to cater to very large demands. On the other hand, factors like warmer climate as well as humidity, a large proportion of the young population, may favour India. With the lockdown now in practice, the experts believe that the pandemic may reach its peak in mid November.[55]

China graph analysis

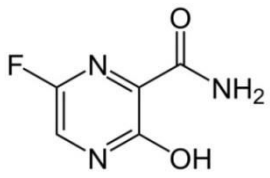
As the cases in China began to decrease, there was relaxation in the lockdown. This caused a spike in the confirmed cases giving rise to a second wave in China [56].

Fig.4. An analysis of CoViD-19 active cases and mortality [52].



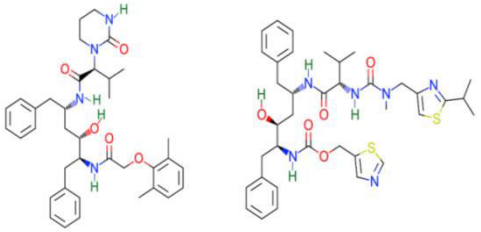
Source: American Chemical Society https://www.acs.org/content/acs/en/moleculeoftheweek/archive/r/remdesivir.html?cid=home_motw

Fig.5. Remdesivir



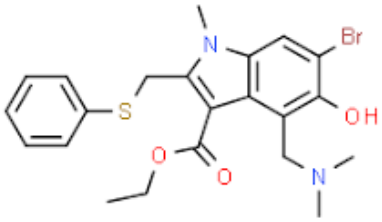
Source: Huateng Pharma https://en.huatengsci.com/article/122.html

Fig.6. Favipiravir



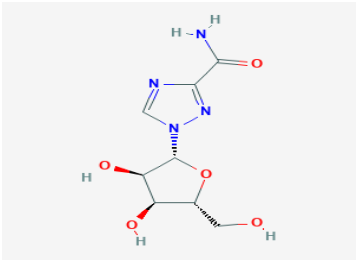
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Lopinavirhttps://pubchem.ncbi.nlm.nih.gov/compound/ritonavir

Fig.7. Lopinavir **Fig.8. Ritonavir**



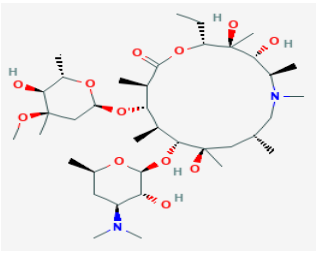
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Umifenovir

Fig.9. Umifenovir



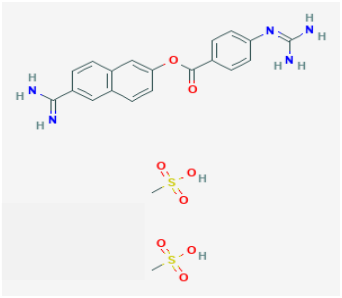
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Ribavirin

Fig.10. Ribavirin



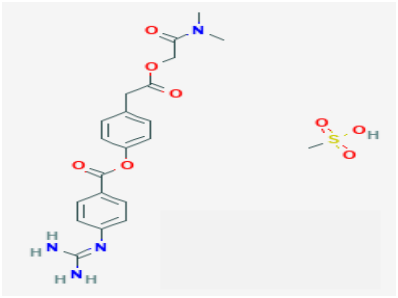
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Umifenovir

Fig.11. Azithromycin



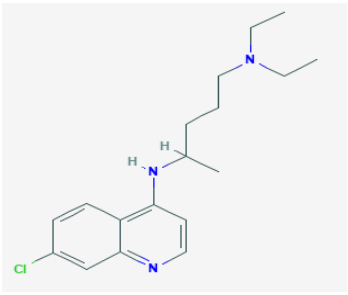
Source: Pubchem**https://pubchem.ncbi.nlm.nih.gov/compound/Nafamostat mesylate**

Fig.12.Nafamostatmesilate



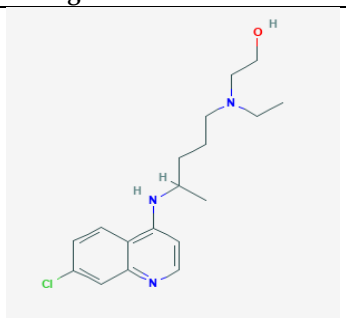
Source: Pubchem**https://pubchem.ncbi.nlm.nih.gov/compound/Camostat mesylate**

Fig.13. Camostatmesilate



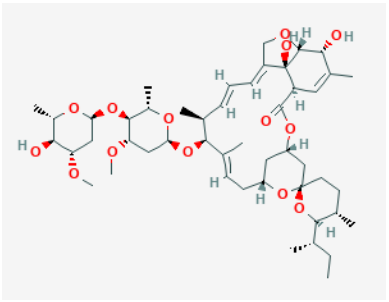
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Chloroquine

Fig.14. Chloroquine (CQ)



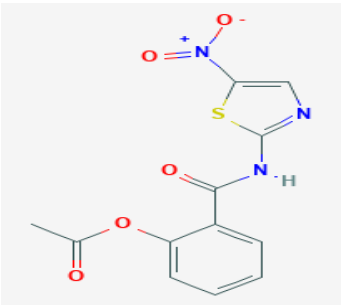
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/hydroxychloroquine

Fig.15. Hydroxychloroquine (HCQ)



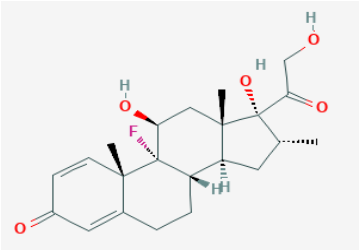
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/ivermectin

Fig.16. Ivermectin



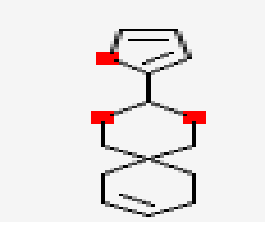
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/nitazonanide

Fig.17.Nitazoxanide



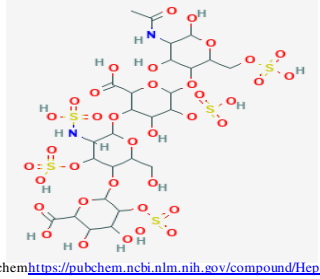
Source: Pubchem: https://pubchem.ncbi.nlm.nih.gov/compound/Dexamethasone

Fig.18. Dexamethasone



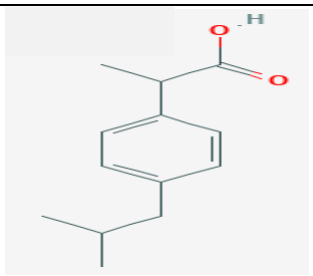
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Ulinastatin

Fig.19. Ulinastatin



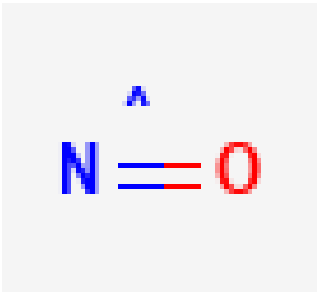
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Heparin

Fig.20. Heparin



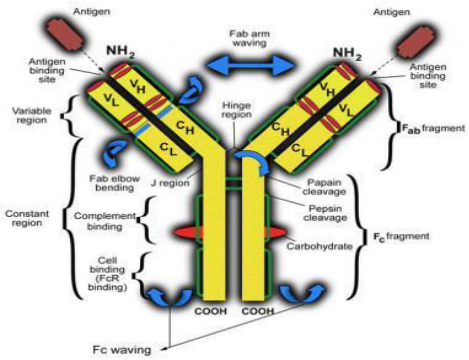
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Ibuprofen

Fig.21. Ibuprofen



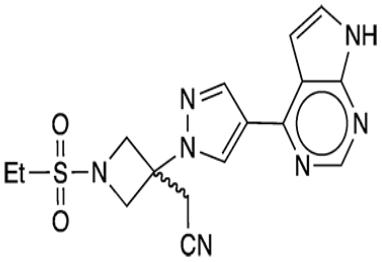
Source: Pubchemhttps://pubchem.ncbi.nlm.nih.gov/compound/Nitric-oxide

Fig.22. Nitric oxide



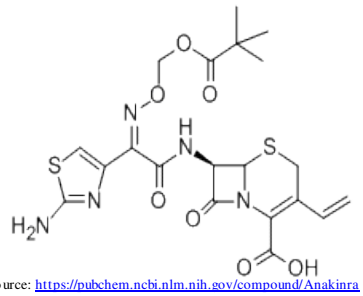
Source: https://emedicine.medscape.com/article/210367-overview

Fig.23. Intravenous Immune Globulin (IVIg)



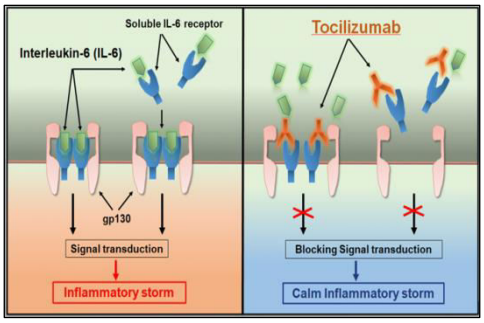
Source: https://pubchem.ncbi.nlm.nih.gov/compound/Baricitinib

Fig.24. Baricitinib



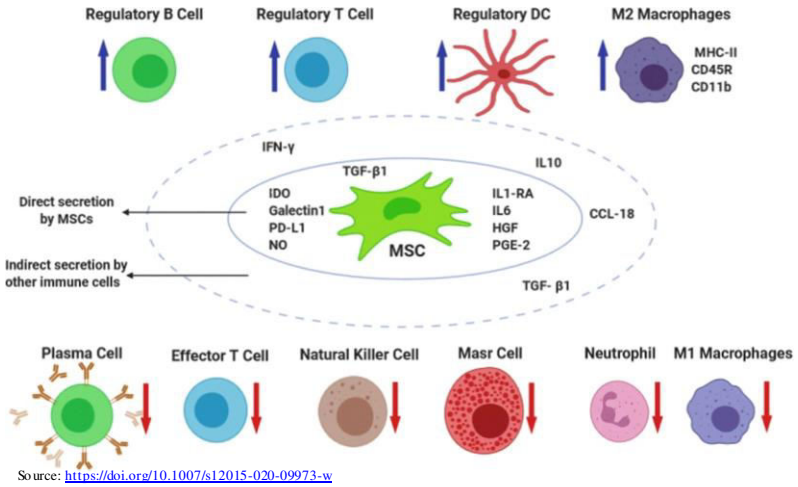
Source: https://pubchem.ncbi.nlm.nih.gov/compound/Anakinra

Fig.25. Anakinra



Source: https://doi.org/10.1186/s12967-020-02339-3

Fig.26. IL -6 inhibitors:



Source: https://doi.org/10.1007/s12015-020-09973-w

Fig.27. Mesenchymal Stem Cells (MSC)

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RESEARCH ARTICLE

A Study of Spreading Rate of COVID 19 using Non-homogeneous Rough Graph Cellular Automaton

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ABSTRACT

Rough Graph Cellular Automaton is an important mathematical model that captures the benefit of rough set theory and graph cellular automaton. In real time problems at each time 't' the system dynamically changes its behaviour. Our objective is to provide a suitable mathematical model namely non homogeneous rough graph cellular automaton (NRGCA) that provides an appropriate solution in predicting the systems having dynamical behaviour. This is appropriately achieved by defining the NRGCA. The generations of non-homogeneous rough graph cellular automaton are also defined. The algorithm is elaborated with the suitable examples. The spreading rate of COVID19 according to various factors is analysed. Using the generations of NRGCA the definite and possible transitions between suspicious, infected and recovered groups of the population under study are clearly obtained. The novelty of this proposed model is that it clearly indicated the parameter that induces more number of definite and possible transitions, so that the spreading rate of the virus can be minimized.

AMS Classification 11B85, 20M35, 37B15, 68Q45, 68Q80

Keywords: Cellular Automaton, Finite Automaton, Graph Cellular Automaton, Information System, Rough set, Rough graph cellular automaton, Non-homogeneous function.

INTRODUCTION

Generally rough set was defined in two different manners one is constructive method and other is algebraic method. In constructive method the approximation space is defined using the equivalence relation and in the algebraic method the approximation operators plays the role of abstract operators [Yao, 2003]. In [Yao, 2003], the author generalized rough set theory and he developed the formulation to deal with the different generalized rough set theory. He discussed about the two methods in his article and also he discussed about the rough set covering. In [Praba, 2020], the authors discussed about the concept graph cellular automaton using basic linear rules. In [M artinez, 2012], the authors discussed about the rate of spreading of a disease using the concept of graph cellular

automaton. Hassan [2011] build a hybrid system for cellular automaton and rough set theory. They used cellular automaton for the multi-agent simulation model which lies in adopting the behaviour of the individual party using rough set approximation. As an application they deal with the traffic system construction. Bartlomiej, [Placzek, 2013] extract a low level features in medical images using the concept of cellular automaton. He used the concept of rough set theory in the techniques of data mining. Eiichiro [2003] proposed a new model of cellular automaton based on the concept of rough set theory to simulate a car in vehicular traffic. The article combined the ideas from machine learning and artificial intelligence. In [Das, 2018], the authors deal with the improvement in accuracy of cancer classification. In this they filter out the redundant genes. Using the proposed concept of cellular automaton and rough set theory and from the Pareto dominant solution the gene subset is obtained to improve the accuracy. David J warne [Warne, 2013] presented a polynomial algorithm to solve the eden problem for GCA. The unused pre-image was removed using the algorithm elimination operation. The time complexity is also discussed. In [2018], Jane discussed about rough set based approach in identifying H1N1. This paper focuses on the dynamical behaviour of RGCA. This is achieved by defining NRGCA in which a graph cellular automaton is equipped with an equivalence relation R_t on the set of vertices at time 't' and a neighbourhood function η_t of the vertices of GCA. In section 2 some of the basic definitions were discussed. In section 3 we define non homogeneous rough graph cellular automaton and section 4 deals with the generations of NRGCA. The illustration taken place in section 5 followed by a conclusion.

Preliminaries

In this section we discuss the basic definitions which are required to study the rest of the sections.

Definition 2.1. Cellular automaton is a collection of cells which is in form of grid. Each cell's life is represented by a cell's state on/off (or) 1/0. The generation of the cellular automaton is predicted using the basic linear rules.

Definition 2.2. Graph cellular automaton is defined by $G = (V, I, \delta)$, where V is the vertices of the graph cellular automaton, I is the input symbols and δ is the time evolution function defined by : $V \times I \rightarrow V$.

Definition 2.3. Graph information system is denoted by $I_0 = (G, \tilde{R}, \eta)$ where G is a graph cellular automaton (V, I, δ) and $\tilde{R}$ is an equivalence relation defined on the vertices of G and η is a neighborhood function with respect to the input symbol x.

Definition 2.4. Adjacency matrix for the graph G is denoted by $A(G)$, and it is defined by $A(G) = \begin{cases} x \; if \; x \in E(Vi, Vj) \\ 0, otherwise \end{cases}$

Definition 2.5. Rough Graph Cellular Automaton (RGCA) is defined by an ordered pair, $G(I_0) = (G(I_0)_-, G(I_0)^-)$ where $G(I_0)_-$ is the lower approximation rough graph cellular automaton defined by $G(I_0)_- = \{V, I, \delta_-\}$ and $G(I_0)^-$ is the upper approximation rough graph cellular automaton.

Definition 2.6. K^{th} generation rough graph cellular automaton is defined by $G_k(I_0) = (G_{k-1}(I_0)_-, G_{k-1}(I_0)^-, R)$ where, K^{th} generation lower approximation rough graph cellular automaton is $G_k(I_0)_- = (G_{k-1}(I_0)_-, R)$ which is defined by $A(G_k(I_0)_-) = R \circ A(G_{k-1}(I_0)_-)$ where $A(G_{k-1}(I_0)_-$ is the $(k-1)^{th}$ generation of lower approximation rough graph cellular automaton and $A(G_k(I_0)_-)$ is the k^{th} generation lower approximation rough graph cellular automaton, R is the rule matrix. Smilarly for upper approximation rough graph cellular automaton.

Rough Graph Cellular Automaton

Graph cellular automaton plays an important role in many real time situations. The generations of GCA leads us to predict the future behaviour of a system. A graph information system was defined by $I_0 = (G, R, \eta)$ where G is a

graph cellular automaton, R is an equivalence relation defined on the vertices of G and η is the neighbourhood function which is defined as $\eta_x : V \to P(V)$. The generations of GCA is defined by $G_k = (G_{k-1}, R)$ where G_{k-1} is the $(k-1)^{th}$ generation of GCA and G_k is the k^{th} generation GCA and R is a rule matrix. This concept was extended to RGCA; in which we have graph information $I_0 = (G, R, \eta)$ where R is an equivalence relation defined on the vertices of graph cellular automaton. Using this information system the RGCA was defined and its generations with respect to lower and upper approximation are also predicted. But we apply this concept in real time problems the equivalence relation defined on the vertices of G need not be same at all time t. Hence an attempt is made to define non-homogeneous RGCA. In this section we extend the concept of graph information system to non-homogenous graph information system.

Non-Homogeneous Graph Information System

Consider a graph information system $I_0 = (G, R, \eta)$. Now let $I_0^t = (G, R_t, \eta_t)$. where G is a graph cellular automaton (V, I, δ),R_t is a non-homogeneous equivalence relation defined on time t and η_t is a neighbourhood function at time t defined by $\eta_t : V \to P(V)$ such that $\eta_t(X) \subseteq V$ is the neighbourhood of x at time t. For $X \in V$, $[x]$ denotes the equivalence class corresponding to x with respect to equivalence relation R_t. This graph information system is called as non homogeneous graph information system.

Non-Homogeneous Rough Graph Cellular Automaton

Consider an non-homogeneous graph information system I_0^t, then the non-homogeneous rough graph cellular automaton is defined by $G(I_0^t) = (G(I_0^t)_-, G(I_0^t)^-)$ where $G(I_0^t)_-$ is the lower approximation non-homogeneous rough graph cellular automaton and $G(I_0^t)^-$ – is the upper approximation non-homogeneous rough graph cellular automaton.

Example 3.1 Consider the GCA defined in figure 1 The corresponding adjacency matrix of figure 1 is $A(G) = \begin{pmatrix} a,b & a & b & 0 \\ a & b & a & 0 \\ 0 & 0 & a,b & a,b \\ 0 & 0 & 0 & a,b \end{pmatrix}$

Then the equivalence classes induced by R_1 at time t = 1 is given by, $X_1 = \{q_0, q_2\}$ and $X_2 = \{q_1, q_3\}$. The function μ is defined in the table (table.2) for the input symbol a and b.

The function η is defined as follows in table 2 on taking $\delta_a = 2$ and $\delta_b = 1$,

Hence $RS(\eta_a(q_0)) = \{U, U\}$, $RS(\eta_a(q_1)) = \{U, U\}$ and $RS(\eta_a(q_2)) = \{U, U\}$, $RS(\eta_a(q_3)) = \{U, U\}$, $RS(\eta_b(q_0)) = \{U, U\}$, $RS(\eta_b(q_1)) = \{\varphi, U\}$ and $RS(\eta_b(q_2)) = \{X_1, U\}$, $RS(\eta_b(q_3)) = \{X_1, U\}$

Then the lower approximation non homogeneous rough graph cellular automaton and upper approximation non homogeneous rough graph cellular automaton is defined in figure.2 and figure.3 respectively,

The corresponding adjacency matrix of figure 2 is $A(G(I_0^1)_-) = \begin{pmatrix} a,b & a,ba,b & a,b \\ a & a & a & a \\ a,b & a & a,b & a \\ a & a & a & a \end{pmatrix}$

and for figure 3, the adjacency matrix is $A(G(I_0^1)^-) = \begin{pmatrix} a,b & a,ba,b & a,b \\ a,b & a,ba,b & a,b \\ a,b & a,ba,b & a,b \\ a,b & a,ba,b & a,b \end{pmatrix}$ At time $t = 2$ the equivalence classes induced by R_2 is given by, $X_1 = \{q_0, q_1\}$ and $X_2 = \{q_2, q_3\}$ then the value of η for the input symbol a and b is same as table 4, Hence $RS(\eta_a(q_0)) = \{U, U\}$, $RS(\eta_a(q_1)) = \{U, U\}$ and $RS(\eta_a(q_2)) = \{U, U\}$, $RS(\eta_a(q_3)) = \{U, U\}$

$RS(\eta_b(q_0)) = \{U, U\}$, $RS(\eta_b(q_1)) = \{X_1, X_1\}$ and $RS(\eta_b(q_2)) = \{X_2, U\}$, $RS(\eta_b(q_3)) = \{X_2, U\}$. Then the lower approximation non-homogeneous rough graph cellular automaton and upper approximation non-homogeneous

rough graph cellular automaton at time t = 2 are shown in figure.4 and figure.5 respectively. The corresponding adjacency matrix $A(G(I_0^2)_-) = \begin{pmatrix} a,b & a,b & a,b & a,b \\ a,b & a,b & a & a \\ a & a & a,b & a,b \\ a & a & a,b & a,b \end{pmatrix}$

The corresponding adjacency matrix $A(G(I_0^2)^-) = \begin{pmatrix} a,b & a,b & a,b & a,b \\ a,b & a,b & a & a \\ a,b & a,b & a,b & a,b \\ a,b & a,b & a,b & a,b \end{pmatrix}$

Generations of Non-Homogeneous Rough Graph Cellular Automaton (NRGCA)

Let $G\,(I_0^t)$ is a non-homogeneous rough graph cellular automaton, then the k^{th} generation NRGCA is defined by $(G_k\,(I_0^t) = (\,G_k(I_0^t)_-, G_k(I_0^t)^-, R)\,, t \geq 1$ where $G_k\,(I_0^t)$is the K^{th} generation NRGCA,$G_k(I_0^t)_-$ is thek^{th} generation of lower approximation NRGCA which is defined by $G_k(I_0^t)_- = (G_{k-1}(I_0^t)_-, R)$, and it is calculated by $A(G_k(I_0^t)_- = R \circ \mathrm{A}(\mathrm{G_{k-1}}(\mathrm{I_0^t})_-)$. Similarly for upper approximation NRGCA it is calculated.

Example 4.1

Consider example 3.1, $A(G_1(I_0^1)_- = M_4 \circ \mathrm{A}(\mathrm{G_0}(\mathrm{I_0^1})_-)$,

$$\begin{pmatrix} 0 & 00 & 01 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 10 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 10 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 01 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 01 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 10 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 10 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 01 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \\ 0 & 00 & 00 & 00 & 00 & 00 & 00 & 00 & 0 \end{pmatrix} \begin{pmatrix} a,b \\ a,b \\ a,b \\ a,b \\ a \\ a \\ a \\ a \\ a,b \\ a \\ a,b \\ a \\ a \\ a \\ a \\ a \end{pmatrix} = \begin{pmatrix} a \\ a \\ 0 \\ a \\ a,b \\ 0 \\ a,b \\ a \\ 0 \\ a \\ a \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Hence $A(G_1(I_0^1)_-) = \begin{pmatrix} a & a & 0 & a \\ a,b & 0 & a,b & a \\ 0 & a & a & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

Similarly for upper approximation non-homogenous rough graph cellular automaton using rule 4,

$A(G_1(I_0^1)^-) = \begin{pmatrix} a,b & a,b & 0 & a,b \\ a,b & 0 & a,b & a,b \\ 0 & a,b & a,b & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$At time t = 2 the corresponding next generation non homogenous rough graph cellular automaton using rule 4 were shown below

$A(G_0(I_0^2)_-) = \begin{pmatrix} a,b & a,b & a,b & a,b \\ a,b & a,b & a & a \\ a & a & a,b & a,b \\ a & a & a,b & a,b \end{pmatrix}$ then $A(G_1(I_0^2)_-) = \begin{pmatrix} a,b & a,b & 0 & a \\ a & 0 & a,b & a,b \\ 0 & a & a,b & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

$A(G_0(I_0^1)^-) = \begin{pmatrix} a,b & a,b & a,b & a,b \\ a,b & a,b & a & a \\ a,b & a,b & a,b & a,b \\ a,b & a,b & a,b & a,b \end{pmatrix}$ then $A(G_1(I_0^2)^-) = \begin{pmatrix} a,b & a,b & 0 & a \\ a,b & 0 & a,b & a,b \\ 0 & a,b & a,b & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$

Simulation

In this illustration, we propose a mathematical model using non homogenous rough graph cellular automaton which effectively captures the dynamical spreading of the disease COVID19. Also this model analyse the parameters that causes the spreading rate and can predict the parameters to which priority should be given. This model is the study of a disease that has dynamically changing spreading rate. Here the study is made for the population of 100 people denote by the universal set $U = \{x_1, x_2, x_3, \ldots, x_{10}\}$ (by using the concept reduction 100 people were grouped into 10 objects . An information table is drawn for the elements of U with attribute set A as the symptoms of the virus that causes the disease, let $A = \{bodypain\ (a_1), cough\ (a_2), temperature\ (a_3)\}$. For all $a_i, i = 1,2,3$, the function $\mu_{a_i} : U \to [0,1]$ represents the degree of membership that the object posses the symptom a_i. Using this the elements of U are classified into 3 groups, $V = \{suspicious\ (S), Infected\ (I), Recovered\ (R)\}$. Now consider a NRGCA $G_t = (V, R_t, \eta_t)$, where $V = \{suspicious\ (S), Infected\ (I), Recovered\ (R)\}$, the transition from one node to other node is determined by $\eta_t . \eta_t : U \to [0,1]. R_t$ is the set of equivalence classes of the objects at time 't'. The equivalence classes are taken according to the behaviour of a system at 't'. The transition between the nodes at time t = 1 is made using the lower and upper approximation of the elements of V. $R_1 = \{(objects\ having\ their\ age > 60 (X_1), 30 < age < 59\ (X_2), age < 29\ (X_3)$

Using the neighborhood function η_1,

$\eta_{1_{a_i}}(x_i) = \{y \in U | \mu_{a_i}(x_i) - \mu_{a_i}(y) < \delta\}$, where δ is the threshold value,

$\mu(x) = \Sigma_{x \epsilon A} \mu_{a_i}(x)/car(A)$; When $\delta = 0.2$ the rough set of the node S, I and R is calculated as follows $\eta_1(S) = \cap_{x \epsilon S}\ \eta_1(x); RS(\eta_1(S)) = \{X_2, X_2\}; RS(\eta_1(I)) = \{\emptyset, \emptyset\}; RS(\eta_1) = \{\emptyset, \emptyset\}$. Then the lower approximation NRGCA and the upper approximation NRGCA depicted in following figures.

At time t = 1 the definite transitions and the possible transitions has been figured out by the above illustration. This implies that in the lower approximation there is transition from S to R implies among the people in the neighbor hood of suspicious group there some who get recovered in time t = 1. Similarly the edge from S to R in upper approximation implies that there is a possibility of having some people who get recovered in the neighbor hood of suspicious people. The corresponding adjacency matrix for lower approximation non homogeneous rough graph cellular automaton using rule 4 is,

$A(G_1(I_0^1)_-) = \begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$ The next generation adjacency matrix

$A(G_2(I_0^1)_-) = M_4 \circ \mathrm{A}(\mathrm{G}_1(\mathrm{I}_0^1)_-)$,

$$\begin{pmatrix} 0 & 0 & 00 & 1 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 10 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 1 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 1 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \end{pmatrix} \begin{pmatrix} 1 \\ 0 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Hence $A(G_1(I_0^1)_-) = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$

Similarly for upper approximation non-homogenous rough graph cellular automaton using rule 4,

$A(G_1(I_0^1)^-) = \begin{pmatrix} 1 & 0 & 1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$, the next generation adjacency matrix is $A(G_2(I_0^1)^-) = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$. Note that this is a null matrix. This indicates that there is no transition between G at next generation. The spreading rate of the disease doesn't depend on the age. At time t = 2 by the history of the person hospital record such as cholesterol, diabetics, heart disease, lung disease, the equivalence classes in R_2 is as follows, $R_2 = \{people\ having\ more\ than\ 2\ disease\ (X_1), disease \leq 1\ (X_2), disease = 0 (X_3)$.

By taking the threshold value as 0.1,

Using the neighborhood function the rough set of the node S, I and R is calculated as follows, ,
$RS(\eta_2(S)) = \{\emptyset, (X_1, X_2)\}; RS(\eta_2(I)) = \{\emptyset, \emptyset\}; RS(\eta_1) = \{\emptyset, \emptyset\}$. Since the lower approximation of the nodes are empty, there is no definite transmission of the disease and the upper approximation NRGCA depicted in the following figure. The adjacency matrix for the upper approximation non homogeneous rough graph cellular automaton is

$A(G_1(I_0^1)_-) = \begin{pmatrix} 1 & 1 & 1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$ The next generation adjacency matrix

$A(G_2(I_0^1)_-) = M_4 \circ \mathrm{A}(\mathrm{G}_1(\mathrm{I}_0^1)_-)$,

$$\begin{pmatrix} 0 & 0 & 00 & 1 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 10 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 1 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 1 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \end{pmatrix} \begin{pmatrix} 1 \\ 1 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Hence $A(G_1(I_0^1)_-) = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$;

By taking the threshold value as 0.3,

In time t = 3 the equivalence classes in R_3c is calculated using the density of the population for the respective persons.$R_3 = \{persons\ who\ lives\ in\ high\ density\ area(X_1), low\ density\ area\ people\ (X_2)\}$

$X_1 = \{x_1, x_2, x_3, x_4\}, X_2 = \{x_5, x_6, x_7, x_8, x_9, x_{10}\}$. Then the rough set of the vertices is $RS\ (\eta_3\ (S)) = \{\varphi, U\}; RS\ (\eta_3\ (I)) = \{\varphi, \varphi\}; RS\ (\eta_3\ (R)) = \{X_2, X_2\}$. The lower approximation and upper approximation non homogeneous rough graph cellular automaton is depicted in the following figure respectively,

$A(G_1(I_0^1)_-) = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & 1 \end{pmatrix}$ The next generation adjacency matrix $A(G_2(I_0^1)_-) = M_4 \circ \mathrm{A}(\mathrm{G}_1(\mathrm{I}_0^1)_-)$,

$$\begin{pmatrix} 0 & 0 & 00 & 1 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 10 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 1 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 1 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \end{pmatrix} \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \\ 1 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$A(G_2(I_0^1)_-) = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 1 & 1 \\ 0 & 0 & 0 \end{pmatrix}, A(G_3(I_0^1)_-) = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & 0 \end{pmatrix}$ and $A(G_4(I_0^1)_-) = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$.

Similarly for upper approximation non homogeneous rough graph cellular automaton,

$A(G_1(I_0^1)^-) = \begin{pmatrix} 1 & 1 & 1 \\ 0 & 0 & 0 \\ 0 & 1 & 1 \end{pmatrix}$ The next generation adjacency matrix $A(G_2(I_0^1)^-) = M_4 \circ A(G_1(I_0^1)^-)$

$$\begin{pmatrix} 0 & 0 & 00 & 1 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 10 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 1 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 1 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \\ 0 & 0 & 00 & 0 & 00 & 0 & 0 \end{pmatrix} \begin{pmatrix} 1 \\ 1 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \\ 1 \end{pmatrix} = \begin{pmatrix} 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

Hence $A(G_3(I_0^1)^-) = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 1 & 0 \end{pmatrix}$ and $A(G_4(I_0^1)^-) = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$.

By comparing the generation at time t = 1, 2, 3. At time t = 3, the number of transition are increases note that R_3 is based on the density of the population. This indicates that due to the density of the population the transitions between the suspicious, Infected and recovered group objects in the population gets increased. Also the generations of NRGCA vanishes in the third generation at time t = 3, this means that in a population with high density it will take time to restrict the transitions in suspicious, Infected and recovered groups. Mores priority should be given for the population with high density, as the spreading rate depends more on the density of the population than age and the medical history of the person.

Limitations This model doesn't clearly indicate the method of grouping the people initially and at each time period the same grouping is maintained. Our future work is to accommodate the elements dynamical change of elements of S, I and R.

CONCLUSION

In this paper we defined non homogeneous rough graph cellular automaton. The generations of the NRGCA are also defined. For a real time study the spreading rate of COVID19 is discussed induced by the parameters age, medical history and density of the population are analysed. It is found the spreading rate is higher in a population with high density. Hence more precaution measures can be made in a population with high density to minimize the spreading rate. The future work is to accommodate the dynamical change of elements of V. Also, in future this work can be extended to other real time application and the generation can be calculated by appropriate rule matrix.

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Table 1: Description

V	μ_a	μ_b
q_0	0	1
q_1	0	0
q_2	2	2
q_3	2	2

Table 2: Neighborhood

V	η_a	η_a
q_0	q_0, q_1, q_2, q_3	q_0, q_1, q_2, q_3
q_1	q_0, q_1, q_2, q_3	q_0, q_1
q_2	q_0, q_1, q_2, q_3	q_0, q_2, q_3
q_3	q_0, q_1, q_2, q_3	q_0, q_2, q_3

Table 3: Information Table

U	body pain	cough	temperature
x_1	0.6	0.4	0.7
x_2	0.8	0.5	0.6
x_3	0.5	0.4	0.8
x_4	0.9	0.7	0.3
x_5	0.4	0.3	0.2
x_6	0.2	0.2	0.2
x_7	0.3	0.1	0.1
x_8	0.7	0.5	0.1
x_9	0.3	0.3	0.2
x_{10}	0.7	0.6	0.1

Table 4: Description

U	x_1	x_2	x_3	x_4	x_5	x_6	x_7	x_8	x_9	x_{10}
age	40	50	36	62	25	16	10	46	28	52

U	η_1
x_1	x_1, x_2, x_3, x_{10}
x_2	x_1, x_2, x_3, x_{10}
x_3	x_1, x_2, x_3, x_{10}
x_4	x_4
x_5	x_5, x_6, x_7, x_8, x_9
x_6	x_5, x_6, x_7, x_9
x_7	x_5, x_6, x_7, x_9
x_8	x_5, x_8, x_9
x_9	x_5, x_6, x_7, x_8, x_9
x_{10}	$x_1, x_2, x_3, x_8, x_{10}$

Table 6: Neighbourhood Function

U	η_1
x_1	x_1, x_2, x_3
x_2	x_1, x_2, x_3
x_3	x_1, x_2, x_3
x_4	x_4

x_5	x_5, x_6, x_7, x_8
x_6	x_5, x_6, x_7, x_9
x_7	x_5, x_6, x_7, x_9
x_8	x_5, x_8, x_9, x_{10}
x_9	x_5, x_6, x_7, x_8
x_{10}	$x_1, x_2, x_3, x_8, x_{10}$

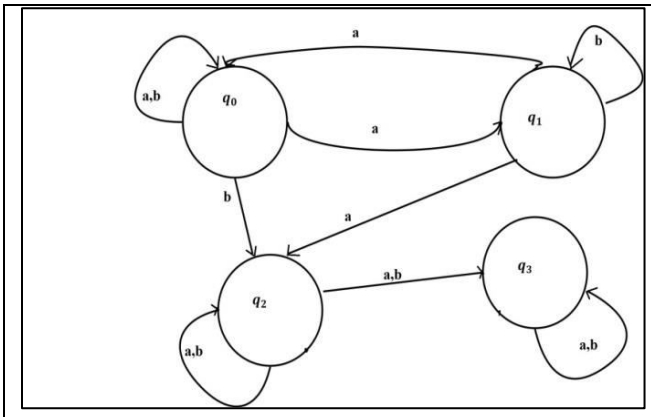

Figure 1: Graph Cellular Automaton G with input symbols I = {a, b}

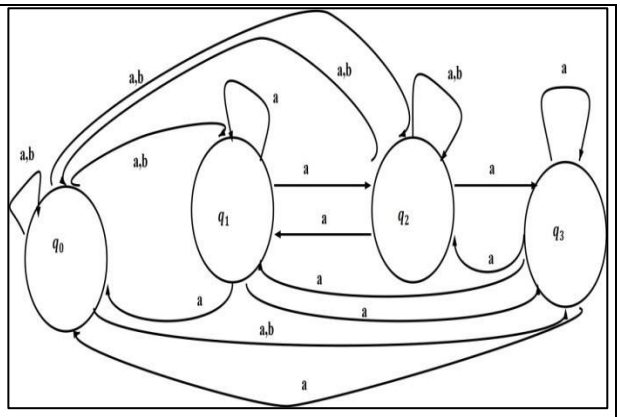

Figure 2: Lower approximation non-homogeneous rough graph cellular automaton $G(I_0^t)_-$

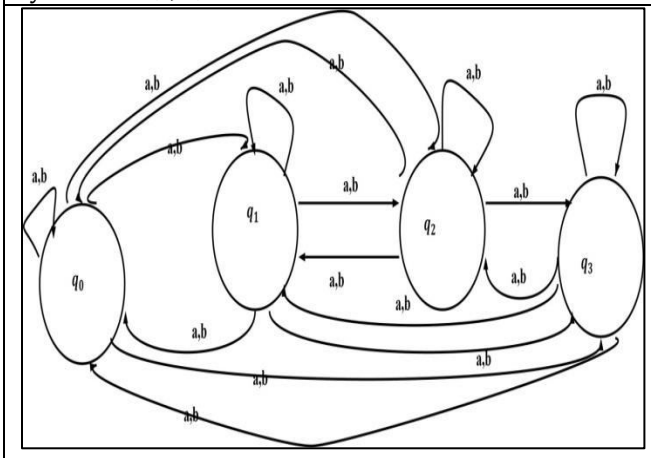

Figure 3: upper approximation non-homogeneous rough graph cellular automaton $G(I_0^t)^-$

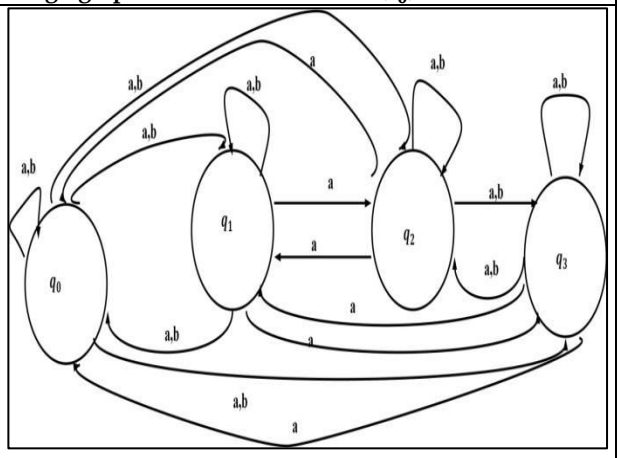

Figure 4: Lower approximation non-homogeneous rough graph cellular automaton $G(I_0^2)_-$

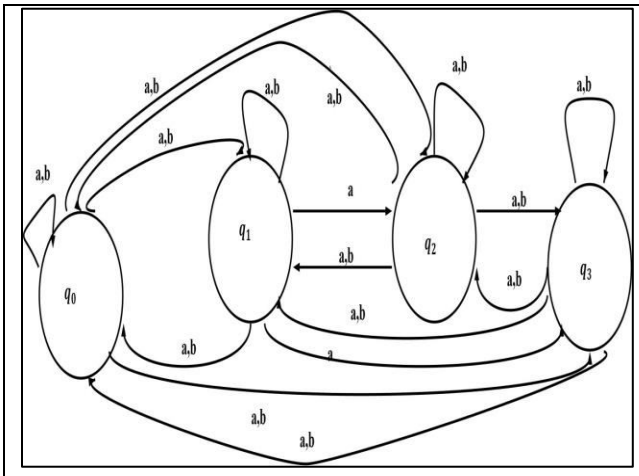

Figure 5: Lower approximation non-homogeneous rough graph cellular automaton $G(I_0^2)^-$

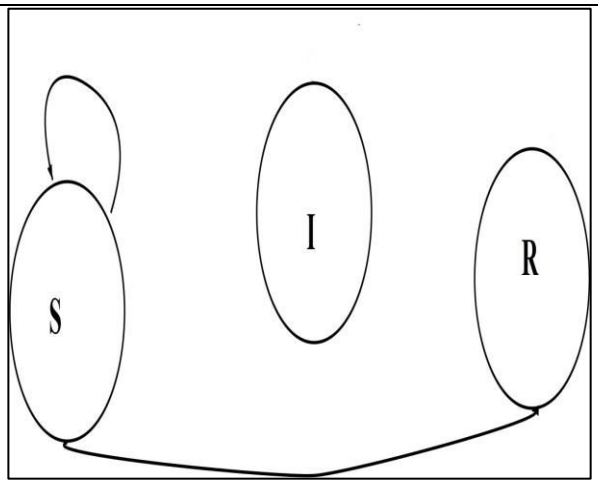

Figure 6: lower approximation non homogeneous rough graph cellular automaton $G(I_0^1)_-$

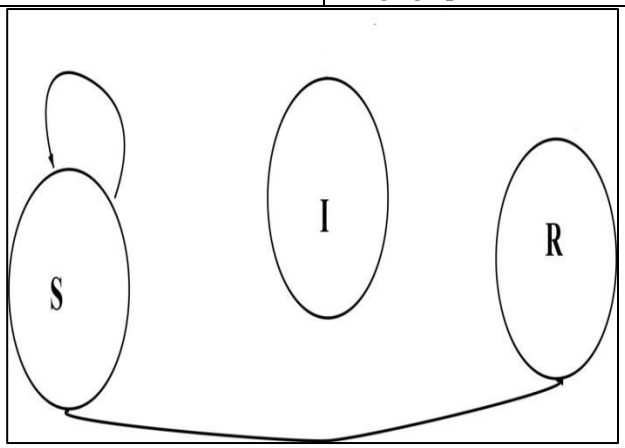

Figure 7: upper approximation non homogeneous rough graph cellular automaton $G(I_0^1)^-$

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REVIEW ARTICLE

Binders in Process of Granulation- Review

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ABSTRACT

Binders are the agents, which are employed to impart the cohesiveness to the granules. This ensures that the tablet remain intact after the compression. The Natural binders like different starch, gums, mucilages, dried fruits possesses the binding capacity as well as some other properties like filler, disintergrant and the natural polymers which are safe & economical than the synthetic polymers like PVP. The Granulation is the process which is mainly used to improve the flow and the compressibility of the powders so as to prevent the segregation of the blend components to improve the content uniformity, and to eliminate the excessive amounts of the fines. Methods of Granulation, Some of the available methods in the industrial field for the preparation of granules are Wet Granulation, Dry granulation and Direct compression methods. The factors which affect the binding properties are Binder concentation, Binder distribution, Granule strength, Type of binder and Particle size and shape. The characterization of binders were evaluated in the angle of repose, the hausner ratio, the Carrs index, the particle size, the hardness test and the disintegration test.

Keywords: Binders, Tablet, Polymers, Natural, Granulation.

INTRODUCTION [1-3]

Binding agent or binders are used to convey the cohesiveness to the granules. Binders are added to the tablet formulation to impart plasticity and enhance the inter-particulate bonding strength in the tablet that make sure the tablet remain intact after compression. To hold different powders together to form a tablet, the binder is added in dry mix or mix in granulating liquid and it form matrix with fillers and the drug embedded in it. On drying the solid binder it forms glue and that holds the particles together, the most significant ingredient is the wet binder which is used in the wet granulation process and the most of the binders are hydrophilic and most times they are soluble in

water. Different starches like rice, potato, maize, corn, wheat, tapioca starch and gums like ferula gum, mosaboiss, *gum olibanum*, *Beilschmiedia* seed gum, okra gum, *Aegle marmelos* gum, gum cordial, okra gum and *cassia roxburghii* seeds gum and the plant fruit such as the date palm fruit and the orange peel pectin shows good potency as a natural binding agent. They also cling to some other properties like filler, disintegrant, thickening agent and are safe and economical than synthetic polymers like PVP.

TYPES OF BINDER [1-5]

Classification on the basis of their source

Natural polymers: Starch, pre gelatinized starch, gelatin,tragacanth,acacia, and gums.
Syntheticpolymer: PVC, HPMC, PEG methyl cellulose and ethyl cellulose.
Sugar: glucose, sucrose, sorbitol.

NATURAL BINDING AGENT

Excipients are additives that is used in active pharmaceutical ingredients which is converted into pharmaceutical dosage form that is suitable for the patients to administrate. In the tablet formulation the binders were added to impart plasticizers andto enhance the inter-particulate bonding strength on the tablet. Granule also increases the degree of compactions when decreasing the brittle fracture tendency during tableting. The selection of a suitable binder for the tablet formulation needs extensive knowledge of the binder properties for enhancing the tablet strength and as well as interaction between different material constituting tablet [4-7]. Gums commonly polysaccharides which are polymeric in nature of natural substance that obtained from woody and non woody plant parts such as bark, seeds, sap, roots, rhizomes, fruit, leaves and plant gums are widely used in the formulation of pharmaceutical dosage forms. The most important application of gum is a tablet, as binding agent [8-9].

Advantage of natural binder

- ✓ Theyare used to modify the release of drug and thereby influencing the absorption and bioavailability of the incorporated drugs [10].
- ✓ The natural binders are widely used in the pharmaceutical and in the food industry as the excipients and additives due to its low toxicity, biodegradability, availability and low cost [11].

Disadvantage of polymer binders

- ✓ Processing difficulties can occur during usage of polymer binder such as, high tablet hardness, rapid over-granulation & decrease in dissolution performance [12-14].
- ✓ When polymer binders are selected addition of strong disintegrates characteristicallyrequired but these are considerably expensive and have a negative effect on the product stability [15].

TYPES OF NATURAL BINDERS

A. Starch as binder
B. Dried fruits as binding agent
C. Natural gums as binder

STARCH AS BINDER [16]

There are several types of natural polymers such as starch, gums, pre-gelatinized starches are used as binding agent. Starches like rice starch, maize starch, potato starch, wheat starch, corn starch are well defined for their binding and disintegrating properties but some other starches like enset starch and banana starch may also be used as binding agent. Starch is also used as fillers. Starch is broadly used as thickening, stabilizing, gelling and/or filling agent in many food applications and it is measured as the mainly used excipients in pharmaceutical formulations. In tablets it

is mainly used as tablets filler, binder or disinter grant. Starch is the main carbohydrate reserve in plant tubers and seed endosperm which is determined as granules. It contains mainly two types of polymer molecules several million of highly branched amylopectin molecules (normally 70-80%) accompanied by a higher number of largely linear amylase molecules (normally 20-30%).

Starch 1500 as a binding agent [17-21]

Starch 1500 acts as the binder producing a granulation that is compressible and produced Lamivudine tablets of increased hardness and friability compared with those prepared with the povidone. The formulation of the Lamivudine tablets with Starch 1500 surpassed the disintegration and the dissolution performance of the povidone formulation that utilized a super disintegrant. The nature and the quantity of the binders were found to correct the disintegration and dissolution rates of the tablets by reducing their wet ability as measured by the adhesion tension of water. During pharmaceutical granulation, the objective is to produce granules that contain a uniform distribution of drug particles within the bulk carrier solid. This can be complicated to achieve and both drug depletion and enrichment in granules may occur. The tapioca starch of the natural product is used as binding agent in the formulation of Diclofenac tablets were determined. To establish the other two normally used disintegrating agent is the potato starch and the maize starch were selected and formulated for comparison. Different formulations were prepared by using the three disintegrants in the concentration of 20mg per tablet. By the wet granulation technique the tablets were prepared.

Tapioca starch as a binding agent [22]

The use of a natural product like tapioca starch as the binding agent within the formulation of Diclofenac tablets was determined. To establish two other commonly used disintegrating agents such as potato starch and maize starch were selected and formulated for comparison. During pharmaceutical granulation, the objective is to produce granules that contain uniform distribution of drug particles within the bulk carriersolid. This can be difficult to achieve and the both drug depletion and the enrichment in granules mayoccur.

Extraction of Different Starches

Extraction of corn starch [23-25]

Stage 1

Consisted of crushing the dry kernels with a hammer, collecting the starch without drying it under the fan, removing the seed coat andseparating the germs.

Stage 2

Three corn kernels were positioned in screw-top 25-ml test tubes. Sodium meta-bisulfite 0.45% (2 ml) is added to each oneof the tube before incubation in a 50°C water bath for 48 hr (± 2 hr) to soften the kernel, increase peeling of the seed coat, and protect the kernel during steeping.

Extraction of potato starch [26,27]

Enzyme solutions were prepared by mixing thoroughly 1g of the enzyme in 10ml of distilled water by a glass rod in a 20ml test tube. The potatoes were washed in the tap water so that any dirt adhered to it may be removed. After washing the potatoes they were cut into small pieces without peeling with a stainless steel knife to facilitate grinding. Grinding were completed in Commercial grinder having motor rpm of 15000 for 1 min and 15 s after standardizing the time. The ground potato meal is then transferred to a 500 ml conical flask and appropriate amount of water was added to the meal. The prepared enzyme solution was poured to the potato meal by using a pipette. For the concentration of 0.1g per 100g of potato meal, the enzyme solution of 1ml was added to 100g of potato meal. The flask should be cotton plugged and kept in the incubator cum shaker at 45°C with a shaking speed of 125 rpm. The pH of all the samples varied between 6 and 7 and cellulose enzyme is effective between pH 3 and 7. So, the natural pH of the broth was not changed. The resultant slurry were screened by a nylon tea strainer of mesh size #100 into a 400 ml beaker Post Incubation. In the, method of screening, the pomace is washed two times in 150 ml of tap water.

Sedimentation was completed for 1h to separate the starch from the other components of the filtrate containing starch. Starch was separated from flour using a modified protein digestion procedure.

DRIED FRUITS AS BINDING AGENT

A potential natural tablet binder from *Grewia optiva* [29]

The gum mucilage was separated from the bark of *Grewia optiva*. The rheological behavior gum mucilage was compared with the starch. The mucilage was then subjected to the physiological characterization & the gum mucilage obtained from the *Grewia optiva* obtained superior rheological properties. A comparative analysis was held that shows the granules bound with *G.optiva* mucilage gum that is relatively bigger and harder than the ones obtained with the starch. The disintegration time, the hardness and the dissolution rate increased with increase in concentration of the gum mucilage. They concluded that *Grewia optiva* gum mucilage as a cheap economic and easily obtainable& suitable for the use of pharmaceutical tablet binder.

Preliminary evaluation of *Bauhinia racemosa* Lam caesalpinaceae seed mucilage as tablet binder [28]

The *Bauhinia racemosa* Lam. Caesalpinaceae seed mucilage is suitable like the binder for the pharmaceutical tablet formulations. Granules were formulated with its varying concentrations and estimated tablet characteristics. The wet granulation techniques were used for the preparation of amoxicillin trihydrate granules. The four different Concentrations was used in the formulation. The estimation for granules size, angle of repose were performed. The evaluation of tablet showed good flow properties and optimum disintegration with more than 90% dissolution in 60 min. 8% w/w binder concentration showed more optimal results as the tablet binder. The mucilage was found to be useful like the uncoated tablet dosage form.

Evaluation of *Mangifera indica* gum as tablet binder [30-32]

The *Mangifera indica* gum is suitable as the binder for pharmaceutical tablet formulations. Paracetamol were used as model drug, Through the wet granulation technique the tablets were prepared. For the physicochemical characteristics, the prepared tablets were evaluated. The tablets friability ranges from 1.12 to 0.26% &disintegration time 3 to 8 min. The *Mangifera indica* binding efficiency is compared with the standard binder gum acacia at similar concentration (5% w/w) the hardness of the prepared tablet from 6.3 to 6.8 kg/cm^{2}they are comparable with those standard binder gum acacia (4.8kg/cm^2).

NATURAL GUMS AS BINDER [33]

Natural gum and mucilage as binder

Through the high molecular weight carbohydrates most of the natural polymer (gum and mucilage) were formed. It is biodegradable, biocompatible and non-hazardous polymers which shows irregular physical-chemical properties and environmentally sustainable features. Carbohydrates represent the most abundant biological molecules, covering a large arrangement of fundamental roles in living things: from the reserve and transport of energy, to the development of structural components, to the linking between intercellular walls. The high molecular weight carbohydrates were derived, are known as the polysaccharides. They may be detected as condensation polymers in which carbohydrates have been joined together by glycosidic linkage with the elimination of molecules of water.

SYNTHETIC/ SEMISYNTHETIC BINDERS [34]

They are most widely used and required a low amount in the formulation. For example Polyvinyl Pyrrolidone, Methylcellulose, Sodium Carboxy Methyl Cellulose, Hydroxy Propyl Methyl Cellulose, Polymethacrylates, Polyethylene Glycol and Methylcellulose, etc.

Advantages of synthetic polymer[35]

- Controllable degradability by manipulating the crystallinity, molecular weight and copolymer ratio.
- Biocompatibility.

Disadvantages of synthetic polymer [36-40]

Though, the utility of synthetic polymers were increasing day by day, these shows certain disadvantages. These are as follows:

- Certain processing difficulties can be created by the Polymer binders like rapid over granulation, increase in the tablet hardness and decrease in the dissolution performance.
- The synthetic polymers are non recyclable, creates environmental pollution throughout synthesis, very high in cost, poor patient compliance and produces side effects.

IDEAL PROPERTIES OF A TABLET BINDER [41-45]

- ✓ It must be physiologically inert.
- ✓ Binder should not interfere with the bioavailability of the drug.
- ✓ Binders must be commercially available in a stable form.
- ✓ Physiologically and chemically stability must be considered.
- ✓ The binding agents should be acceptable to the regulatory agencies.
- ✓ Standards of regulatory requirements must be met by the binding agents.
- ✓ They must be able to produce cohesive compacts for directly compressed tablets.

GRANULATION [46,47]

Granulation is that the process during which the primary powder particles are done to stay and to form larger, multi-particle aggregates known as granules. After the granulation process the granules may either be packed, or they may be mixed with other excipients that is prior to tablet compaction or capsule filling. Granulation is mainly used to improve flow and compressibility of powders so that it prevents segregation of the blend components to improve content uniformity, and remove excessive amounts of fines. The granulate particle size is mainly affected by the quantity and feeding rate.

Granulation method can be widely classified into three types:

i. Wet granulation.
ii. Dry granulation.
iii. Direct compression.

GRANULATION TECHNIQUES

WET GRANULATION

Wet granulation is that the most generally used method of granulation within the pharmaceutical industry. The addition of a liquid solution to powders is involved, to form a wet mass or it forms granules by adding the powder together with an adhesive, instead of compaction [48]. The wet mass is dried and then sized to get the granules. The liquids were added that binds with the wet powder particles by a combination of the capillary and the viscous forces with the wet state. More stable bonds were formed during the subsequent drying which leads to the formation of agglomerates [49].

MERITS

- It improves the flow property and the compression characteristics and increases the density of the granules.
- It prevents segregation of powders.
- There is better distribution of color and soluble drugs if added in the binding solution.
- It converts hydrophobic surfaces into hydrophilic.

DEMERITS

- The thermo labile and the moisture sensitive drugs were poor candidates. Multiple processing steps were involved in the process which adds complexity.

- There is loss of material occurred during various stages of processing.
- Process is high cost because of labor, space, time, special equipment and energy requirement.

WET GRANULATION TECHNIQUES

The4 major techniques of the following process were used for wet granulation process.

EXTRUSION-SPHERONIZATION[56]

This process is mainly used as a technique to generate multi-particulates for controlled release application. It is a multiple step process that involves at least 5 steps capable of making uniform sized spherical particles.

1. There is dry mixing of materials to achieve homogeneous dispersion.
2. Wet granulation of the reported mixture to form wet mass.
3. The extrusion of the wet mass to form the rod shaped particles.
4. Rounding off (in spheronizer)
5. Drying

The optional screening of dried spherical particles can be performed to attain a targeted mean size distribution. The diagram explains schematically the steps involved in the extrusion spheronization process.

SPRAY DRYING [57-60]

It is a continuous process in which a dry granular product is obtained by providing a binding solution or a suspension of active agent with or without excipients to the drying system where the feed is atomized and dried with a heated gas steam. Particle agglomeration were brought by spraying the binder solution on the bed of powder particles in fluidized state achieved with the channel of air followed by drying using hot air.

The spray drying process involves three fundamental steps

1. Atomization of the liquid feed into fine droplets.
2. Partition of the dried powderfrom the gas stream.
3. Mixing of these sprays droplets with a heated gas stream, letting the liquid to evaporate and leave dried solids.

Spray drying is widely applied in formulation of dry syrup and dusting powders. This process must be followed accurately to avoid size variation of particles. It is used for thermo-labile substances. But, it should be noted that this is a continuous rapid process which is economic and reduces operator exposure to dust.

FLUID BED GRANULATION[53-55]

Fluidization is the process by which transformation of fine solids into a fluid like state takes place through contact with a gas. The fluid will maintain the particles giving them free mobility without entrapment at certain gas velocity. Procedure by which granules are produced in single equipment by spraying a binder solution onto a fluidized powder bed is called Fluid bed granulation. The material processed by the fluidized bed granulation are finer, free flowing and homogeneous. The system comprises of heating of air and followed by passing it through the pre-processed material. Then, the same air exit through the voids of the product. Fluidized bed system consists of various components such as

- Spray Nozzle
- Air-Handling Unit (AHU)
- Control System
- Product Container and Air Distributor
- Disengagement Area and Process Filters

- Exhaust Blower or Fan
- Solution Delivery System.

The diagram presents a typical fluid bed granulator (Glatt Type). It reduces loss of product with improvement of safety for workers. The dust formation during this process is minimum. Non-Reproducibility and higher manpower and long processing time are some of the disadvantages of this type of granulation. This type of granulation is used for drying, coating and mixing.

HIGH SHEAR MIXTURE GRANULATION [50,52]

High shear mixture has been applied widely in Pharmaceutical industries for blending and granulation. In this type of equipment, the particles swing into movement by an impeller rotating at a high speed of 100 rpm. The equipment also includes a chopper which rotates about 1500 – 4000 rpm. The prime function of chopper is to cut bulky lumps into smaller fragments therefore it increases the binder distribution into the blend. The liquid binder is added by pouring, pumping or spraying from the top. Wet agglomeration in a high-shear mixer involves 3 phases:

1. Dry Powder mixing with a time period of 2-5 mins
2. Liquid binder addition with a time period of 1-2 mins
3. Wet massing.

After the wet mass is formed, it is further processed to obtain dried grade particle size granules.

1. Wet sieving of granules.
2. Dry sieving of granules.
3. Drying

The diagram shows details of a typical high shear mixer granulator equipment i.e Rapid Mixer Granulator.

After mixing of materials in dry condition, liquid is poured during mixing. Then the moist mass is wet massed in order to attain a narrow particle size distribution. Then the granules were wet sieved, followed by secondary sieving after drying. The liquid quantity is significant, because the process is vulnerable for over wetting, which leads to uncontainable agglomerate growth. Variations in raw materials may influence the liquid necessity. The impeller torque and the power consumption of mixers were used to observe the properties of wet masses during agglomeration. The above method of measurement gives a measure of the amount of resistance the impeller experiences to maintain a certain rotational speed.

FREEZE GRANULATION [61,66]

The integrated Biosystems, Inc. had patented freeze GT that results in the spherical and free flowing granules with optimal homogeneity. Freeze Granulation involves spraying of suspension containing powder into liquid nitrogen where the drops were immediately frozen to form granules which upon subsequent freeze-drying yields dry granule. There are several advantages in this process like a higher practical yield, absence of cavity formation, better reproducibility, etc. There are certain disadvantages associated with this graduation like chances of degradation may occur for volatile substance or low melting point substances, which is lesser than 0°C. Freeze granulation is widely applied in formation of injectable granules.

ADVANCED GRANULATION TECHNIQUES[67]

Over a time period, due to technological development and to improve commercial output various, modern granulation technologies have been developed such as,

- Foam Granulation
- Moist Granulation Technique (MGT)
- Melt/Thermoplastic Granulation

- Moisture Activated Dry Granulation (MADG)
- Steam Granulation
- Thermal Adhesion Granulation Process (TAGP)

DRY GRANULATION [61-65]

This method is the inexpensive method of granulation and suitable for hydro sensitive products. In this method granules were prepared without binding solution and heat. Two steps involved in this method. Such as,

- Preparing large particles called slugging.
- Milling and screening of slugs into the small granules.

Advantages

- Requirement of equipments is minimum
- Eliminate binding solution process

Disadvantages

- It tends to produce more dust with respect to wet granulation.
- It increases the potentiality of cross contamination.

Applications

- It is suitable for hydrophobic and lipophilic substances.

DIRECT COMPRESSION [59,68]

Direct compression is the simplest and most economical method for the tablet manufacture because it requires less processing steps other than techniques. Introduction of spray dried lactose and avicel had modified the tablet manufacturing process and opened avenues of direct compressing tableting. The term direct compression is used to define the process by which tablets are directly compressed from powder blends of active ingredient and excipients, which flow uniformly in the dyes and forms a film compact.

Advantages

- Direct compression requires minimum number of equipment, power consumption, space, time and labor leading to reduced production cost of tablets.
- Better stability of API
- Cost effective production can be achieved.

Disadvantages

- Lubricant sensitivity
- Poor compressibility of API

Applications of direct compression techniques [70,71]

- This technique can now be applied to mouth dissolving tablets because of the availability of improved tablet excipients, especially tablet disintegrants and sugar-based excipients
- The tablets include high loading API with poor compatibility is manufactured by direct compression method. Strong compatibility can achieve by using direct compression-binder.

FACTORS AFFECTING BINDING PROPERTY

BINDER CONCENTRATION [72-73]

The concentration of binders have been shown to affect the degree of plastic deformation imparted on a model non plastic deforming system. In another study, the concentration of starch in a dicalcium phosphate system was found to reach an optimum of ten percent. A quantity greater than ten percent led to cohesion between starch molecules an increase number of fine particles which led to poor granule properties for tabletting.

BINDER DISTRIBUTION

In each system stated that the main factor which effects binder effectiveness is binder distribution within the granule or directly compressible system. Binder distribution was evaluated in model formulations and unique patterns were identified which depend upon method of manufacture. Using a solvent extraction method these authors were able to identify the regions of binder distribution in granules prepared by wet massing, slugging (pre-compression) and spray drying. The wet massing granules tended to have a matrix-like binder distribution while the granules prepared by spray drying had a localized binder shell on the surface of the granule. The pre-compression process tended to produce a binder distribution of discrete particles[74-76]. The distribution of a binding agent is affected by processing conditions and formulation factors which inhibit the wetting of the substrate particles. This was illustrated by evaluating granule qualities of a system granulated with a surfactant compared to using modified starch and starch paste. The surfactant may increase the spreading of the binding liquid but leads to granules with decreased strength[77].

GRANULE STRENGTH [78-81]

Though binder type and concentration have been shown to affect the granule strength, the granule strength does not correlate with tablet strength. A greater influence of compaction force and binder concentration was seen on tablet strength. A correlation was determined between the degree of fragmentation of a granule and tablet tensile strength. Granules that tend to fragment during compaction tend to produce good tablets due to a great number of formed areas for inter-particulate binding. The fragmentation is also identified as a critical parameter in the tablet formation by direct compression. The effect of binding agent is evaluated, on the ability to influence the plasticity of a non-plastic deforming model material. The binding agents were shown to contribute to the plasticity of the studied granulation.

TYPE OF BINDER [81,82]

To elucidate the influence of type of binding agents on bond formation during tabletting, the effect of different agents on the energy utilized to form tablet bonds as measured by the net work of compaction, after multiple compactions of a dicalcium phosphate dihydrate based formulation was identified. By dividing the total work of compaction into components of work derived to form the tablet and work lost through elastic recovery, the influence of six commonly used binding agents on the plasto/elastic properties of a granulated system was studied. The six compounds were rank ordered on their ability to influence the plasticity of the system. The use of multiple tablet compaction as a model to determine bond formation may be limited by the heat formation within a tablet which occurs during compaction. If allowable time is not permitted between compaction cycles heat not dissipated may have an influence on inter-particulate bond formation.

PARTICLE SIZE AND SHAPE [83-86]

The effect of particle size on the ability of a material to bond was shown to be dependent on the substances mechanism of deformation. This was illustrated by evaluating the mechanisms of two drugs: sulfadimethoxine which deforms by particle fragmentation; and sulfaphenazole which deforms plastically, with a series of drugs and excipients, and excipients alone. In the case where substances deform by fragmentation larger particles tend to form bonds more effectively than smaller particles. In the case of plasticly deforming compounds, tablet structure and the ability to form bonds was not affected by particle size. These evaluations were made in model homogenous systems. In a practical formulation setting particles in a tablet formulation may deform by both mechanisms and possibly

have an elastic component also. In this respect, particle size may be an important factor in bond formation during compaction. As with particle size, particle shape factors may have an influence on binding depending upon the materials ability to fracture or deform.

CHARACTERIZATION FOR BINDERS[87-102]

Angle of Repose

Angle of repose is defined as the physical property by which steepest angle of dip is relative to the horizontal surface. It can range from 0-90 °. This is a pre-formulation property which is related to inter-particulate friction between particles.

Hausner Ratio

Hausner ratio is defined as the ratio of taped density to bulk density. It is an essential flow property which is widely used in preformulation studies in various pharmaceutical industries.

Carr's Index

Carr's index is otherwise known as compressibility is outlined because the ability of the powder to decrease in volume once subjected to pressure. it's measured by getting the density determination as follows:

Percentage Compressibility = (Tapped density - Bulk density/Tapped density)*100

The compressibility measurement provides an idea on the flow property of the granules as per carr's index:
The Carr's index is an indication of the compressibility of the powder. The Carr's index is normally used in pharmaceutics as an indication of the flow ability of a powder.

PARTICLE SIZE

The granule size affects the disintegration time, drying rate kinetics of the wet granulation, variation, granule friability, average tablet weight, and granulation flow ability. The formulator estimates the tablet quality, that affects the granule size and distribution. The measurements generally used for the size and distributions that include the Conductivity Test, Microscopy and Sieving.

HARDNESS TEST

Hardness show the capability of a tablet to withstand shocks will handling, the har tablet hardness that were determined using Erweka hardness tester, which is expressed in kg/cm^2, ten tablets were randomly selected from each formula and tablets hardness can be determined.

CONCLUSION

The binders are the agents which are mainly used to impart the cohesiveness to the granules in the pharmaceutical industries. The binders are classified according to their source like natural and synthetic binders, the binders include the granulation process which is mainly used to improve the flow and the compressibilityof the powders, the granulation methods are wet granulation, dry granulation and direct compression. The binding properties were evaluated as angle of repose, Hausner ratio, Carr's index, particle size, hardness test and disintegration test.

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Table 1: Angle of repose and quality of flow

ANGLE OF REPOSE	TYPE OF FLOW
< 25	Excellent
25 – 30	Good
30 – 40	Passable
> 40	Very Poor

Table 2: Hausner's ratio and quality of flow

HAUSNER RATIO	TYPE OF FLOW
Less than 1.25	Good Flow
1.25 - 1.5	Moderate
More than 1.5	Poor Flow

Table 3: % compressibility and quality of flow

% Compressibility	Flow Description
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair
23 – 28	Poor
28 – 35	Poor
35 – 38	Very Poor
> 40	Extremely Poor

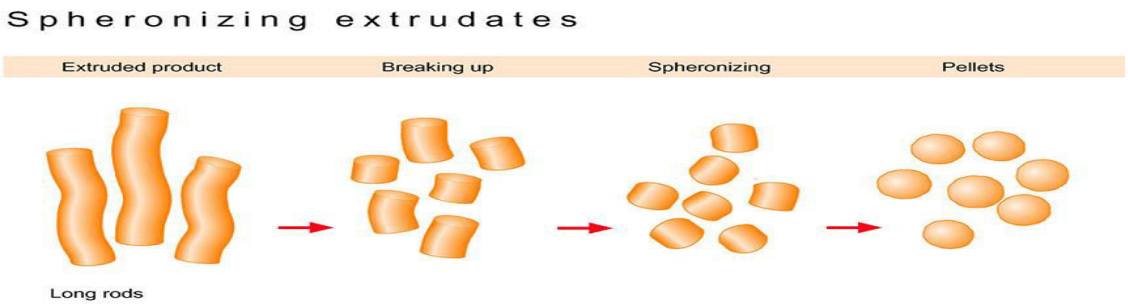

Fig.1. Different Steps Involved In The Extrusion- Spheronization Process

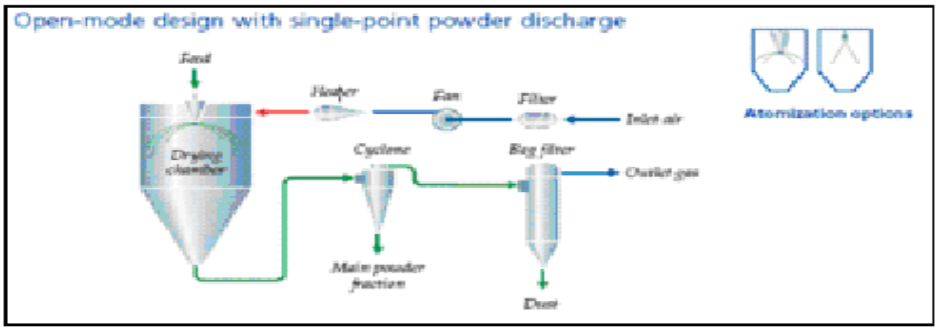

Fig.No:2Spray Dryer Configurations (from GEA Niro)

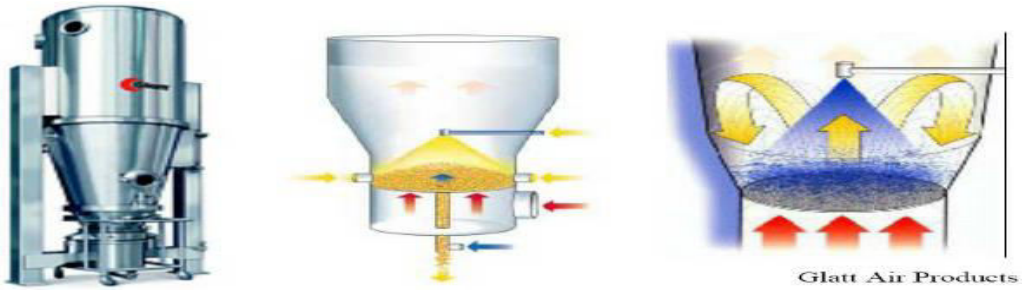

Fig.No:3Fluidized Bed Granulator(Glatt)

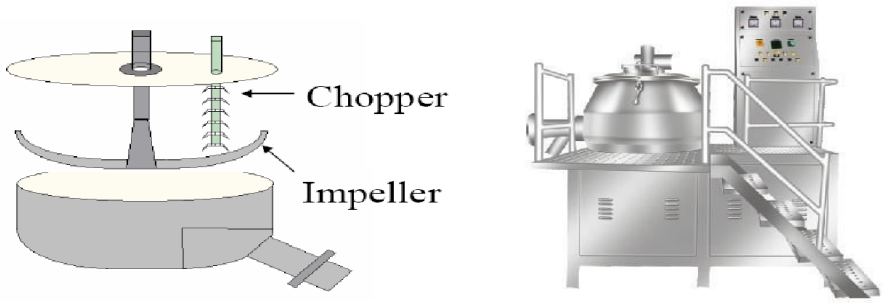

Fig.No:4Rapid Mixer Granulator (RMG)

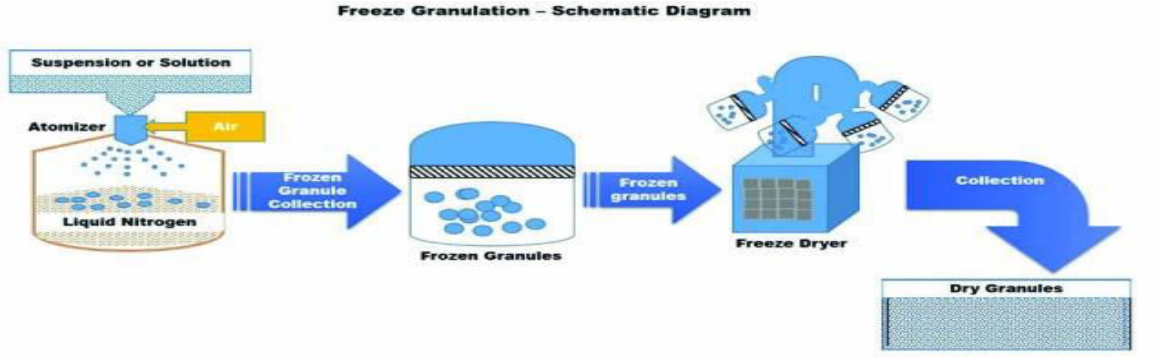

Fig.No:5 Freeze Granulation- Schematic Diagram

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RESEARCH ARTICLE

Green Synthesis of Antimicrobial Nanoparticles from Indian Lichens

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ABSTRACT

Indian being a mega diversity country exhibit rich diversity of plant groups including lichens and the country is a hotspot of lichen diversity with 2917 lichen species, which is about 13% of the known lichens in the world. Since ancient times, lichens have been a household item in India, used as spice and traditional medicine mentioned in Ayurvedic and Unani system of medicine and More than 160 species are known to be medicinally important lichens. Most of the secondary metabolites present in lichens have been reported to have various biological activities well evident with the leads available. Lichen secondary metabolites exhibit a wide variety of biological actions including antimicrobial (fungus, bacteria, virus, protozoa), anti-inflammatory, analgesic, antipyretic, antiproliferative, antioxidant and cytotoxic effects. Being a slow growing organism in nature, lichens were quite neglected for their use in development of pharmaceutically important drugs, however after the advent of nanotechnology, in recent year a large number of lichen species are utilize for development of antimicrobial nanomaterials throughout the world. So far, few uses of lichens as nanoparticles formation are available from India. Thus, the present review will provide a detailed account of potential lichen species for development on antimicrobial nanoparticles.

Keywords: Lichens, nanosilver, phytochemical, antimicrobial.

INTRODUCTION

In recent years the synthesis of green nanoparticles from plants or other natural resources has gained more attention as the synthesis does not require use of high pressure, energy and temperature. A part from toxic free nature of

nanoparticles, the green chemistry is eco-friendly, cost-effective, suitable for pharmaceutical and biomedical applications. Though, a number of higher groups of plants and fungi (Table 1-3) are used for the synthesis of nanoparticles and screened for their antimicrobial properties, however few taxa of Algae, fungi, lichens and bryophytes are employed for green synthesis. Recently studies on the progress and application of nanoparticles received greater attention and a number of reviews on the subject are available. [1-5]. Among lichens the species of lichen taxa such as *Evernia, Parmotrema, Parmelia, Parmeliopsis, Punctelia, Usnea* and *Xanthoparmelia* are widely used for synthesis of nanoparticles.

Shahi and Patra [6] synthesized bioactive nanoparticles of 50-200 nm size using lichen taxa *Usnea longissima*. The nanoemulsion showed antibiotic activity against a number of dermatophytoses human fungi during preliminary in vivo investigations.

Kumar *et al.*[7] evaluated the synergistic efficiency of lichen extracts of *Parmotrema pseudotinctorum* and *Ramalina hossei* and silver nanoparticles alone and in combination against gram negative and gram positive bacteria causing food poisoning. The lichen extracts were more effective against gram positive bacteria while silver nanoparticle on gram negative bacteria. The lichen extract of *Ramalina hossei* was found to affect bacteria more extent than *Parmotrema pseudotinctorum*. In combination trails, the result was found to be superior to that of individual treatment *Ramalina hossei* in combination of nanoparticles exhibits higher inhibition of *Escherichia coli* and *Salmonella typhei* than the standard antibiotic. The lichen extracts individually have lesser activity than the combination with silver nanoparticles.

Dasari *et al.*[8] carried out biosynthesis of silver nanoparticles from four foliose lichens such as *Parmeliopsis ambigua, Punctelia subrudecta, Evernia mesomorpha* and *Xanthoparmelia plitti* after characterization of the nanoparticles antimicrobial activity of synthesized SNPs were tested against Gram negative (*Pseudomonas aeruginosa* (ATCC 9027) and gram positive (Proteus vulgaricus Staphylococcus aureus (ATTCC 6538), *Streptococcus pneumonia* (ATCC 4969) and *Bacillus subtilis* (ATCC 98). The antioxidant activity of all the four lichen nanoparticles was also studied. *Evernia mesomorpha* shows potent antimicrobial activity against the five tested bacterial strains while *Punctelia subrudecta* shows the potent antioxidant activity.

Yildiz *et al.*[9] biosynthesized the silver nanoparticles from AgNo3 using extract of *Cetraria islandica* a foliose lichen reducing and stabilizing. Response surface methodology (RSM) was used to investigate the effects of temperature, reaction time and AgNo3/ lichen ratio caused a decrease of particle size and the increase in temperature resulted in bigger particles.

Mie *et al.* [10] reported the synthesis of silver nanoparticles from the reduction of silver nitrate and an aqueous extract of the lichen *Parmotrema praesorediosum* as a reductant as well as a stabilizer. The synthesized nanoparticles have an average particle size of 19nm with a cubic structure and showed potential antibacterial activity against gram-negative bacteria.

Din *et al.*[11] successfully synthesized the silver nanoparticles by reduction of silver nitrate with an aqueous extract of lichen *Ramalina dumeticola*. The synthesized AgNPs showed potential antibacterial activity against Gram-positive and Gram- negative bacterial such as *Proteus vulgaris , Pseudomonas aeruginosa, Serratia marcescens, Salmonella typhi, Staphylococcus epidermidis, MRSA, Bacillus subtilis, Streptococcus faecalis* with a inhibition zone of range between 7.5-10.5 mm in 100/ ug/ml. AgNPs.

Mie *et al.* [12] developed a simple biological method for green synthesis of silver nanoparticles using two lichen species, *Parmotrema praesorediosum* and *Ramalina dumeticola* .The TEM analysis showed synthesis of 20nm and 42nm average sized silver nanoparticles in *R. dumeticola* and *P. praesorediosum* respectively.

Debnath *et al.*[13] accomplished biogenic synthesis of gold nanoparticles using dried biomass of two high altitude lichen species collected from the alpine regions of Arunachal Pradesh. The XRD study showed formation of face-centered cubic structure of gold nanoparticles in a case of *Ascroscyphus* sp. Produced while *Sticta* sp. has multiply twinned nanomaterials.

Leela and Anchana [14] synthesized characterized silver nanoparticles using the aqueous extract and using the purified compounds obtained from the methanolic extract. The nanoparticles showed antimicrobial, antioxidant and antidiabetic activities.

Siddiqui *et al.*[15] synthesized / fabricated the silver nanoparticles from aqueous ethanolic extract of *Usnea longissima* and tested it for antimicrobial activity against both gram positive and gram negative bacteria after characterization by UV-Vis, FTR spectroscopy, TEM and SEM analysis.

Singh *et al.* [16] developed a herbo-metalic colloidal nao-formulation containing Swarna (Gold) nanoparticles and polyphenolic rich *Usnea longissima* lichen extract and evaluated its antiquorum sensing property against Streptococcus mutant. The synthesized Uh-Au@ Nano-CF (herbometallic colloidal) nano formation with nano particles of 28 nm sized was characterized by TEM and FTIR. The data from the inhibition of violacein production revealed that the Uh-Au@Nano-CF at sublethal concentration of 5,10 and 15% show potent antiquorum sensing activity. The treatment of Uh-AU@Nano-CF was found to inhibit the secretion of Streptococcus mutant virulence factors, including acid production.

Abdolmaleki *et al.*[17] considered biosynthesis of silver nanoparticles by two lichens of *Usnea articulate* and *Ramalina sinensis* had a maximum absorption at the wavelengths of 450 and 480 nm. Also, the presence of silver nanoparticles was confirmed by XRD method. The size of silver nanoparticles produced by *Usnea articulata* was about 10 to 50 nm and the nanoparticles produced by *Ramalina sinensis* around was 50 to 80 nm. The antibacterial test of the nanoparticles showed a good inhibitory effect against all four bacteria.

Thakkar *et al.*[5] and Sajjadi *et al.* [18] lichens exhibit vast array of secondary metabolites which can be used as an excellent natural source to synthesize nano materials. Glycosides and alkaloids produced by plants, fungi and bacteria including lichens are widely used in medication drugs and have other applications.

Silver nanoparticles have unique properties thus a number of organism are employed to synthesize the silver nano particles both for diagnostic and therapeutic purpose. India being a mega diversity country exhibit rich diversity of different plant group including lichens. More than 2700 species of lichens are recorded from India; however, medicinally potential of only 160 lichens are listed from the country.

Few studies [17, 11, 14] regarding synthesis of lichen nano materials from are available thus the present study is carried out with an aim to list the lichens together with their characteristic features, chemicals present and distribution for further development of green, antimicrobial nano particles from India lichens species.

Potential India Lichen Species for Synthesis of Nanomaterial

Based on the leads available on medicinal properties of Indian lichens, their distribution and availability of high biomass, following species may be considered for development/ synthesis of medicinal nanomaterials from lichens. Some common secondary metabolites chemical structure present in lichen species are present below.

Acroscyphus sphaerophoroides Lév

A pulvinate-fruticose lichen found growing over rock, soil and some time on dead wood, thallus upto 5 mm tall yellowish orange, solid, cylindrically branched lichen globular, terminal mazaedioid apothecia, apothecia terminal,

black. The species found growing on alpine areas of Indian Himalayan regions between altitudes of 4000-4400 m from Arunachal Pradesh and Sikkim. The species has Calycin, gyrophoric acid, zeorin as its secondary metabolites.

Anzia physoidea A.L. Sm.
Thallus cortiocolous, foliose, upto 5 cm across, branched, lobes upto 2 mm wide, upper side greyish green to brownish. The species widely distributed in temperate regions of Arunachal Pradesh, Darjeeling and endemic eastern Himalaya region. The species have lobaric acid and atranorin as its major secondary metabolites.

Aspicilia almorensis Räsänan
A crustose lichen growing on exposed boulders with peltate thallus, areolate in centre and lacinate at periphery. The species widely distributed in temperate Indian Himalayan regions in the state of Himachal Pradesh, Jammu & Kashmir, Uttarakhand and West Bengal hills between altitudes of 2500-3750 m. The species has norstictic acid as its major secondary metabolites.

Bryoria bicolor (Hoffm.) Brodo & D. Hawksw.
A fruticose lichen with erect to caespitose 2-7 cm tall, black thallus growing in soil, bark of trees and rock. The lichen widely distributed in higher temperate and alpine Indian Himalayan regions in Sikkim, Uttarakhand, Arunachal Pradesh and West Bengal hills between altitudes of 3500-4500 m. The species has Fumarprotocetrraric acid as its major secondary metabolites.

Bryoria himalayensis (Motyka) Brodo & D. Hawksw.
A fruticose lichen growing mostly on trees with 20 cm long, grey brown to black thallus with pseudocyphellaean spinules branches. A endemic widely distributes in upper temperature and alpine Indian Himalayan regions between altitudes of 3000-4000 m in Arunachal Pradesh, Nagaland, West Bengal-Darjeeling Hills and Sikkim. The species has fumarprotocetraric acid as its major secondary metabolites.

Bulbothrix isidiza (Nyl.) Hale
A foliose lichen growing mostly on trees, with 8 mm wide lobes, bulbate cilia along margins of lobes. Apothecia upto 4 mm in diam. A common lichen species in tropical to subtropical regions between altitudes of 800-1500 m in different localities of Karnataka, Kerala, Maharashtra, Manipur, Meghalaya, Nagaland and Uttarakhand. The species has salazinic acid as sits major secondary metabolites.

Bulbothrix meizospora (Nyl.) Hale
A foliose lichen growing mostly on bark of trees upto 12 cm in diam. with upto 8 mm wide adnate lobes with bulbate cilia on axils. The species is widely distributes in subtropical to lower temperate regions of India between altitudes of 1500-2500 m in Meghalaya, Nagaland, Sikkim, Tamil Nadu-Nilgiri and Palni Hill, Uttarakhand, West Bengal-Darjeeling district. The species has salazinic acid as its major secondary metabolites.

Bulbothrix setschwanensis (Zahlbr.) Hale
A foliose lichen growing mostly on trees, upto 10 cm in diam., lobes upto 6 mm wide with bulbate cilia only with distinct bulb, apothecia upto 5 mm in diam. The species is commonly distributed in tropical to subtropical regions of India between 360-1500 m in different localities of Arunachal Pradesh, Manipur, Nagaland, Uttarakhand and West Bengal-Darjeeling Hills. The species has salazinic acid as it major secondary metabolites.

Canoparmelia aptata (Kremp.) Elix & Hale
A foliose lichen growing on trees, forming a patch upto 8 cm across with 4 mm wide postulate sorediate lobes. The species is distributes in tropical to lower temperate regions of India between altitudes of 1000-3000 m in different

localities of Karnataka, Madhya Pradesh, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has perlatolic and stenosporic acids as its major secondary metabolites.

Canoparmelia ecaperata (Müll Arg.) Elix & Hale
A foliose lichen growing on trees, forming a patch upto 8 cm across lobes 5 mm wide, maculate, cracked, isidaite upper surface. The species is common in tropical and lower temperate region between altitudes of 1300-2350 m in Kerala, Nagaland, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has atranorin, usnic and divercatic acids as its secondary metabolites.

Canoparmelia texana (Tuck.) Elix & Hale
A foliose lichen growing mostly on bark of trees, upto 10 cm across with maculate cracked postulate sorediate lobes of 4 mm wide. The species is common in tropical and lower temperate region between altitudes of 100-2500 m in Karnataka, Kerala, Maharashtra, Manipur, Meghalaya, Nagaland, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand. The species has divercatic, nordivercatic and stenosporic acids as its major secondary metabolites.

Cetraria islandica (L.) Ach.
A foliose shrub like lichen growing on soil upto 5 cm tall branches upto 5 mm wide with marginal continuous pseudocyphallae. The species is common in upper temperate and alpine Indian Himalayan regions in Arunachal Pradesh, Sikkim and Uttarakhand, between altitudes of 3450-4500 m. The species has fumerptotocetraric, protocetraric and protolichenestrinic acid and its major secondary metabolites.

Cetraria laii Divakar, A. Crespo & Lumbsch
A cushion forming lichen, growing on soil upto 5 cm tall with 3 mm wide yellow to brownish lobed. The apothecia are marginal to submarginal to lobes upto 10 mm in diam. The species is widely distributed in upper temperate to alpine regions between altitudes 300-3500 m of Jammu & Kashmir, Sikkim and Uttarakhand and have usnic, lichensterinic, protolicheterinic, secaloni and endocrocin pigment.

Cetraria pinastri (Scop.) Gray
A foliose to subfruticose lichen commonly growing on bark, twigs of trees, thallus adnate upto 3 cm across, lobes compact, 2-3 mm wide upper side yellow to deep yellow, marginally sorediate; soredia yellow granular, lower side yellow, reticulately lacunose, sparsely rhizinate. Apothecia not known. The species reported from upper temperate regions of the Himalaya between altitudes of 3300-3600 m from Himachal Pradesh, Uttarakhand. The species has Vulpinic and pinastric acid as its secondary metabolites.

Cetrelia ceterioides (Delise ex Duby) W. L. Culb. & C. F. Culb.
A foliose lichen, growing on tree bark, forming patch of 16 cm across with 15 mm wide lobes upper surface with wide psaeudocyphellae and finely sorediate at margin. A common species in temperate regions of Indian Himalayan regions found growing between altitudes of 1500-3000 m in Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Manipur, Nagaland, Sikkim, Uttarakhand, West Bengal-Darjeeling district. The species has atranorin, perlatolic and imbriaric acids as its major secondary metabolites.

Cladonia cartilaginea Müll. Arg.
A dimorphic lichen growing on decaying wood or soil with upto 15 mm tall simple to sparingly branched podetia lacking scyphi. A common species distributed in subtropical to lower temperate in Indian Himalayan regions and higher altitudes of Western Ghats between altitudes of 1100-2000 m in Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Karnataka, Kerala, Manipur, Meghalaya, Sikkim, Tamil Nadu, Uttarakhand, West Bengal-Darjeeling district. The species has fumarprotocetraric acid as the major secondary metabolite together with other strain of stictic, consticite, cryptosticite, psoromic, usnic and isousnic acids.

Cladonia corniculata Ahti & Kas.
A dimorphic lichen found growing on soil or decaying wood, upto 50 mm tall, farinose sorediate podetia brown hymenial disc lacking scyphi. A common lichen species widely distributes in lower temperate regions of Indian Himalayan regions and higher altitudes of Western Ghats between altitudes of 1650-2500 m in the state of Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Kerala, Meghalaya, Sikkim, Tamil Nadu-Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has fumarprotocetraric and protocetraric acid as its major secondary metabolites.

Cladonia corymbescens (Nyl.) Nyl.
A dimorphic lichen found growing on soil with upto 35 mm tall, repeatedly subcroymsosely branched, longitudinally fissured, ecorticate podetia with brown hymenium. The species shows its common occurrence in the temperate Indian Himalayan regions and higher altitudes of Western Ghats between altitudes of 1500-4000 m, in the state of Arunachal Pradesh, Sikkim, Tamil Nadu, Uttarakhand and West Bengal-Darjeeling district. The species has fumarprotocetraric, protcetraric acid as its major secondary metabolites.

Cladonia furcata (Huds.) Schrad.
A dimorphic lichen found growing on decaying wood or on soil upto 50 mm tall, dichotomously to irregularly branched subulate or tapering never scyphose, esorediate, irregularly squamulose, podtia with brown hymenial disc. The species is common in temperate Indian Himalayan regions between altitudes of 1700-3900 m found growing on soil or dead wood in the state of Arunachal Pradesh, Himachal Pradesh, Nagaland, Sikkim, Uttarakhand, West Bengal-Darjeeling district. The species has fumarprotocetraric acid as its major secondary metabolites.

Cladonia furticulosa Kremp.
A dimorphic lichen found growing on soil and decaying wood upto 30 mm tall, simple to rarely branched blunt escyphose, sorediate podetia with brown hymenial disc. The species is widely common in temperate Indian Himalayan regions and higher altitudes of Western Ghats between altitudes of 1500-2400 m in the state of Arunachal Pradesh, Karnataka, Kerala, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, Tamil Nadu-NIlgiri and Palni Hills, Uttarakhand and West Bengal-Darjeeling district. The species has psoromic usin, fumarptotocetraric, protcetraric and lichenternic acids as its major secondary metabolites.

Cladonia ochrochlora Flöerke
A dimorphic lichen found growing on decaying wood or soil with sorediate large primary squamulose upto 20 mm tall, esyphose, simple farinose sorediate podetia with brown hymenial disc. The species is widely distributed in lower to upper temperate regions of Indian Himalayan regions and Western Ghats between altitudes of 1500-3500 m, found on decaying wood and soil in the state of Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Kerala, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand and West Bengal-Darjeeling district. The species has fumarprotocetraric acid as its major secondary metabolites.

Cladonia pyxidata (L.) Hoffm.
A dimorphic lichen found growing on decaying wood or soil upto 10 mm tall pseudopodia upto 5 mm wide ecyphi with pellate disc and brown hymenial disc. The species is common in temperate Indian Himalayan regions between altitudes of 2000-3000 m found growing on decaying wood and on soil in association with mosses, in the state of Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Sikkim, Uttarakhand and West Bengal-Darjeeling district. The species has fumarprotocetraric acid as its major secondary metabolites.

Dirinaria aegialita (Afz.in Ach) Moore
A foliose lichen mostly growing on bark or on rocks, forming patches of 6 cm across, with flabellate, plicate, grey lobes with isidioid verrucose or dactyls becoming sorediate. The species is distributes in tropical to subtropical

regions of India between altitudes of 500-1500 m in the state of Andaman Island, Kerala, Madhya Pradesh, Tamil Nadu-Palni Hills, Uttar Pradesh, Uttarakhand. The species has divercatic acid as its major secondary metabolites with a number of triterpin.

Evernia mesomorpha Nyl.
A fruticose shrub like lichen found growing on bark of trees or rarely on rocks and soil. Thallus erects to pendulous upto 13 cm long tapering yellow brown wrinkled isidiate-sorediate throughout upper surface. Species reported from upper temperate regions of Himachal Pradesh, Sikkim, Uttarakhand. Thallus contains divaricatic and usnic acid as its secondary metabolites.

Flavoparmelia caperata (L.) Hale
A foliose lichen found growing on bark of trees or sometimes rocks, with closely adnate thallus forming patches of upto 20 cm across lobes yellow with postulate granular soredia. The species is widely distributes in lower Indian temperate to alpine regions and Western Ghats between altitudes of 1500-3500 m in the state of Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Manipur, Meghalaya, Nagaland, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has usnic, caperatic and protocetraric acid as its major secondary metabolites.

Flavopunctelia flaventior (Stirton) Hale
A foliose lichen growing over bark, twigs rarely on rock, upto 10 cm across, lobes upto 10 mm wide, upper side yellow green to grey with marginal pseudochphellae sorelia marginal to sumargianl capitate to linear. The species is common in lower temperate Indian Himalayan regions and higher altitudes of Western Ghats between altitudes of 1500-3300 m in the state of Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has lecanoric acid as it major secondary metabolites.

Heterodermia diademata (Taylor) D.D. Awasthi
A foliose lichen found growing on bark of trees or on soil or rocks forming patches upto 15 cm across with upto 5 mm wide lobes, lacking soredia and isidia with numerous apothecia upto 7 mm in diam. The species is widely distributed in subtropical to temperate Indian Himalayan regions and central south and western parts of India between altitudes of 1200-2500 m in the state of Arunachal Pradesh, Assam, Andhra Pradesh, Jammu & Kashmir, Himachal Pradesh, Madhya Pradesh, Maharashtra, Manipur, Meghalaya, Nagaland, Rajasthan, Sikkim, Tamil Nadu-Nilgiri and Palni Hillls, Uttarakhand, West Bengal-Darjeeling Hills. The species has zeorin as its major secondary metabolites together with other triperpins.

Hypogymnia physodes (L.) Nyl.
A foliose lichen found growing on bark of trees or on soil or rocks, thallus with branched lobes up to 4 mm wide lobes grey brown with globose sorelia and lacking lateral perforations. The species is common in lower temperate to alpine regions of Indian Himalayan regions between altitudes of 2200-3500 m in the state of Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Sikkim, Tamil Nadu-Nilgiri Hills, Uttarakhand, West Bengal-Darjeeling Hills. The species has physodic, physodalic and protocetraric acids as its major secondary metabolites.

Hypogymnia vittata (Ach.) Parrique
A foliose lichen mostly found growing on bark of trees with branched lobes upto 4 cm long lobose, sorediate perforated on lower side. The species is common in temperature and alpine India Himalayan regions between altitude of 2500-4000 m in the state of Arunachal Pradesh, Himachal Pradesh, Nagaland, West Bengal-Darjeeling Hills. The species has physodic acid as its major secondary metabolites.

Hypotrachyna adducta (Nyl.) Hale
A foliose lichen moistly found growing on twigs of trees, forming patches up to 4 cm across with soft lobes dense dichotomously branched rhizines. The species is common in subtropical to temperate Indian Himalayan region between altitude of 1500-3600 m in the state of Arunachal Pradesh, Assam, Manipur, Nagaland, Sikkim and West Bengal-Darjeeling Hills. The species has protocetraric acid as its major secondary metabolites.

Hypotrachyna awasthii Hale & Patw.
A foliose lichen found growing on trees bark, forming patches upto 10 cm across, lobes upto 10 mm wide, round, isidiate, presence of dense dichotomously branched rhizines at lower side. The species is common in subtropical to lower temperate Indian Himalayan regions and Western Ghats between altitudes of 1100-2000 m in the State of Arunachal Pradesh, Assam, Kerala, Karnataka, Maharashtra, Manipur, Nagaland, Tamil Nadu-Nilgiri Hills, West Bengal-Darjeeling Hills. The species has norstictic and salazinic acids as its major secondary metabolites.

Hypotrachyna cirrhata (Fr.) Divakar, A. Crespo, Sipman, Elix & Lumbsch
A foliose lichen found growing on bark of trees on soil or some times on stones forming patches of upto 12 cm across with canaliculated lobes of 2-4 mm, dark grey, lacking sorediate and isidia. The species is widely distributes in subtropical and Indian Himalayan region and Western Ghats of India in the state of Arunachal Pradesh, Assam, Himachal Pradesh, Jammu & Kashmir, Karnataka, Manipur, Meghalaya, Nagaland, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has salazinic and protlichesterinic acid as its major secondary metabolites.

Lobaria retigera (Bory) Trevis.
A foliose lichen found growing on bark of trees or on soil rocks along with mosses, forming patches upto 30 cm across or larger with upto 30 mm wide pale brown scrobiculate reticulately ridge lobes with granular to cylindrical simple to coralloid or lobulated isidia on ridge, lower side with tometose rhizinate in grooves. The species is reported from lower temperate to upper temperate regions between altitudes 1600-3500 m in the State of Arunachal Pradesh, Assam, Himachal Pradesh, Manipur, Meghalaya, Nagaland, Sikkim, Tamil Nadu Hills, Uttarakhand, West Bengal-Darjeeling district. The species has triterpenoid and thelephonic acid as its secondary metabolites.

Lobothallina praeradiosa (Nyl.) Hafellner
A crustose, effigurate lichen found growing on exposed rocks forming patches upto 4 cm across with 2-5 mm long, 1-3 mm wide marginal lobes with powdery surface, apothecia 3.0 mm in dia. The species is common in temperate Indian Himalayan regions between altitudes of 1800-3400 m in the State of Himachal Pradesh, Sikkim, Uttarakhand, West Bengal-Darjeeling district. The species has fumarprotocetraric and caperatic acid as its secondary metabolites.

Myelochroa aurulenta (Tuck.) Elix & Hale
A foliose lichen found growing mostly on bark of trees forming patches upto 10 cm across with blue black mimed upto 5 mm wide postulate granular sorediate lobes. The species is known from subtropical to lower temperate to upper temperate regions of Indian Himalayan regions and Western Ghats regions of India between altitudes of 100-3000 m in Arunachal Pradesh, Kerala, Madhya Pradesh, Manipur, Nagaland, Sikkim, Tamil Nadu-Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has secalonic acid zeorin and leucotylin as its secondary metabolites.

Myelochroa subaurulenta (Nyl.) Elix & Hale
A foliose lichen found growing on bark of trees forming patches upto 10 cm across with 4 mm wide esorediate and non-isidiate lobes bearing cilia on the axils. The species is known form lower temperate regions of Indian Himalayan regions and Western Ghats in south India between altitudes 1000-3000 m Kerala, Manipur, Nagaland, Sikkim, Tamil

Nadu-Palni Hills, Uttarakhand, West Bengal-Darjeeling Hills. The species has Secalonic acids, Zeorin, leucotylin acid, terpenes as its secondary metabolites.

Nephroma helveticum Ach.
A foliose lichen found growing on bark of trees, soil or along with mosses, forming patches of upto 8 cm across with upto 10 mm wide, suborbiculate isidiate lobes. Apothecia on the lower side with dentate margin and nephoromoid. The species is known from Indian Himalayan regions and higher altitudes of Western Ghats in south India between altitudes of 1500-3600 m in Arunachal Pradesh, Himachal Pradesh, Manipur, Nagaland, Sikkim, Tamil Nadu-Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has Nephrin and some unknown substances as its secondary metabolites.

Nephromopsis laii (Thell & Randl.) Saag & Thell
A foliose lichen found growing on bark of trees, forming patches of upto 12 cm across with convolute, rounded greenish yellow lobes, bearing plug-like outgrowth of pseudocyphellae. Apothecia marginal on lobes, rounded to reniform. The species is known from Indian Himalayan regions between altitudes of 2500-3500 m in Arunachal Pradesh, Nagaland, Sikkim, Uttarakahand, West Bengal-Darjeeling district. The species has usnic, lichesterinic and proto lichensterinic acids as its secondary metabolites.

Nephromopsis nephromoides (Nyl.) Ahti & Randl.
A foliose lichen found growing on bark of trees, forming patches upto 20 cm across with coriaceous rounded, inovoluted 2-4 cm wide lobes, lower side with lacunose rugose, depressed pseudocyphellae. Apothecia marginal on lower side, nephromoid. The species is known from temperate to alpine regions of Indian Himalayan regions between altitudes of 2500-3600 m in Arunachal Pradesh, Himachal Pradesh, Uttarakhand, West Bengal-Darjeeling district. The species has usnic, lichesterinic, protolichesterinic and caperatic acid together with some pigments as secondary metabolites.

Nephromopsis pallescens (Schaer.) Park
A foliose lichen found growing on bark trees forming patches upto 16 cm across with convolute upto 20 mm wide greenish yellow scrobiculate-rugose lobes, lower side with pseudocyphellae on laminllae and plug like outgrowths. Apotheica laminal to submarginal. The species is known from temperate Indian Himalayan regions between altitudes of 2400-3500 m in Arunachal Pradesh, Sikkim, Nagaland, Manipur, Uttarakhand, West Bengal-Darjeeling district. The species has usnic, lichensterinic, protolichesterinic, alectoronic and alpha collatolic acid as its secondary metabolites.

Nephromopsis stracheyi (C. Bab.) Müll. Arg.
A foliose lichen found growing on trees bark, forming patches upto 15-20 cm across with convoluted upto 4 cm wide, yellow grey scrobiculate lacunose lobes, lower side with nemoerous regose, pseudocyphellae at level. Apothecial marginal on lower side reniform. The species is known from temperate Indian Himalayan regions between altitudes of 2100-3500 m in Arunachal Pradesh, Manipur, Nagaland, Sikkim, Uttarakhand, West Bengal-Darjeeling district. The species has usnic, anzianic, lichesterinic and protolichestrinic acid as its secondary metabolites.

Pannaria complanata P.M. Jørg.
Thallus subfoliose to foliose growing over bark of trees, closely adnate, orbicular lobed lobes upto 2 cm wide, upper side brownish. Apothecia upto 2 mm in diam. The species are known from lower temperate regions between altitudes of 1800-3000 m in Tamil Nadu-Nilgiri and Palni Hills. The species has pannarin as its secondary metabolites.

Parmelia adaugescens Nyl.
A foliose lichen found growing on decaying wood or bark of trees forming patches upto 10 cm across with 3-5 mm wide densely maculate lobes lacking soredia and isidia. Apothecia substipitate. The species is known from temperate Indian Himalayan regions between altitudes of 3000-3600 m in Arunachal Pradesh, Manipur, Nagaland, Sikkim. The species has salazinic and consalzinic acids as its major secondary metabolites.

Parmelia saxatilis (L.) Ach.
A foliose lichen mostly growing on rocks forming patches upto 6 cm across with sublinear dentate grey brownish maculate lobes the maculae turned into effigurate pseudocyphellae and becoming isidiate. The species is known from upper temperate Indian Himalayan regions between altitudes of 3000-3500 m in Arunachal Pradesh, Jammu & Kashmir, Sikkim, Uttarakhand. The salazinic, lobaric acids are the major secondary metabolites present in the species.

Parmelia squarrosa Hale
A foliose lichen mostly growing on bark of trees and rarely on rock forming patches upto 11 cm across, lobes sub linear upto 5 mm wide, upper side pale to mineral grey with angular pseudocyphellae forming reticulate network and cylindrical isidia, branched rhizines. Apothecia 2 mm in diam. The species is known from temperate regions between altitudes of 3000-3800 m from Sikkim. The species has Salazinic, consalalzinic and fatty acid as its secondary metabolites.

Parmelinella wallichiana (Taylor) Elix & Hale
A foliose lichen found growing on bark of trees, soil or some time on rock, forming patches upto 20 cm across with upto 10 mm wide, rounded lobes isidate on axils bear simple to branched isida. Apotrhecia upto 15 mm in diam. The species is commonly known from tropical to temprate Indian Himalayan regions and higher altitudes in Western Ghats and other central Indian regions between altitudes of 500-3000 m in Arunachal Pradesh, Karnataka, Madhya Pradesh, Manipur, Meghalaya, Nagaland, Sikkim, Tamil Nadu, Uttarakhand, West Bengal-Darjeeling district. The species has atranorin, salazinic, consalazinic acids as its major secondary metabolites.

Parmotrema andinum (Müll.) Arg.
A foliose lichen found growing on bark of trees, forming patches upto 15 m across with upto 20 mm wide, eciliate, maculate lobes, lacking isidia and soredia. Apothecia upto 20 mm in diam. The species is known from tropical to lower temperate region between altitudes of 500-2100 m in Andhra Pradesh, Jharkhand, Himachal Pradesh, Karnataka, Madhya Pradesh, Odisha, Tamil Nadu-Palni Hills, Uttarakhand. The species has lecanoric and orsellinic acid as its secondary metabolites.

Parmotrema austrosinense (Zahlbr.) Hale
A foliose lichen found growing on tree of bark, or sometimes on rocks forming patches upto 10 cm across with rounded eciliate faintly maculate soredaite lobes. Apothecia upto 5 mm in diam. The species is commonly known from tropical to lower temperate regions of central India between altitudes of 750-3000 m in Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Karnataka, Kerala, Maharashtra, Manipur, Meghalaya, Nagaland, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand. The species has lecanoric acid as its major secondary metabolites.

Parmotrema cooperi (J. Steiner & Zahlbr.) Sërus.
A foliose lichen found growing on bark of trees and forming patches upto 15 cm across, 80 mm wide lobes, convolute, ciliate upper side grey to grey green, white maculate, sorelia marginal, soredia granular, lower side centrally black. The species found to growing in lower temperate regions between altitudes of 1500-2100 m from Kerala, Tamil Nadu. The species has lecanoric acid as secondary metabolites.

Parmotream hababianum (Gyeln.) Hale
A foliose lichen found growing on bark of trees and forming patches of upto 10 cm across with upto 15 mm die lobes, lobes crenate, ciliate, upper side grey to brownish grey, white maculate, sorelia marginal, sorediate lobes revolute, lower side centrally brown black. Apothecia not known. The species is known from tropical to lower temperate regions between altitudes of 800-2300 m from Himachal Pradesh, Kerala, Manipur, Nagaland, Tamil Nadu-Palni Hills, Uttarakhand, West Bengal-Darjeeling district.

Parmotream nilgherrense (Nyl.) Hale
A foliose lichen found growing on bark of trees on soil or rocks, forming patches of upto 15 cm across with convolute ciliate, maculate upto 30 mm wide lobes, lacking soredia and isidia. Apothecia upto 20 mm diameter and perforated. The species is widely distributes in temperate Indian Himalayan regions and higher altitudes of Western Ghats in south India between altitudes of 1500-4500 m in Arunachal Pradesh, Assam, Jammu & Kashmir, Himachal Pradesh, Kerala, Manipur, Meghalaya, Nagaland, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand. The species has alecctoronic and $\acute{\alpha}$-collatolic acid as its secondary metabolites.

Parmotrema praesorediosum (Nyl.) Hale
A foliose lichen growing on bark of trees or rock, forming patches of upto 10 cm, adnate, lobes upto 5-8 mm wide, upper side grey to darker, emaculate, sorelia usually marginal, soredia granular, lower side centrally black. Apothecia upto 4 mm in diam. The species widely distributed from tropical to lower temperate regions between altitude of 300-1750 m from Andhra Pradesh, Arunachal Pradesh, Assam, Himachal Pradesh, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Manipur, Nagaland, Orissa, Rajasthan, Tamil Nadu. The species has protopraesorediosic and praesorediosic acids as secondary metabolites.

Parmotrema pseudonilgherrense (Ashina) Hale
A foliose lichen growing on bark of trees, some time on soil and forming patch upto 10 cm across, lobes upto 10-15 mm wide, dentate at centre, marginally ciliate, upper side grey to darker in the central, densely white maculate, sorelia on apices of dent in central part. Soredia granular, white on lobes. Apothecia rare upto 2-5 mm in diam., the species are widely distributed in temperate regions between altitude of 1666-3500 m from Himachal Pradesh, Karnataka, Maharashtra, Manipur, Sikkim, Tamil Nadu and Uttarakhand. The species has alectoronic, $\acute{\alpha}$-collatolic acid as its secondary metabolites.

Parmotrema pseudoreticulatum (C. Tav.) Hale
A foliose lichen growing only on bark of trees and forming thallus upto 20 cm across with upto 5-15 mm wide lobes, lobe sciliate, upper side grey, densely white maculate, sorelia marginal to linear, maculae reticulately fissured. Apothecia not seen. The species is reported from Andaman Island, Jammu & Kashmir, Tamil Nadu Hills between altitudes of 500-1500 m. The species has its salazinic acid and consalazinic acid as its secondary metabolites.

Parmotream pseudotinctorum (Abbayes) Hale
A foliose lichen found growing on rock and rarely on bark and twigs forming upto 6 vm across, bears lobes upto 2-6 mm wide, eciliate, upper side grey, isidiate, isidia thick, irregularly inflated branched, lower side centrally black. Apothecia not seen. The species reported between altitudes of 1600-1900 m from Uttarakhand. The species has lecanoric acid as its secondary metabolites.

Parmotrema reticulatum (Taylor) Choisy
A foliose lichen found growing on bark of trees, rock, or soil, forming patches upto 20 cm across, with upto 15 mm wide, ciliate densely maculate reticulately fissured sorediate lobes, lacinules of palmate lobes, sorediate at tips. Apothecia rare. One of the most widely distributed lichen species in India reported from subtropical to temperate regions between altitudes of 1500-2500 m in Arunachal Pradesh, Assam, Chhattisgarh, Himachal Pradesh,

Meghalaya, Sikkim, Maharashtra, Odisha, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has salazinic and consalizinc acids as its major secondary metabolites.

Parmotrema saccatilobum (Taylor) Hale
A foliose lichen growing over bark of trees, and forming upto 10 cm across patch with 4-10 mm wide lobes, eciliate, upper side grey, emaculate, cracked at centre, isidiate, isidia granular to filliform, simple, lower side centrally black. Apothecia not seen. The species widely growing in tropical to subtropical regions between altitudes of 500-2500 m from Andaman Island, Assam, Goa, Nagaland, Uttarakhand, West Bengal-Kolkata and Darjeeling. The species has protocetraric acid as its secondary metabolites.

Parmotrema sancti-angelii (Lynge) Hale
A foliose lichen found growing over bark and some time on rock, forming patch upto 15-20 cm across with upto 8-15 mm wide lobes, ciliate, upper side grey to dark emaculate cracked in older parts, sorelia marginal to submarginal, soredia farinose or brown, lower side centrally black. Apothecia not seen. The species found growing between tropical to lower temperate region between altitudes of 300-2300 m of Assam, Kerala, Maharashtra, Manipur, Madhya Pradesh, Meghalaya, Nagaland, Rajasthan, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling Hills. The species has gyrophoric and lecanoric acid as its secondary metabolites.

Parmotrema subsumptum (Nyl.) Hale
A foliose lichen growing on trees upto 15 cm across, with 10 mm wide lobes upper surface maculate, sorediate along margin. The species is commonly distributes in subtropical to lower temperate regions of Indian between altitudes of 1500-2250 m in Manipur, Meghalaya.

Parmotrema subtinctorium (Zahlbr.) Hale
A foliose lichen, growing on bark, soil or rock upto 10 cm across, lobes 20 mm wide with maculate upper side cracked in older parts, filiform isidiate marginally. The species is common in tropical to lower temperate region between altitude of 450-2500 m in different localities of Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Manipur, Nagaland, Tamil Nadu-Nilgiri and Palni Hills, Uttarakahand, West Bengal-Darjeeling district. The species has salazinic acid as its major secondary metabolites with norlobarinic and Ioxodin.

Parmotrema thomsonii (Stirt.) A. Crespo, Divakar & Elix
A foliose lichen found growing on bark of trees, forming patches upto 12 cm across with 15 mm wide dentate, marginally ciliate esorediate non isidaiate lobes, lower side centrally black with rhizines marginal zone brown nude without rhizines. Apothecia upto 15 mm in diameter perforated. The species is known from temperate Indian Himalayan regions between altitudes of 1800-3600 m in Arunachal Pradesh, Himachal Pradesh, Jammu & Kashmir, Nagaland, Sikkim, Uttarakhand, West Bengal-Darjeeling district. The species has atranorin, alectoronic and ά-collaltotic acids as its secondary metabolites.

Parmotrema tinctorum (Despr. ex Nyl.) Hale
A foliose lichen found growing on tree bark, rock, forming patches upto 20 cm across with upto 30 mm wide eciliate, isidaite lobes, isidia simple to coralloid. Apothecia rare upto 10 mm in diam., imperforate. The species is known from tropical to lower temperate Indian Himalayan regions and other parts of the country between altitudes of 400-2500 m in Andhra Pradesh, Arunachal Pradesh, Assam, Chhattisgarh, Himachal Pradesh, Jammu & Kashmir, Jharkhand, Karnataka, Kerala, Madhya Pradesh, Manipur, Meghalaya, Nagaland, Odisha, Rajasthan, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has lecanoric acid and orselinic acid as its secondary metabolites.

Peltigera pindarensis D.D. Awasthi & M. Joshi
A foliose lichen growing on rock, soil and some time on mosses, forming patches upto 6 cm across, lobes upto 5-17 mm wide, margins crisp, upper side pale brown to brown tometose lacking isidia and soredia, rhizines simple. Apothecia horizontal rounded upto 2-7 mm in diam. The species reported from temperate to alpine regions of Indian Himalayan regions between altitudes of 250-3000 m, from Arunachal Pradesh, Himachal Pradesh and Uttarakhand. The species has no secondary metabolites.

Peltigera polydactylon (Neck.) Hoffm.
A foliose lichen growing on soil, rock, or along with mosses forming patches upto 15 cm across, with 10-15 mm wide, 4-5 cm long, greyish brown etometose lobes lacking isidia and soredia, lower side reticulate brown black veined. Apothecia centrally saddle shaped upto 7 mm in diam. The species is known from temperate Indian Himalayan regions between altitudes of 2000-3500 m, from Arunachal Pradesh, Assam, Jammu & Kashmir, Manipur, Meghalaya, Sikkim, Uttarakhand, West Bengal-Darjeeling district. The species has gyrophoric acid, Tenuiorin, dolichorrizin as its secondary metabolites.

Peltigera praetextata (Flörke) Zopf.
A foliose lichen growing over soil, mosses, rock and bark, forming patches upto 16 cm across and about 5 cm long lobes and 7-20 mm wide, upper side greyish brown to brown, tometose, becoming smooth towards centre, lower side reticulate, brown black veined in central part and pale brown veined in marginal area; rhizines simple, photobiont a Nostoc. Apothecia upto 10 mm in diam. The species found growing in temperate regions between altitudes of 1950-3600 m from Himachal Pradesh, Jammu & Kashmir, Nagaland and Uttarakhand. There are no secondary metabolites found.

Peltigera rufescens (Weiss) Humb.
A foliose lichen found growing on soil, rock, bark and forming patches upto 8 cm, lobes 5-10 mm wide, margin crisp reflexed or deflexed, often lobulated, upper side brown to dark brown, tometose, lacking isidia and soredia; lower side reticulate, elevated, dark veined, rhizines squarrosely branched long, photobiont a nostoc. Apothecia vertical, saddle shaped upto 3-6 mm in diam. The species reported from upper temperate regions of the Himachal Pradesh, Jammu & Kashmir, Nagaland, Uttarakhand, West Bengal-Darjeeling. There is no secondary metabolite found.

Physcia dilatata Nyl.
A foliose lichen found growing over bark and some time on rock, forming patches between 5-10 cm across; it's a narrow lobed lichens lobes upto 10 mm wide; upper side whitish grey to pruinose, lacking isidia and soredia, lower side grey to darker, lower cortex parapectenchymatous. Apothecia upto 1.5 mm in diam. Species reported from subtropical to lower temperate regions of Manipur, Uttarakhand. The species has zeorin as secondary metabolites.

Platismatia erosa W.L. Culb.& C.F. Culb.
A foliose lichen found growing on bark and forming patches upto 12 cm across, lobes 5-20 mm wide; upper side grey, marginal area brownish, reticulately ridged and veined, isidiate minutely pseudocyphellate, isidia simple to coralloid, lower side jet black. Apothecia rare. The species reported from Sikkim, West Bengal-Darjeeling district. The species has atranorin and caperatic acid as its secondary metabolites.

Pseudocyphellaria aurata (Sm. ex Ach.) Vain.
A foliose lichen found growing over bark, and forming patches upto 8 cm across, lobes 2-10 mm wide, upper side reddish brown, sorediate, sorelia on underside of upturned margins of lobes, linear yellow lower side ochraceous brown, with yellow pesudocyhpellae, photobiont a green alga. Apothecia absent. The species reported from subtropical to lower temperate regions between altitudes of 1300-2300 m, from Arunachal Pradesh, Manipur,

Nagaland, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand. The species has triterpenoids as its secondary metabolites.

Pseudocyphellaria crocata (L.) Vain.
A foliose lichen found growing on bark of trees and some time on soil and mosses, forming patches upto 8 cm across, lobes upto 10 mm wide, upper side brownish, foveolate, sorelia, marginal linear, yellow side brownish, pseudocyphellae yellow, photobiont nostoc. Apothecia absent. The species reported from lower temperate regions of Arunachal Pradesh, Nagaland, Tamil Nadu-Nilgiri Hills, Uttarakhand. The species has Triterpenoids, tenuiorin, gyrophoric and methylgyrophorate acid as its secondary metabolites.

Punctelia rudecta (Ach.) Krog.
A bigger lobes foliose lichen, found growing over bark of trees, rock upto 8-10 cm across, crisp and fragile lobes between 3-6 mm wide, upper side grey to dark, psudocyphellae punctiform to elongate, isidia simple, coralloid and lacinulate, lower side pale brown. Apothecia rare, upto 5 mm in diam. The species reported from subtropical to temperate regions between altitudes of 1500-3200 m, from Himachal Pradesh, Jammu & Kashmir, Kerala, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand. The species has lecanoric acid as secondary metabolites.

Pyxine cocoes (Sw.) Nyl.
A foliose lichen found growing over bark of trees and forming patches upto 6 cm across, lobes 0.5-2 mm wide, upper side yellowish grey, maculate laminal to marginal turning into pseudocyphellae and then into sorelia. Apothecia upto 1 mm in diam. The species reported from subtropical to lower temperate regions between altitudes of 1000-3000 m, from Kerala, Maharashtra, Manipur, Odisha, Tamil Nadu-Chennai and Palni Hills, Uttar Pradesh, Uttarakhand, West Bengal-Kolkata. The species has lichenoxanthones and triterpens as its secondary metabolites.

Pyxine subcinerea Stirt.
A foliose lichen found growing over bark and twigs of trees and forming patches upto 7 cm across, lobes 1-2 mm wide; upper side greyish margins intermittently pseudocyphellate; pseudocyphellae developing into sorelia and spreading on to lamina, soredia white. Apothecia 1-2 mm in diam. The species reported from subtropical regions between altitudes of 450-1500 m from Uttarakhand, West Bengal-Darjeeling Hills. The species has lichenoxanthone and triterpenes as its secondary metabolites.

Ramalina conduplicans Vain.
A fruticose, erect to pendulosus lichen found growing on bark and twigs of trees or sometimes on rocks with upto 10 cm long, grey to yellowish brown branches upto 7 mm wide, raised pseudocyphellate on margin of branches. Apothecia upto 7 mm in diam. The species is widely distributed in tropical to lower temperate regions on Indian Himalayan regions between altitudes of 2500 m Andaman Island, Arunachal Pradesh, Assam, Andhra Pradesh, Himachal Pradesh, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Manipur, Meghalaya, Nagaland, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand, West Bengal-Darjeeling district. The species has usnic, slazinic, sekikaic acid as its secondary metabolites.

Ramalina himalayensis Räsänen
A fruticose lichen erect to pendulous lichen found growing on rock upto 3 cm across patches, yellowish brown, branched, branches upto 1.5 cm tall, and upto 2 mm in diam, sub cylindrical, sparsely pseudocyphellate at apices of secondary digitiform branches, lacking isidia and soredia. Apothecia upto 3 mm in diam. The species reported from upper temperate regions between altitudes of 3200-3500 m, from Uttarakhand, West Bengal-Darjeeling Hills. The species has evernic acid as its secondary metabolites.

Ramalina hossei Vain.

A fruticose erect to pendulous lichen found growing over bark and twigs of trees, about 6 cm tall, yellowish grey to brownish branched, branches upto 2 mm wide, nervosa, marginal pseudocyphellae turning into sorelia, soredia granular. Apothecia upto 1 mm in diam. The species reported from subtropical to lower temperate regions between 1200-2500 m altitudes from Meghalaya, Uttarakhand, West Bengal-Darjeeling. The species has usnic and sekikaic acid as its secondary metabolites.

Ramalina nervulosa (Müll. Arg.) Abbayes

A fruticose erect to pendulous lichen found growing over bark twigs and about 05-20 cm long, yellowish grey, branched, branches flattened upto 4 mm wide angular or terete towards apices, pseudocyphellae in longitudinal striae causing nervosa appearance; sorelia marginal. Apothecia upto 2.5 mm in diam. The species reported from Karnataka, Kerala, Tamil Nadu-Nilgiri Hills. The species has usnic and sekikaic acid as its secondary metabolites.

Rhizoplaca chrysoleuca (Sm.) Zopf.

A foliose umbilicate lichen found growing mainly on rock, thallus monophyllous to polyphyllous upto 3 cm across, lower side brown at centre, bluish black in outer part. Apothecia upto 5 mm in diam. The species reported from upper temperate to alpine regions of Indian Himalaya from Himachal Pradesh and Uttarakhand. The species has placodialic acid as its secondary metabolites.

Roccella montagnei Bel em. D.D. Awasthi

A fruticose lichen found growing over bark and twigs of trees and rarely on rock, thallus erect to pendulous upto 25 cm long, profusely branches, branches irregularly widened 5-10 mm at base or in middle part tapering, greenish grey with marginal to laminal orbicular sorelia. Apothecia not known. The species luxuriantly goring near coastal area of India like Gujarat, Karnataka, Kerala, Odisha, Pondicherry, Tamil Nadu. The species has Erythrin acid as its secondary metabolites.

Rusavskia elegans (Link) S. Y. Kondr. & Kärnefelt

A foliose lichen found growing over rock and forming patches upto 7 cm, suborbicular, lobes radiating, compact 0.25-1 mm wide, convex, nodulose with densely crowded. Apothecia upto 1 mm in diam. The species is reported from temperate to alpine regions of Indian Himalayan area between altitudes of 3000-6000 m from Himachal Pradesh, Jammu & Kashmir and Uttarakhand. The species has parietin as its secondary metabolites.

Stereocaulon foliolosum Nyl.

A dimorphic lichen found growing over rock, rarely on soil, upto 4 cm tall, sparingly branched, decorticated, subglabrous, brownish, phyllocladia flattened, leafy 1.5-2.5 mm long. Cephalodia 1-2 mm in diam, brown cell lumina enclosing nostoc. Apothecia terminal upto 2 mm in diam. The species is reported temperate regions of Indian Himalayan regions between 2000-4000 m altitudes of Sikkim, Uttarakhand. The species has atranorin and lobaric acid as its secondary metabolites.

Stereocaulon massartianum Hue

A dimorphic lichen found growing over rock, upto 7.5 cm tall, 1 mm thick at base, sparingly branched, decorticate yellow to brownish; phyllocladia cylindrical upto 2-5 mm long, dense at base, sparse above. Cephalodia upto 2.5 mm in diam., brownish, sacculate, enclosing Sytonema or Stigonema. Apothecia terminal on short lateral branches upto 1 mm in diam. The species found growing in temperate regions of Indian Himalayan area between altitudes of 2500-3550 m Arunachal Pradesh, Sikkim, West Bengal-Darjeeling district. The species has atranorin and stictic acid as its secondary metabolites.

Stereocaulon piluliferum Th. Fr.
A dimorphic lichen, primary thallus found growing over rock, rarely on soil upto 6 cm tall, 0.5-0.8 mm thick at base, simple or sparingly branched in apical regions, brownish corticated. Phyllocladia cylindrical simple to branched upto 5 mm long, more dense on one side. Cephalodia 0.5-1.0 mm in diam., brownish enclosing Nostoc. Apothecia terminal arising on pyriform clavulae, 2-3 mm in diam. The species reported from temperate area of Indian Himalayan regions between 1800-3900 m altitudes of Arunachal Pradesh, Assam, Meghalaya, Sikkim, Uttarakhand and West Bengal-Darjeeling district. The species has atranorin, sticitc, norstictic acid as its secondary metabolites.

Sticta nylanderiana Zahlbr.
Thallus foliose found growing over bark, rarely on soil and rock, patches upto 14 cm across, lobes 3-30 mm wide, upper side pale grey to darker, lacking isidia and soredia, lower side pale brown to brown cyphellate, cyphellae initially minute, later 0.4-2.00 mm in diam., endotropic cephalodia with nostoc. Apothecia 2-8 mm in diam. The species reported from temperate regions between altitudes of 1800-3600 m from Manipur, Sikkim and Uttarakhand. The species has atranorin and gyrophoric acid as its secondary metabolites.

Sticta praetextata (Räsänen) D.D. Awasthi
A foliose lichen found growing over bark of trees, and forming patches upto 12 cm across, lobes 7-30 mm wide, margins repeatedly incised lacinulate to squamiform-isidiose; upper side grey to brown, lacking isidia and soredia; lower side brownish, cyphellae upto 2 mm wide. Apothecia not known. The species reported from temperate regions between altitudes of 2400-3500 m from Arunachal Pradesh, Himachal Pradesh and Uttarakhand. The species has atranorin and gyrophoric acid as its secondary metabolites.

Sticta weigelii (Ach.) Vain.
A foliose lichen found growing over bark of trees sometimes found over rock, soil and forming patches upto 12 cm across, lobes rounded 10-15 mm wide, incised, margins notched or torn, densely isidiate, upper side grey to chestnut brown, isidiate in submarginal and long cracks in lamina; isidia granular to cylindrical; lower side brown to black, cyphellae 0.5-3.0 mm wide. Apothecia upto 4 mm in diam. The species reported from subtropical to lower temperate regions between altitudes of 800-2250 m from Arunachal Pradesh, Assam, Kerala, Manipur, Meghalaya, Nagaland, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand. There is no secondary metabolite reported in this species.

Sulcaria sulcata (Lev) Byste. ex Brodo & D. Hawksw.
A fruticose lichen found growing over bark and twigs of trees, attached by a basal disc, erect to pendent upto 12 cm long, 03 mm thick at base, branched cylindrical, tapering pale brown to brown-black with slit like or widened scalariform pseudocyphellae. Apothecia upto 8 mm in diam. The species widely growing in temperate area of Himalaya between 2700-4200 m altitudes of Arunachal Pradesh, Sikkim, Uttarakhand and West Bengal-Darjeeling district. The species has psoromic acid as its secondary metabolites.

Sulcaria virens (Taylor) Byste. ex Brodo & D. Hawksw.
A fruticose lichen found growing over bark and twigs of trees, pendulous upto 40 cm long, branched, branches flattened, ribbon like, upto 2 mm wide, becoming cylindrical in apical region surface greyish yellow to deep yellow, upper side with scalariform pseudocyphellae. Apothecia not known. The species ground growing in temperate regions of Himalaya between altitudes of 2400-3900 m in Arunachal Pradesh, Sikkim and Uttarakhand. The species has vulpinic, virensic and pulvinic acid as its secondary metabolites.

Teloschistes flavicans (Sw.) Norm.
A fruticose lichen found growing over bark, twigs of trees rarely on soil, erect to pendent, irregularly branched, forming entangled clumps; branches teret upto 0.5 mm thick, surface yellow to orange red smooth to scabrid; sorelia

orbicular to elongate, soredia white, granular fibrils black tipped scattered. Apothecia not known. The species found growing in Karnataka, Kerala, Tamil Nadu-Nilgiri and Palni Hills and Uttarakhand.

Thamnolia vermicularis (Sw.) Schaer.
A fruticose podetioid lichen growing over soil, and mosses, attached basally cylindrical upto 5 cm tall, 2 mm thick at base, tapering, centrally hollow, surface milky white to greyish smooth. The species reported from temperate alpine area of Indian Himalayan regions of Arunachal Pradesh, Sikkim and Uttarakhand. The species has Thamnolic and decarboxythamnolic acid as its secondary metabolites.

Umbilicaria indica Frey
A foliose to umbilicate lichen found growing over rock, polyphyllous, thallus 3-9 cm across, margins incised, often ciliate, weakly to strongly undulating and wrinkled, upper side grey to brownish, smooth to tumid often with holes with protruding rhizomorphs; lower side brown-black smooth, rhizinomorphs cylindrical, simple or irregularly branched. Apothecia upto 2 mm in diam, gyrose. The species reported from temperate to alpine regions of Indian Himalayan regions between altitudes of 1800-5050 m from Sikkim, Uttarakhand and West Bengal-Darjeeling Hills. The species has gyrophoric acid as its secondary metabolites.

Umbilicaria virginis Schaer.
A foliose to umbilicate lichen found growing over rock, monophyllous, upto 10 cm across, orbicular, upper side buff to yellowish brown, irregularly wrinkled, finely granulose, white pruinose, with necral layer, lower side ochraceous or pink red; rhizomorph cylindrical or flat, simple or branched, brownish. Apothecia numerous upto 4.5 mm in diam., omphalodiscus. The species reported from temperate to alpine regions between altitudes of 3700-4000 m in Himachal Pradesh, Jammu & Kashmir, Uttarakhand and Sikkim. The species has gyrophoric acid as its secondary metabolite.

Usnea aciculifera Vain.
A fruticose pendulous lichen found growing over twigs and bark of trees, thread like tahllus upto 13 cm long, brown to yellow brown to blackish brown, dichotomous to sybsympodial branching, 0.25-0.75 mm in diam., tapering, surface annularly cracked, smooth to verrucose-isidiate. Apothecia absent. The species found growing in subtropical to temperate regions between altitudes of 1200-2250 m from Arunachal Pradesh, Assam, Nagaland, Sikkim and Uttarakhand. The species has stictic and constictic acids as its secondary metabolites.

Usnea baileyi (Stirt.) Zahlbr.
A fruticose sub erect to pendulous lichen found growing on bark, twigs of trees and some time on rock, branched upto 25 cm long greenish grey to brown, dichotomously to subsympodially branched; main branches 1.5-2.0 mm in diam., tapering transversely cracked at intervals, pseudocyphellate andisidaite; isidia dense on contex. Apothecia rare upto 5 mm in diam. The species widely found growing in lower temperate regions between altitudes of 1300-2600 m from Arunachal Pradesh, Assam, Kerala, Manipur, Meghalaya, Nagaland, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand. The species has Norstictic and salazinic acids as its secondary metabolites.

Usnea complanata (Müll. Arg.) Mont.
A fruticose lichen found growing on bark and twigs of trees, thallus bushy upto 8 cm tall, yellowish brown to grey brown; branching subdichotomous to sympodiual; several branches arising from near base; main branches upto 2 mm in diam., lateral spinules and branches dense upwards, surface sparsely annularly cracked; papillae, pseudocyphellae, isidia and soredia absent; central axis solid. Apothecia are terminal. The species found growing over on lower temperate regions between 1800-2100 m altitudes from Tamil Nadu-Nilgiri and Palni Hills. The species has galbinic, norstictic and salazinic and stictic acid complexes as its secondary metabolites.

Usnea ghattensis G. Awasthi

A fruticose lichen found growing over twigs of trees, thallus erect, bushy, upto 6 cm tall, light to dark brown; branching sympodial; several main branches arising from near the base; main branches stiff upto 3 mm in diam., lateral branches dense, stiff, blackish at apices; surface sparsely palilliate; pesudocyphellae; isidia and soredia absent. Apothecia terminal upto 8 mm in diam., margin ciliate. The species reported from Karnataka and Maharashtra only. The species has usnic acid as its secondary metabolites.

Usnea himalayana Bab.

A fruticose lichen found growing over twigs of trees, thallus pendulous upto 25 cm long, longer in nature, pale grey, greyish green, yellow brown to dark brown in herbarium, branching dichotomous throughout; branches articulate, inflated upto 3 mm in diam., in between articulations, branches attenuate; surface annularly sparsely cracked, pseudocyphellae orbicular, linear, elongate, white; isidia and soredia absent; central axis solid. Apothecia rare, terminal upto 3 mm in diam. The species found growing mainly on temperate regions between altitudes of 1800-3300 m from Arunachal Pradesh, Himachal Pradesh, Manipur, Nagaland, Sikkim, Tamil Nadu-Nilgiri and Palni Hills, Uttarakhand and West Bengal-Darjeeling district. The species has Norstictic, salazinic, stictic acids as its secondary metabolites.

Usnea longissima Ach.

A fruticose lichen found growing over twigs and bark of trees, thallus pendulous, filamentous, branches upto 60 cm long to several meters, pale yellow, greyish green to light brownish; 0.5-1.0 mm in diam., laternal branches dense, perpendicular, 2-5 cm long, cracked near base with soredia and isidia; central axis solid. Apothecia rare upto 5 mm in diam., margin ciliate. The species reported from temperate regions of Himalaya between altitudes of 2100-3600 m from Arunachal Pradesh, Assam, Himachal Pradesh, Sikkim, Uttarakhand and West Bengal-Darjeeling district. The species has barbatic, squamatic, diffracrtic, evernic and fumerprotecetraric acids as its secondary metabolites.

Usnea perplexans Stirt.

A fruticose lichen found growing over bark and twigs of trees, thallus shrubby 8-10 cm tall, greenish grey to yellowish grey, sympodially branched; primary branches upto 2 mm in diam., subsequent and lateral branches dense, giving thallus a bushy appearance, surface of branches papillate, sorediate, isidia absent; central axis solid. Apothecia not known. The species reported from lower temperate regions of Himalaya between altitudes of 2100-2700 m from Himachal Pradesh, Jammu & Kashmir and Uttarakhand. The species has salazinic acid as its secondary metabolites.

Usnea subfloridana Stirt.

A fruticose lichen found growing over bark, twigs and rarely soil; thallus 3-9 cm tall basally black, upwards brownish; branching dichotomous to sympodial branches, branches lax to dense, major branches upto 1.5 mm in diam., lateral branches dense, surface of branches minutely papillate, branches soridate and isdiate; sorelia excavate; soredia granular; isidia developing on soralia as well as directly on cortex; central axis solid. Apothecia not known. The species is reported from temperate regions of Himalaya between altitudes of 2200-3700 m from Himachal Pradesh, Jammu & Kashmir Kerala and Uttarakhand. The species has norstictic, salazinic, squamatic and thamnolic acids as its secondary metabolites.

Xanthoparmelia stenophylla (Ach.) Ahti & D. Hawksw.

A foliose lichen found growing over rock forming patches upto 18 cm across, usually pulvinate, in dense mats; lobes sub linear, 1.5-5.0 mm wide, brownish at apices; secondary lobules developing at centre, often erhizinate; upper side yellow green lacking isidia and sredia, lower side brownish, rhizinate. Apothecia rare 3-9 mm in diam. The species reported from upper temperate regions between altitudes of 2100-4500 m from Himachal Pradesh, Jammu & Kashmir and Uttarakhand. The species has salazinic and consalazinic acid as its secondary metabolites.

Xanthoparmelia terricola Hale, Nash & Elix
A foliose lichen found growing over soil and forming patches upto 5 cm across; lobes upto 2 mm wide; black rimmed; upper surface yellowish green, lacking isidia and soredia; lower side brown. Apothecia are not known. The species is reported from upper temperate to alpine regions between altitudes of 3900-4500 m from Uttarakhand. The species has salazinic, consalazinic and norstictic acid as its secondary metabolites.

Xanthoria perietina (L.) Th. Fries
A foliose lichen found growing on bark trees and rarely on rock, forming patches upto 5 cm across in rosettes pattern; lobes upto 3 mm wide, ascending and flabellate at apices; upper side orange-yellow or darker orange, lacking isidia and soredia; lower side pale grey. Apothecia crowded, 1.5-3 mm in diam. The species reported from lower temperate regions of Indian Himalayan area between altitudes of 1650-3000 m from Jammu & Kashmir. The species has parietin as its secondary metabolites.

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Table 1. Silver nanoparticles from higher plants

Serial no.	Targeted taxa	References
1.	*Lippa citriodora, Helianthus annus, Camellia sinensis, Aloe vera, Acalypha indica*	Krishnaraj*et al.* [19]
2.	*Morenda citrifolia*	Suman *et al.* [20]
3.	*Parthenium* leaf extract	Parashar *et al.* [21]
4.	Plant extract used for biosynthesis of silver nanoparticle	Gilaki [22]
5.	Widely available Indian plants leaf extract	Banerjee *et al.* [23]
6.	*Raphanus sativus*	Tamilashwari *et al.* [24]
7.	Waste vegetable peel	Sharma *et al.* [25]
8.	*Catharanthus roseus*	Panneerselvam *et al.* [26]
9.	*Ficus amplisima, lippia nodiflora, cycas circinalis* leaf extract	Johnson and Prabhu[27]
10.	Papaya fruit extract	Jain *et al.* [28]
11.	*Lippia citriodera*	Cruz *et al.* [29]
12.	*Terminalia chebula* fruit extract	Edison and Sethuraman [30]
13.	*Achyranthus aspera*	Bobbu et al.[31]
14.	*Ocimum sanctum* leaf extract	Singhal *et al.* [32]
15.	*Pulicarea glutinosa* extract	Khan *et al.* [33]
16.	*Rhinacanthus nasutus* leaf extract	Pasupuleti [34]
17.	*Acacia leucophloea* extract	Kasi*et al.* [35]
18.	*Desmodium gangeticum*	Thirunavoukkarasu et al.[36]

Table2. Silver nanoparticles from lower groups of plants (Fungi, Algae)

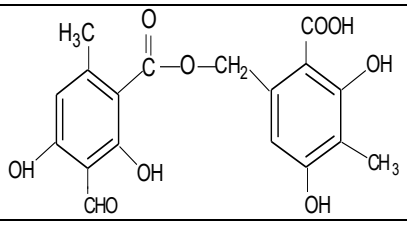
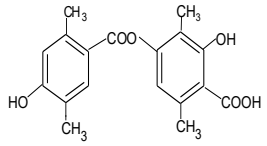
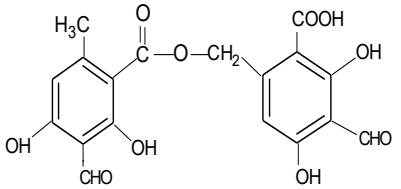
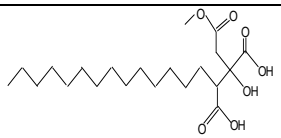
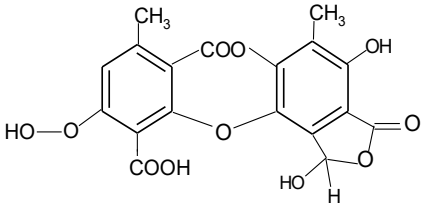
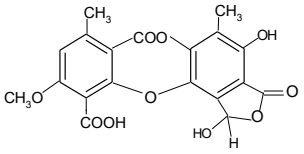
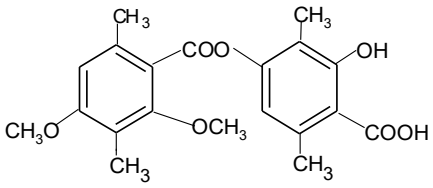
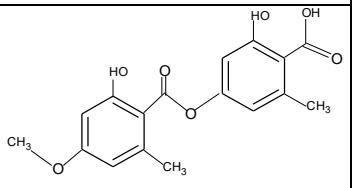
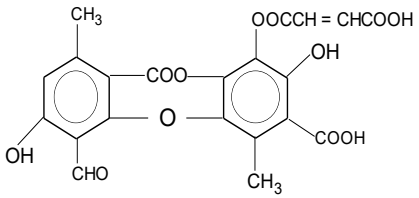
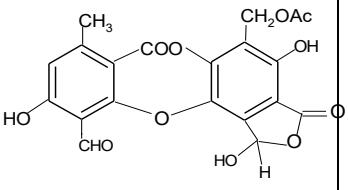
Serial no.	Targeted taxa	References
1.	Endophytic fungus *Pestalotiopsis microspora*	Netala et al.[37]
2.	Filamentous fungal strain isolated from Sugarcane plantation	Basso *et al.* [38]
3.	Endophytic fungus *Aspergillus clavatus* isolated from *Azadirachta indica*	Verma et al.[39]
4.	*Fusarium oxysporum*	Ahmad et al.[40]
5.	*Penicillium brevicomapactum*	Shaligram et al.[41]
6.	*Ganoderma lucidum*	Paul et al.[42]
7.	*Phellinus igriearis*	Leela and Devi [14],Revathy et al.[43]
8.	Endophytic fungi isolated from *Gloriosa superba*	Devi et al.[44]
9.	*Ceropegia thwatesii*	Muthukrishnan *et al.* [45]
10.	*Aspergillus terreus*	Li et al.[46]
11.	*Neurospora intermedia*	Li et al.[46]
12.	*Amylomyces rouxii*	Javed et al.[47]
13.	*Humicola* species	Asad et al.[48]
14.	*Puccinia graminis*	Kirthi et al.[49]
15.	*Arthroderma fulvum*	Xue et al.[50]
16.	Fungus mediated biosynthesis	Jaidev [51]
17.	*Schizophyllum radiatum*	Metuku et al.[52]
18.	*Yeast*	Ortega [53]
19.	*Candida albicans*	Rahimi et al.[54]
20.	Synthesis of metal nanoparticles from microbes	Narayanan et al.[55]
21.	*Escherichia coli*	Gurunathan et al.[56]
22.	Probiotic *Bacillus licheniformis*	Shanthi et al.[57]
23.	Macroalga *Padina tetrastomatica*	Princy and Gopinath [58]
24.	Ability of potential cynobacterium and microalgae silver nanoparticles	Patel et al.[59]
25.	*Fusarium semitectum*	Sawle *et al.* [60]
26.	*Fusarium oxysporum*	Korbekandi *et al.* [61]
27.	*Penicillium* sp.	Hemanth*et al.* [62]
28.	Soil fungus	Jain *et al.* [63]
29.	Marine fungus (*Aspergillus terreus, A. flavipes, Fennellia flavipes* and *Trichoderma hamatum*)	Barakat and Gohar [64]
30.	*Aspergillus flavus*	Vigneshwaran *et al.* [65]
31.	*Penicillium citrinum* and *Penicillium walesmani*	Honary *et al.* [66]

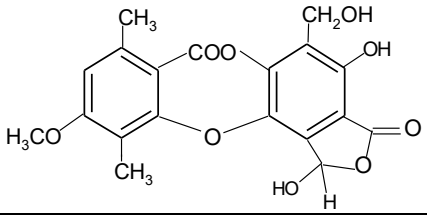
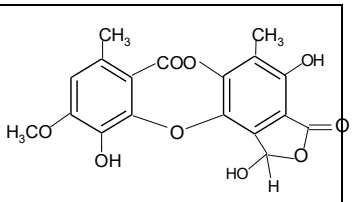
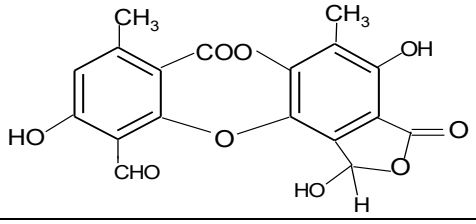
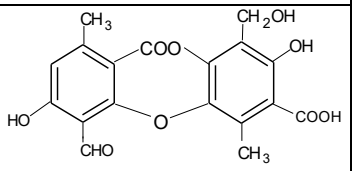
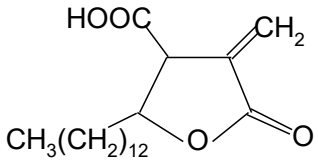
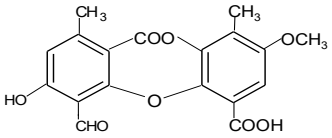
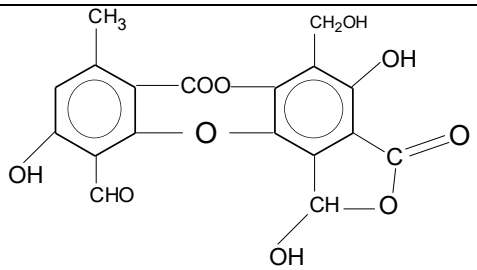
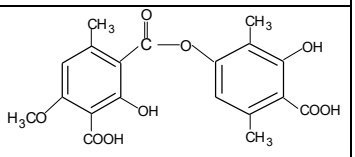
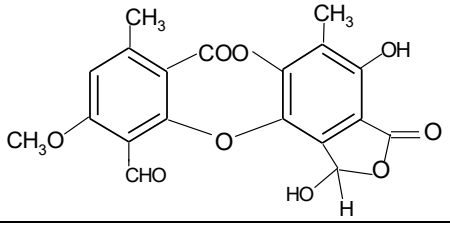
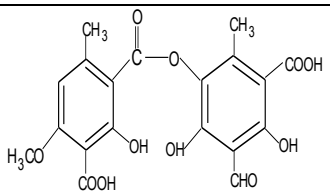
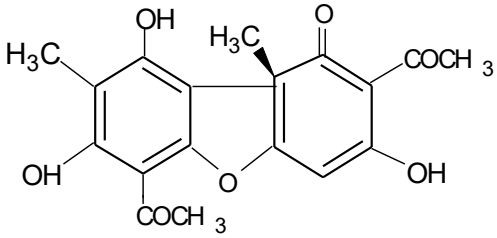
Table 3. Lichen species used for silver nanoparticle formation

Serial no.	Targeted taxa	References
1.	*Cetraria islandica*	Yildiz et al.[67]
2.	*Acroscyphus sphaerophoroides Sticta nylanderiana*	Debnath et al.[68]
3.	*Parmotrema pseudotinctorum Ramalina hossei*	Kumar *et al.* [69]
4.	*Parmeliopsis ambigua, Punctelia subrudect*	Dasari *et al.* [8]

	Xanthoparmelia plitti *Evernia mesomorpha*	
5.	*Usnea articulata,* *Ramalina sinensis*	Abdolmaleki et al.[70]
6.	*Parmelia perlata*	Paul et al.[42]
7.	*Usnea longissima*	Shahi and Patra [71]
8.	*Parmotrema praesorediosum*	Mie et al.[72]
9.	*Ramalina dumeticola*	Din *et al.* [72],Mie et al.[12]
10.	*Cladonia rangiferina*	Rai and Gupta [73]
11.	*Parmotrema perlatum*	Revathy *et al.* [43]

Table 4. Some common secondary metabolites present in lichen species and their chemical structure.

Secondary metabolites	Structural information	Secondary metabolites	Structural information
Alectorialic acid		Barbatic acid	
Barbatolic acid		Caperatic acid	
Constictic acid		Cryptostictic acid	
Differactaic acid		Evernic acid	
Fumaroprotocetraric acid		Galbinic acid	

Hypoconstictic acid		Menegazzaic acid	
Norstictic acid		Protocetraric acid	
Protolichesterinic acid		Psoromic acid	
Salazinic acid		Squamatic acid	
Stictic acid		Thamnolic acid	
Usnic acid			

RESEARCH ARTICLE

Application of Intuitionistic Fuzzy Graph in Traffic Controls

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ABSTRACT

The aim of this paper is to find the justification for the traffic congestion issue and get the diverse method of accidental zones in a traffic streams utilizing vertex coloring of an intuitionistic fuzzy graph.

Keywords: Traffic light, Vertex coloring, intuitionistic fuzzy graph coloring, accidental zone, Traffic stream.

INTRODUCTION

Zadeh (1965) proposed the fuzzy set, which has been implementing in various area like group decision, engineering etc. Atanassov K.T (1998) introduced the new concepts of intuitionistic fuzzy set (IFS) is a generalization of fuzzy set and described some of their important properties with a suitable example. Graph theory emerged from the Konigsberg bridge problem in 1736 by Swiss mathematician, Leonhard Euler. Graph theory is the study of graphs, which are mathematical structures used to model pairwise relation between objects and play vital role in real life problem. A graph can be defined as a pictorial representation or a diagram that represents data or values in an organized manner. The points on the graph often represent the relationship between two or more things. Fuzzy graph was found by Rosenfeld (1975), he described that fuzzy analogues of different basic graph-theoretic ideas like bridges, paths, cycles, trees, connectedness and some properties. Atanassov K.T (1999) established the concepts of intuitionistic fuzzy graph.

The concept of coloring a graph in graph theory applied in traffic signals, scheduling i.e., time table, etc. The idea of two different approaches to the graph coloring in fuzzy graph and the classical concept of chromatic number of a graph by Munoz et al. (2004). The fuzzy coloring of fuzzy graph was explained by Eslahchi.C and Onagh (2006) and discussed about the chromatic fuzzy sum, strength of fuzzy graph and studied some concepts related to the graphs. Parvathi. R and Karunambigai.M.G (2006) gives a new definition to the intuitionistic fuzzy graph and described

some properties and introduced notion of various concept. Lavanya.S and Sattanathan.R (2009) introduced the concept of total coloring of fuzzy graph and defined fuzzy total coloring in term of a family of fuzzy sets satisfying certain conditions. Myna.R (2015) developed the Application of fuzzy graph in traffic, he uses the fuzzy graph model to represent a traffic network of the city and discuss a method to find the different type of accidental zone in traffic flows using edge coloring of a fuzzy graph. Intuitionistic fuzzy graph coloring was established by Rifayathali. M.A. et al. (2017) and introduced the chromatic excellence of intuitionistic fuzzy graph and its properties.

In this article, intuitionistic fuzzy graph are used in traffic controls and different types of accidental zones using vertex coloring in intuitionistic fuzzy graph and specially denoting intersection part of vehicles met with an accidents and it is concluded by applying chromatic number in graph.

Preliminaries

Definition 2.1.A ***Fuzzy graph*** $G=(\sigma,\mu)$ is a pair of functions $\sigma: V \to [0,1]$ and $\mu: V \times V \to [0,1]$, where for all $u, v \in V$, we have $\mu(u, v) \le \sigma(u) \wedge \sigma(v)$.

Definition 2.2.*Intuitionistic fuzzy graph* (IFG) is of form G = (V,E) where

1. $V=\{v_1, v_2 \ldots v_n\}$ such that $\mu_1: v \to [0,1]$ and $\gamma_1: v \to [0,1]$ denotes the degree of membership and non-membership of the element $v_i \in V$ respectively and $0 \le \mu_1(v_i)+\gamma_1(v_i) \le 1$ for every $v_i \in V$, (i = 1,2,..n)
2. $E \subset V \times V$ Where $\mu_2: V \times V \to [0,1]$ and $\gamma_2: V \times V \to [0,1]$ such that
   $\mu_2(v_i, v_j) \le \min [\mu_1(v_i), \mu_1(v_j)]$
   $\gamma_2(v_i, v_j) \le \max [\gamma_1(v_i), \gamma_1(v_j)]$
   And $0 \le \mu_2(v_i, v_j)+\gamma_2(v_i, v_j) \le 1$ for every $(v_i, v_j) \in E$.

Definition 2.3.A ***k-vertex coloring*** of a graph G is an assignment of k colors, 1,2,…… k, to the vertices of G. The coloring is proper if no two distinct adjacent vertices have the same color. The ***chromatic number*** $\chi(G)$ of a graph G is the minimum k for which, G is k-colorable.

Definition 2.4.A family $C=\{c_1,\ldots,c_k\}$ of intuitionistic fuzzy sets on a set V is called a ***k-vertex coloring*** of G = (V, E) if

a) $\nu c_i(x) = V$, for all x ∈ V

b) $c_i \Lambda c_j = 0$

c) For every strong edge xy of G, $\min\{c_i(\mu_1(x)), c_i(\mu_1(y))\} = 0$ and
$\max\{c_i(\gamma_1(x)), c_i(\gamma_1(y))\} = 1, \quad (1 \le i \le k)$

The least value of k for which the G has a k-vertex coloring denoted by $\chi(G)$, is called the chromatic number of the intuitionistic fuzzy graph G.

Intuitionistic Fuzzy Graph Coloring in Traffic Signal Problem

A graph is an advantageous method of addressing data including relationship between objects. The focus of the graph is addressed by vertices and edges. So, there is ambiguity in the depiction of the object or in its connections or in both. To depict this kind of connection, we need to configuration graph model with parting of intuitionistic fuzzy set. This parting of intuitionistic fuzzy set with diagram is known as intuitionistic fuzzy graph. Traffic signal plays a significant part to stay away from accident. Therefore, we need to manage a traffic stream.

In Fig. 1, the traffic stream is characterized by vertices and edges; the arrow addresses the heading of vehicles. The quantity of vehicles passing in all ways isn't comparable. Since each left turn doesn't meddle with the traffic stream (i.e.) the vehicles can pass with no aggravation. Remaining bearing in Fig. 1 is set apart from A to B show the traffic stream that met with an accident. In this paper, we are presenting the traffic stream as an intuitionistic fuzzy graph problem. In this graph we consider a traffic flow shown below. Each corresponding arrow shows the vehicles will go from one direction to other direction. The number of vehicles is not equal in all paths. For this reason, we consider the intuitionistic fuzzy set whose membership value depends upon on vehicle number.

The quantity of vehicle is high there is a chance of traffic stream and accident. The vehicle passing is between the ranges 5,000 to 10,000 every hour; at that point its membership value is addressed as higher, when vehicle passing is between the ranges 0 to 5,000 every hour; at that point its membership value is addressed as lower. In the event that the speed of vehicles is high there is an opportunity for accident. So, speed limit for vehicles should be controlled in all ways to stay away from crash of vehicles. The non-membership is addressed utilizing the waiting time of a vehicle in the path, if waiting time in any path is high there will be chance for high traffic stream. In this problem we represent each traffic flow using the vertices of intuitionistic fuzzy graph and their membership value depends on the number of the vehicle of that road. The vertices of two adjacent vertices, is corresponding traffic flow crossing each other. Here v_1 and v_2 are adjacent vertices. There may be possibility for the accidents.

Graph Model of Traffic Problem at the Crossroads

Graph Model of Traffic Problem at the Crossroads, as we can see there are 4 flows which are then labelled by A, B, C and D. Direction of traffic stream can be seen at the following figure. The arrow shows that the direction of the vehicles in the traffic stream.

The flows are compatible which can be seen in the following

1. A flow A is compatible with the flows B.
2. A flow B is compatible with the flows A.
3. A flow C is compatible with the flows D.
4. A flow D is compatible with the flows C.

Traffic Light Control

In observation of the crossroads forms are assumptions, including:

There is a free left where vehicles can pass easily, hence every left turn doesn't require a sign for example $v_1 \rightarrow v_4$ and $v_4 \rightarrow v_2$. The table underneath show how signals are utilized to keep away from traffic stream further more accident. In this manner signals assume an incredible part in space of traffic light.

Solution and Phasing of Traffic Lights

Since the number of vehicles in all the path are not equal, therefore we need minimum time duration for low traffic flow, maximum time duration for high traffic flow and medium time duration for medium traffic flow. The traffic light pattern waiting time for each phase is more, due to these total waiting time of vehicles will be more. To minimize the waiting time for vehicles we can follow the following traffic light pattern.

Numerical Example

Consider the Intuitionistic fuzzy graph G = (X,Y) with intuitionistic fuzzy vertex set $X = \{v_1, v_2, v_3, v_4\}$ and intuitionistic fuzzy edge set. $Y = \{v_1v_3, v_1v_4, v_2v_3, v_2v_4\}$.

$\delta = \{x_i\ x_j / ij = 14, 24, 13, 23\}$ the membership function defined as

$$\alpha_1(x_i)\beta_1(x_i) = \begin{cases}(0.4,0.6) & \text{for } i=1\\ (0.7,0.2) & \text{for } i=2\\ (0.3,0.5) & \text{for } i=3\\ (0.6,0.1) & \text{for } i=4\end{cases}$$

$$(\alpha_2(x_i x_j),\beta_2(x_i x_j)) = \begin{cases}(0.4,0.6) & \text{for } i=14\\ (0.6,0.2) & \text{for } i=24\\ (0.3,0.6) & \text{for } i=13\\ (0.3,0.5) & \text{for } i=23\end{cases}$$

Let $\Gamma=\{c_1,c_2\}$ be a family of intuitionistic fuzzy set defined on X as follow

$$c_1(x_i) = \begin{cases}(0.4,0.6) & \text{for } i=1\\ (0.3,0.5) & \text{for } i=3\\ (0,1) & \text{otherwise}\end{cases} \quad c_2(x_i) = \begin{cases}(0.7,0.2) & \text{for } i=2\\ (0.6,0.1) & \text{for } i=4\\ (0,1) & \text{otherwise}\end{cases}$$

Hence the family $\Gamma=\{c_1,c_2\}$ fulfilled the condition of intuitionistic fuzzy vertex coloring of the graph G. Hence the Intuitionistic Fuzzy chromatic number $\chi_v(G)$ is 2.

CONCLUSION

In the concept of crisp incompatibly among the nodes of graph we cannot describe the vagueness or partial information about a problem. In this paper, we represent the traffic stream using an intuitionistic fuzzy graph whose vertices and edges both are intuitionistic fuzzy vertices and intuitionistic fuzzy arcs. By using the intuitionistic fuzzy graph coloring of vertices, we obtain the chromatic number.

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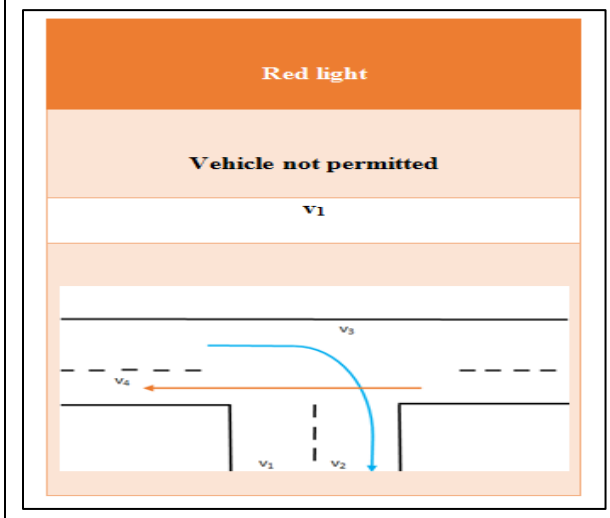
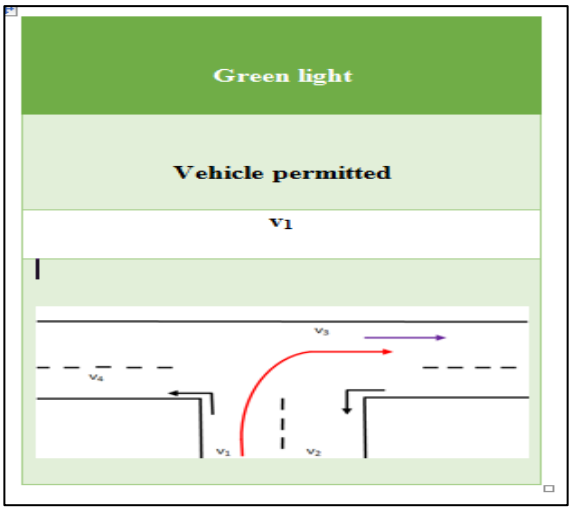
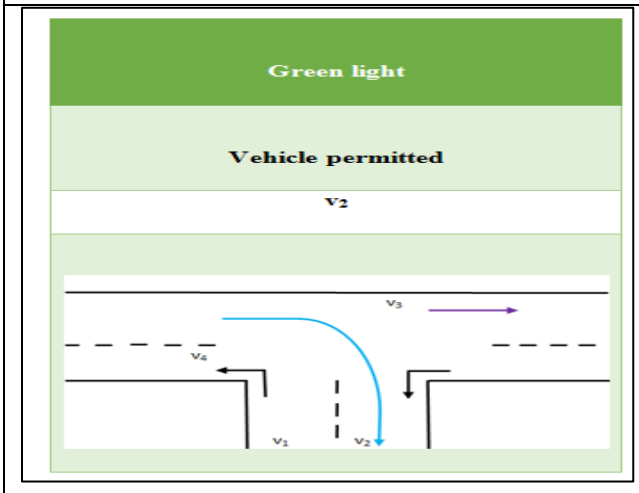
Table 1: Notation of Vertex

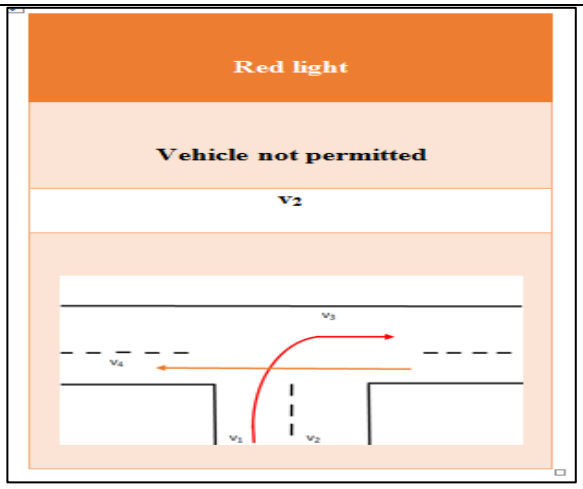
Vertex	A	B	C	D
A	v_1	v_2	v_4	v_3

Table 2: Vehicle Permitted and not permitted









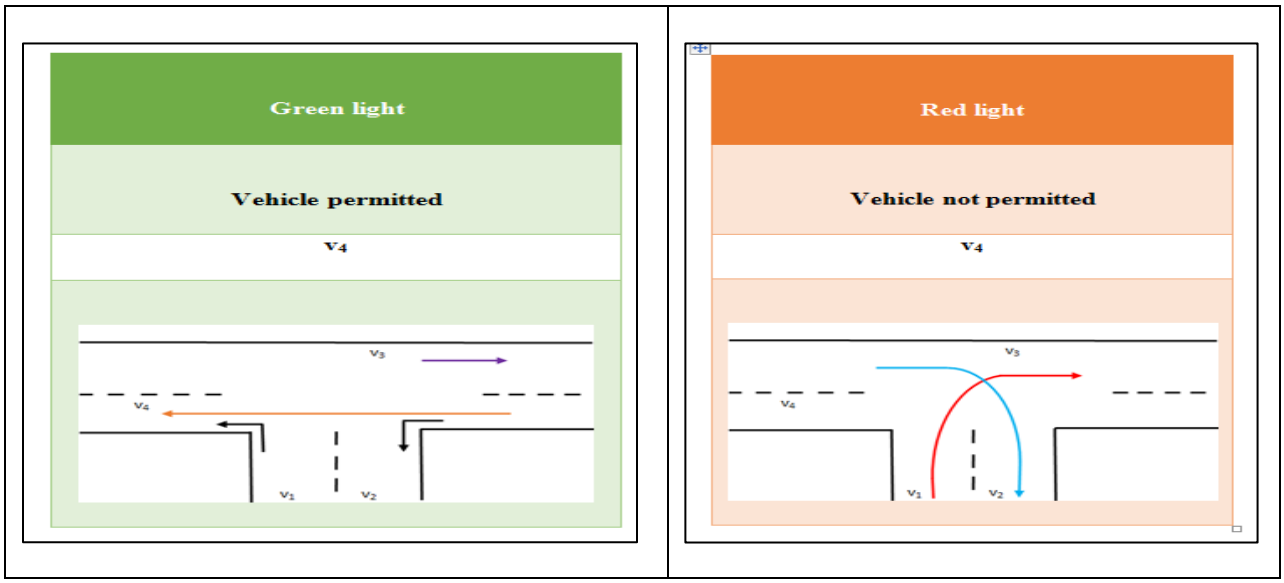


Table 3: Traffic Light Pattern

TRAFFIC LIGHT PATTERN		
PHASE I	PHASE II	PHASE III
Only v_1 and v_4	Only v_3 and v_2	Only v_4 and v_3

Table 4: Vertex Set

Vertex	v_1	v_2	v_3	v_4
X	(0.4,0.6)	(0.7,0.2)	(0.3,0.5)	(0.6,0.1)

Table 5: Edge Set

EDGES	v_1v_3	v_1v_4	v_2v_3	v_2v_4
Y	(0.3,0.6)	(0.4,0.6)	(0.3,0.5)	(0.6,0.2)

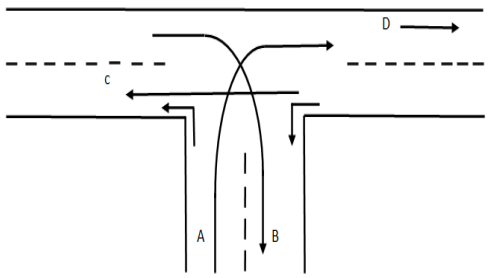


Fig.1. Road Map

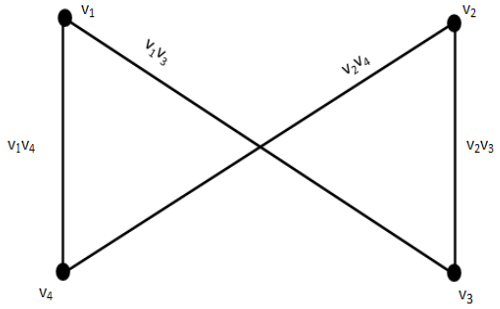


Fig.2. Graph of Road Map

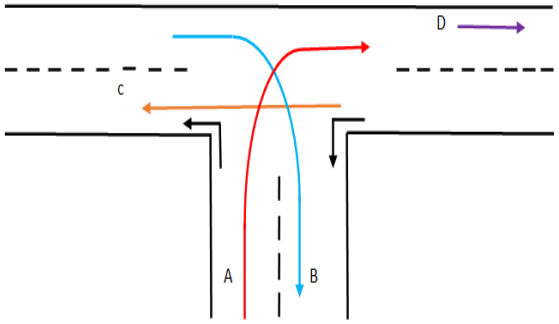


Fig.3. traffic signal control

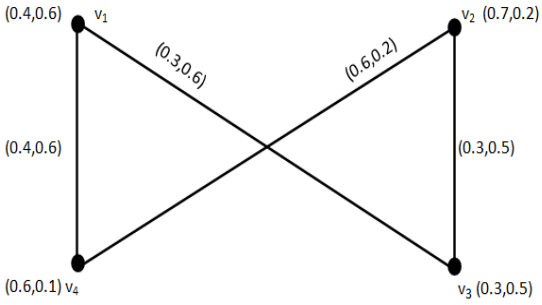


Fig. 4. intuitionistic fuzzy graph

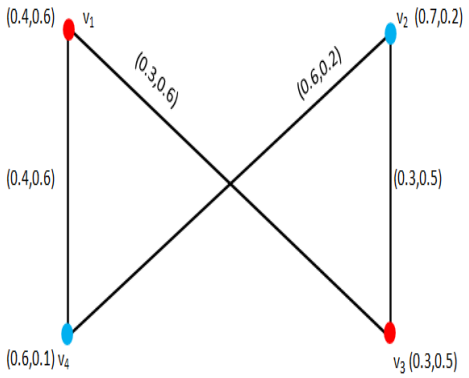


Fig.5. Coloring of intuitionistic fuzzy graph

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RESEARCH ARTICLE

The Role and the Representation of Farm Women in India

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ABSTRACT

This paper aims at projecting the role and the representation of farm women in India. It presents the history of agriculture in the world generally. Particularly, it deals with the women folks living in rural India and their sole dependence on farm and field works. This paper focuses on the vagaries of troubles, sufferings, burdens and the heavy yoke they bear in order to proceed in the life along with their children and family. It is reflection and a mirror of voiceless women in the patriarchal society, how they toil them as if bulls plowing the field to be fed and groom. Their labour are neither recognized nor accepted / appreciated. We could say that they are the bread-winners of the entire nation but living in an at most poverty. This paper also showcases our responsibility to elevate their position and also alleviate their miseries. It also states few more samples from English Literature which portray the role of farm women in their fictions. It reiterates the importance of agriculture for the development of the economy of any nation. The word agriculture comes from the Latin words ager-referring to the soil and culture-to its cultivation. The word 'agriculture' can be defined as the cultivation and production of crop plants, grains, fruits and vegetables or livestock products. It is similar to farming: the field or field dependent production of food and fodder. Agriculture and civilisation go hand in hand and it is possible for primitive man to settle down in places leading to formation of society and civilisation. Asia is considered to be the birth place of agricultural revolution where wild ancestors of wheat and barley and domesticated animals like goat, sheep, pig and cattle are found. The period from 7500-6500 B.C. was the period of discovery of agriculture.

Agriculture was very prominent profession during Vedic age 1500-1000 B.C. Use of iron particularly iron ploughs became prevalent. Buddhist period 600 BC marks the importance of trees. It can be called as a period of Arboriculture and Horticulture. During the first century, the most important development in

agriculture was irrigated cultivation in agriculture. Irrigated cultivation of rice in South India Cauvery River was the most important source of irrigation water. Cultivation of rice, finger millet, Sugarcane, Pepper and turmeric was common. During the British regime, the most important development in agriculture was cultivation of commercial crops like cotton, sugarcane and Indigo as they felt the need of raw materials for their industrial growth and they got huge amount from European market by selling our commercial crops. In India, more than 75% of the population is depending on agriculture. The high density of working population in India is engaged in agriculture. According to India's census figure, 66 per cent of India's working population is engaged in agriculture. Indian Agriculture has been the source of supply of raw materials to our leading industry. Cotton, Jute, textile industry, Sugar, vanaspathi and plantation depend upon agriculture directly or indirectly. There are many other industries such as, small and cottage industries, handloom, oil industry, rice mills and sugar mills depend upon agriculture for their raw materials. Female farmers play a vital role in food production and food security and as such they are the backbone of the development of rural and national economies. Women from rural areas should be admired, recognized and accepted for their day and night work despite many health issues. They play a significant role in the agricultural labour force. Their contributions are extremely significant though their efforts are trivialised and their works are difficult to quantify because of lack of regular data that monitors their agricultural activities. They toil in the land and field to feed the unknown citizen. The wage they receive for their labor is insufficient since their basic needs are not met. The family suffers to fulfill the requirements. While everyone has three meals a day, farm women are so pathetic to have a single meal a day that also she sacrificed it for her children by drinking porridge and water.

Keywords: Biological and social issues and farm women in literature, Family, The farm women in India, The trouble the farm women undergo, The work, The wage.

INTRODUCTION

The day starts before sunrise and continues after sunset. These are the women farmers of India. Those voices often go unheard owing to their gender. They struggle to establish their identity at a grassroots level due to the patriarchal traditions. These voices need to be heard for the progressive India. Women farmers in India perform the most of the farming jobs, from sowing to harvesting. Yet their access to resources is less than their male counterparts. Closing this gender gap is essential to accelerate the pace of growth in the agriculture sector.

"We have been doing farming for ages. My mother in law did it, I am doing it, my daughter and daughter-in-law will do it. But what we need and will cherish is an identity of our own. An identity of being a woman farmer." Bholi Devi, Harpur Village, Bihar. It is a voice of every women farmer in India

Farm women work in agriculture and they are active in all the areas of field works including plowing, manuring, seeding, pruning, watering, and harvesting, supervising, managing the financial aspects incorporated land and cultivation. The role of farm women has drastically changed that they are wives of farmers or independent farmers. Farm is a distinct environment where there is no distinction between home and work. In an urban society, most works are done outside, whereas on a farm the home is a productive place.

Before the cock crows, she wakes up and cleans her home and cowshed. She started feeding her cows and bulls which feed her in return. She trained herself in milking the cow and walked towards the farm which is few miles away from home, packing the yesterday cooked rice or grain soaked in water. As she went earlier, she could work till the twilight and returned home to cook for her husband and children. It is not a feast but food for hungry body

and soul. Sweating odor, the salty face and the cracked hand and heel exhibited their hard labor. Laboring in the farm under the scorching sun which penetrates her body did not affect her body as she could think of her starving kids at home. Nevertheless, she worried about her children's education and their future in the dusty earth. Her world centered on her family, field, the well, the cattle, the expected harvest, monsoon, and rain. She became desperate when anything of these deceived her. The early marriages, incessant childbirth, over workload make her look aged even in her thirties. The uncombed bun hair, unpowdered, wrinkles, sunburnt face, powerful eyes, sharp and sensitive ears, and the innocent and ignorant talk paraded her simplicity.

The whole family works in the field. Rural women involved in farming activities such as weeding, transplanting, and harvesting. They are undergoing problems related to land ownership, security of tenure, land quality issues. Women are preferred in farm works because their wages are lower than men. They work more hours and more intensively. Gathering firewood is another responsibility of women and girls. Men do work such as land preparation; planting; sowing and fertilizer application which could be done in stipulated time. Whereas Women do work, such as weeding, watering are routine daily activities. Women farmers face various problems while working on the farm. These are physical, chemical, occupational, seasonal and biological. The reason for these problems may be inappropriate uses of tools or types of machinery, lack of awareness, high exposure to pesticide, exposure to extreme weather conditions, close contact with plants and cattle, long and lengthy working posture and hours.

Farm women are mostly uneducated. However, they might have got primary level education. Their situation did not permit them to continue their education. If they earn for a day they could feed a day. The farmland is a family business and farm women have to play a multifaceted role to take care of the family, cattle, farms, workers, resources to manage the farm. Compare to urban and suburban women who cook only for her family, farm women cook entirely for all the workers of their farm and their household. They grow, process food and do farm work 24x7, Despite their hard task in the field and everywhere they turn, they do not receive any due respect, recognition or appreciation. They may be the owners of thousand acres of land and their property may worth millions but the simple way of living, the humble way of leading the farming, the least care for them, and their abundant respect for the land which feeds them, and nurtures their nation lifelong. They never anticipate anyone's assistance or governance. They are the masters of their wealth and prosperity. Their assumption and prediction over the production of the farm are absolute always. The loss of monsoon, the natural disaster struck them at times but their strong, indelible, and oak mind allow them to survive and overcome any chaos on their ways.

To fetch drinking water she has to carry a pot on her head and another on her hip to balance the weight and she walked miles away from home and there she has to wait hours together to bring water from the deep well. Sometimes she encountered serious problems by poisonous insects and snakes on her way. The draught and the flood damaged her livelihood to a greater extent.

Bechy Jaber who wrote about farm women narrated her first sixteen years of her life on a farm. She lived in a remote rural area. Her parents were farmers, her grandparents, her uncles, aunts were farmers. The farm determined many aspects of her life. They raised much of their food, raised chickens for eggs and meat, milked cows, sold the eggs, milk, creams and the farm products. They wore clothes that defined their tasks. She disliked that childhood. She found it confining and painful that she could not play with friends after school as she always had to go home to gather eggs, wash eggs, pack eggs, bring the cows from grassing, milk the cows, and help her mother in the house with the domestic chores. Besides, carrying heavy buckets of milk and water which are painful to her arms and shoulders. This was the typical farm life.

An important segment of society is farm women who also had stories to share about their hard life, lose of husband and child and breach with other relations. The novels about the farms bind their experiences in the rural setting and the consistency of the works involved.

The best-known farm novels written by women during the 20th century are Roy Meyer's **The Middle Western Farm,** Willa Cather's **O Pioneers!** and **My Antonia.** Here Alexandra is the heroine who becomes more extraordinary, she saves the family farm, and she runs the business of farming rather than her brothers, Oscar and Lou. She works for the family prosperity and unity. As one thinks of a farm woman, Alexandra, her father depended on her more and more upon her resourcefulness and good judgment and she had kept the family from disintegrating morally and getting careless in their ways. She makes decisions about money and land that is beyond ordinary women. Her commitment to the land isolates her from her brothers, mother, and other women. She has no peer and she is loving and kind and generous to all. One could see the absolute power of Alexandra throughout the novel.

The works of Ruth Suckow especially **Country People** incorporates the elements of world war I and its impact on small communities and farm families. The novel projects two approaches to a farmwife's life. One aspect during her early years of marriage, she is working with her husband to build a strong farm. The second is about the successful farming, moving to a new house, being widowed and having to build a new life. The novel encapsulates an important aspect of a farmer's wife. It delineates how she continues to adopt the hardest of the hard work is done. Suckow's main character is Emma. After marriage, she quit her teaching job and worked with her husband in the field. Much of Emma's life is shown in this excerpt "Emma settled down quickly into a young farm wife. She …got an air of timidity that was an accentuation of her old shyness. She was thin, with skin burned dark, and tired, hollowed eyes…"(56-57).

Suckow also wrote " It all came on Emma. Grandma helped a little, but there was more washing, more cooking and more cleaning. It seemed as if she lived more than ever in the kitchen" (77). Emma looks older, her hair was getting grey, she has been slender but she began to put on flesh now. It makes her look older instead of younger, dumpy and shapeless and middle aged. Suckow describes the country farm women that they are neither flattering nor glamorous. She described one daughter as "aged and hollow-eyed with dark skin but her clothes were shabbier than her mother's. This is the way farm women finished their lives. One could say that 'when money is plenty it is a man's world. When money is scarce it is a women's world. When alleles seem to have failed, the woman instinct comes. This statement address the role of women in household where women's work was integral to the function of the home and farm life which determined the success of her farming operation.

Prem Chand is an Indian writer who made farmers the primary subject matter of his fiction. His stories and novels portray different aspects of a farmer's life. Dr. Ramvilas Sharma says" Prem Chand immersed himself in the life of the farmers and what he wrote was, new for the literary world. He knows the pulse of the farmers. He brought to the fore the untouched realities of their life. "Prmashram" is an epic on peasants' life. Along with it, "Kharmabhoomi" "Godan" complete the triology of the life of Indian farmers. Farmers, laborers, and landlords are present in Prem Chand's literature. But his focus is on the farmers. His farmers till their land. They handle all farming operations. It was they who built India's farm culture. He identifies indebtedness is the biggest problem of the farmer. Prem Chand's farmer is groaning under the weight of debt sometimes he is the victim of the repressive system, sometimes he turns a rebel and on other occasions, he is a typical god-fearing Indian. The main source of worries for farmer is finances. One could experience Indian farm culture in Prem Chan's writings. He projects that the farmer is concerned about his honor and dignity. In Tamil Nadu, particularly, agriculture, food production is majorly carried out by women, with the contribution of men.

The major crops sown in Tamil Nadu are rice, jowar, ragi, bajra, maize, and pulses. Few other crops that are highly cultivated in the regions of Tamil Nadu are cotton, sugarcane, tea, coffee, and coconut. Tamil Nadu has also gained a commendable status in the horticultural sector in its agricultural department. The horticultural products of Tamil Nadu include cash crops and oilseed crops. Bananas and mangoes are cash crops while groundnuts, sesame, and sunflower are oilseed crops. Paddy is the most leading crop in Tamil Nadu and is found in 3 kinds namely Kuruvali, Thaladi, and Samba that varies from season to season. River tanks and wells are the main source of irrigation. Tamil Nadu faced the lease rainfall for the prior 140 years, in 2016. Average annual rainfall decreased to 62% in 2016. The

monsoon season failed over Tamil Nadu with scattered rain in some areas. The highest deficit of rainfall in Indian states in 2016 was in Tamil Nadu. Seeing their crops failing, many farmers began to die of heartbroken and suicides. The Hydrocarbon extracting project implemented in the agricultural fields of Tamil villages like Neduvasal annoyed the Tamil farmers. Tamil Nadu farmers protested, led by Tamil Farmer Ayyakannu.

This is the highly productive Cauvery delta, a region that epitomizes one of the oldest civilizations in the world, where the farmers grew three crops every year to meet local needs and send the surplus to feed the deficit in other regions. This is South India's paddy bowl – the land of prosperity. For example, Selvaraju had about Rs 7 lakh in unpaid debts – crop loans from banks and loans from the informal sources that he borrowed to meet domestic exigencies. He spent at least Rs 5 lakh on two surgeries that his wife Rasati underwent for the removal of a brain tumor over the last two years. This meant recurring health expenses. Karti says the last two years drained the family financially. Added to this were his falling assets. He sold a pair of his bullocks last year. All the family's gold has been pawned to a jeweler in Thanjavur, Karti says. Bank savings are gone. The only possession they have now is the home he built. Climate change and water scarcity have aggravated the farming problems further due to unpredictable rainfall patterns and frequent droughts and flooding.

Problems faced by Women Farmers: There are many serious problems encountered by women farmers. There are not granted land ownership and ignored in inheritance of family property. Most women farmers are small and marginal with the least land holding which deters productivity and investment. The lack of formal sources of credit from banks and money lenders, lack of proper access to resources and modern input like seeds , fertilizers , pesticides are another major problem. Besides, farm women have less role in bargaining power and selling side, more field role. They need to maintain household and children care take, beside agriculture work, bad effect on health; low literacy rate; not Gender friendly machines.

Women are responsible for food for their families. They engage in various stages of processing farm land, harvest, and their maintaining household. In many culture in the world women have the responsibility for the provision of food for their families. They are the provider of basic needs, food, fuel, and water for their families. The tasks performed by women folks in agriculture include crop production, planting, weeding, applying fertilizers and pesticides, harvesting and threshing of the crops, packing, transporting, marketing and animal husbandry.

Self-help groups, village-based financial organizations, comprised soley of women play a crucial role in promoting a shared agenda around health, education and agriculture. These groups are changing the lives of women at the grassroots level.

Self-help groups acts as a catalyst in transforming their role. Selvi, one of the farmers and the members of the self-help groups in Tamil Nadu says: "It is easy to approach women farmers with improved knowledge and practice on sustainable agriculture practices when they are in groups. For the women farmers, it is also easy to come out of their household as the member of a self-help group in which they share their group identity. It provides them confident and courage and independency and socialisation". In India women's contributions to agriculture are significant. Farm women felt the need of their children's education to a large extent, as they realized that only education could bring about great change in the next generation. They are confident that they must provide them with better educational facilities as well as chances to get an education outside their village.

Swaminathan, the famous agricultural scientist describes that it was woman who first domesticated crop plants and thereby initiated the art and science of farming. While men went out hunting in search of food, women started gathering seeds from the native flora and began cultivating those of interest from the point of view of food, feed, fodder, fibre and fuel. Women have played and continue to play a key role in the conservation of basic life support

systems such as land, water, flora and fauna. They have protected the health of the soil through organic recycling and promoted crop security through the maintenance of varietal diversity and genetic resistance.

To empower the women farmers, they should have proper farm training, and proper handling of modern equipments and machines in facilitating their work and capacity building schemes to compete challenges in their ways. Women land ownership plays a vital role to obtain their rights on the agriculture land. They must have easy access to financial resources from banks. Sufficient representatives must be required to raise their voice and to implement their needs. The Government of India has taken steps to improve the condition of rural women through implementing various welfare schemes to alleviate their sufferings and burden.

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REVIEW ARTICLE

Review Study of Various Diluents Employed in Pharmaceutical Industry

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ABSTRACT

Diluents are chemically inactive excipients, mostly used to make up the required bulk of solid dosage form and used up to 80% in a formulation. It introduces soya-bean nugget powder, as novel excipient with nutraceutical value for tablets containing cholesterol lowering drug, (simvastatin). Certain diluents, such as mannitol, lactose, sorbitol, sucrose and inositol, when present in sufficient quantity, can impart properties that will help in disintegration of the tablet in the mouth by chewing. Such tablets are commonly called chewable tablets. Properties such as safety, inertness, etc. are considered. Various studies reported that diluents used in the solid dosage forms shows unwanted effects in body on long term and some time in short duration therapy.

Keywords: Diluents, Lactose, Excipients, Compression, Granulation, Formulation.

INTRODUCTION

Diluents area unit outlined because the style of excipients that area unit added therefore on increase the dimensions of pill for punching. the aim of diluents is to reinforce the majority to sure level therefore on create it convenient for compression. The ordinarily used pill thinner is milk sugar that is convenient in the majority pill formulation owing to its physical properties and therapeutic immobility. milk sugar particles area unit plastic, deform struggling. Hence, they're quite compressible, free flowing if anhydrous, non- absorptive and have high freezing point (202ºC), in order that it's not softened by the friction by the resistance forces of compression. The property which boosts its worth as a thinner is its nature of fast drying. it's thus, convenient for wet granulation [1]. Besides milk sugar, the opposite 2 hexahydric alcohol sugars area unit xylitol, sorbitol and diuretic that area unit convenient for tender tablets owing to the coolness sensation created thanks to negative heat of resolution [2].

Microcrystalline polysaccharide is additionally a decent thinner that has high softness. Its use is restricted thanks to the high-ticket price. Among the opposite diluents area unit saccharose, dextrose, Dicalcium phosphate, carbonate, common salt, starch, mixture oxide, kaolin etc. they will be hand-picked and added to formulation counting on the properties desired [3]. These pharmaceutical ingredients that lack medicine activity however area unit fascinating or necessary in pharmaceutical preparations. Diluents comprise of heterogeneous teams of drugs, designed to create up the mandatory bulk of the pill once the drug indefinite quantity itself is insufficient to get the majority [4]. The pill size ought to be unbroken higher than 2-3 millimeter and weight of pill ought to be higher than 50mg so as to facilitate pill handling throughout manufacture and to attain targeted content uniformity. The thinner vary might vary from 5-80% in a very pharmaceutical formulation. Diluents area unit typically added to pill formulation for secondary reason to supply higher pill properties such as: Enhance flow and regulate weight of pill as per die capability. Ideally diluents shouldn't show any result on the opposite

- To permit direct compression
- provide improved cohesion,
- excipients utilized in the formulation [6].

Diluents ought to be ready to mill into tiny sized once required. It shouldn't promote microorganism growth within the indefinite quantity kind. It should additionally not interfere with the bioavailability of active ingredients. It shouldn't have an effect on the medicine activity of active ingredients [8,9]. Non-active thinner this thinner molecule doesn't contain the active cluster, principally is that the inert solvent, like resolvent within the dilution method doesn't participate within the reaction. By mixing with solvent the consistence is reduced to the best level [10]. Additionally to the dilution result, the mechanical properties, thermal deformation temperature, medium and ageing injury area unit affected. ought to take into consideration the volatile rate of solvents, if the speed of volatility is extremely slow, so within the gum layer to depart the solvent, therefore can have an effect on the bonding strength. Meanwhile, if the speed of volatility is extremely quick, the surface of the adhesive layer is simple to make a movie, deter the interior solvent of the rubber layer escape [12].

This successively, causes the bubble to supply within the rubber layer. it's sometimes accustomed fine-tune the speed of volatilization by commixture various solvents with totally different boiling points. it's utilized in adhesives of rubber-type and epoxy resins. Active thinner could be a thinner containing active teams within the molecule. it's within the method of diluting the adhesive to participate within the reaction, however will|can also} play a toughening role (such as in epoxy adhesives added glycerin epoxy or gas chemical compound radical ether can play a toughening effect) [13].

A DILUENT SHOULD HAVE FOLLOWING PROPERTIES [14, 15]

- Must be physiologically, with chemicals and physically inert by themselves & together with the medicine.
- Economic
- Free from all microorganism contamination, mustn't alter the bioavailability of the drug .Colour compatible.
- Non hepatotoxic, commercially accessible in acceptable grade.

OBJECTIVES OF INCORPORATING DILUENTS

1. So as to provide tablets of affordable size (i.e. minimum diameter of 3mm), it's necessary to feature associate degree inert material referred to as thinner or Filler [16].
2. Thinner boost the majority so as to create the pill a sensible size for compression [16].
3. The dose of some medicine is sufficiently high that no filler is needed (e.g. acetylsalicylic acid and bound antibiotics).

4. Bound diluents, like diuretic drug, lactose, sorbitol, plant product and vitamin B, once gift in spare amount, will impart properties that may assist in disintegration of the pill within the mouth by mastication. Such tablets area unit normally known as tender tablets [15].
5. Diluents used for direct compression formulae offer the powder mixture necessary flow-ability and sponginess [18].
6. To delay or management the speed of unleash of drug from the pill [19].

CHARACTERISTICS OF IDEAL DILUENTS

1. They have to be nontoxic and acceptable to the drug-regulatory agencies all told countries wherever the merchandise is to be marketed [20].
2. They have to be commercially offered in a suitable grade all told countries wherever the merchandise is to be factory-made [21].
3. They have to be with chemicals stable alone and together with the medication and different pill parts [22].
4. They have to be low-cost compared to the active ingredients. they have to be physiologically inert [22].
5. They have to be colour-compatible
6. They have to be freed from any unacceptable microbiologic "load" [23].
7. They have to haven't any negative effects on the bioavailability of the drug(s) within the product [24].

EFFECTS OF DILUENTS [25, 26]

- Degradation of API (hydrolysis).
- Complex formation.
- Sucrose – pill hardness-poor disintegration.
- Capping – low wet.
- Mannitol - punch filming/ choosing.

LACTOSE

Conventional lactose

***Brand name*:** Pharmatose, Respitose.

In pill formulation milk sugar is that the most generally used agent. it's offered in hydrous and anhydrous kind. There are a unit 2 grades of milk sugar area unit commercially offered milk sugar is most well-liked attributable to pleasant style, promptly dissolve in water, non-reactive, show smart unleash rate, less disintegration time and low price diluents[27]. The most limitation is that it reacts with alkane drug bases in presence of alkaline lubricants and manufacture discolouration with time. This reaction is termed Maillard reaction. Three grades of milk sugar area unit commercially available:

LACTOSE MONOHYDRATE[29,30]

***Brand name*:** Pharmatose and lactochem.

Lactose (C12H22O11) is lactose. it's a oligosaccharide composed of 1 sucrose and one aldohexose molecule. Within the pharmaceutical business, milk sugar is employed to assist kind tablets as a result of it's outstanding squeezability properties. it's additionally accustomed kind a diluents powder for dry-powder inhalations. milk sugar could also be listed as milk sugar hydrous , Lactose hydrate isn¬milk sugar anhydrous, milk sugar hydrate, or milk sugar dry out.

CHARACTERISTICS OF LACTOSE HYDROUS

- Lactose monohydrate is not directly compressible and therefore it is convenient for use in wet granulation.
- It has poor flow properties and hydrophillic.
- Lactose is odourless and slightly sweet-tasting; a-lactose is approximately 20% as sweet as sucrose [31].
- It produces a hard tablet and the tablet hardness enhances on storage, disintegrant is needed in formulation.
- Drug release rate is usually not affected.

- Occurs discoloration with amines and alkaline materials [32].
- It contains approximately 5% moisture and hence is a potential source of instability especially with moisture sensitive drugs [33].

SPRAY DRIED LACTOSE[1,34]

Brand name: Spray Process 315; Flow Lac; Lacto press; Super Tab 11SD, 14SD etc.

Now a day's spray dried milk sugar area unit used as a result of it allow direct compression. thanks to cohesive nature, spray dried milk sugar additionally has smart flow characteristics. however spray dried milk sugar is vulnerable to darkening within the presence of excess wet, amines, and different compounds.

FAST-FLO LACTOSE [28]

- It is non- absorbent
- This is way a lot of compressible
- Spherical aggregates of microcrystal's milk sugar hydrate
- Tablets area unit 3 to fourfold more durable than regular spray dried.

MANNITOL[39,40]

Brand name: Mannogen-2080.

It is Associate in Nursing scentless, white, crystalline powder with slight sweet style. It dissolves slowly and imparts a chill sensation within the mouth thanks to its negative heat of answer, thus employed in cuttable pill diluents. Mannitol being inert and non - absorbent is employed in nourishment formulations that area unit wet sensitive. Formulations containing diuretic drug need large amount of lubricants thanks to its less flow ability.

XYLITOL [43-45]

***Brand name*:** Bioxtra, Bioxtra-T.

Xylitol is good like table sugar however while not form of the negative effects Xylitol is a beautiful goods and employed in totally different merchandise that notably relate to your health and well-being .It additionally includes a crystalline, granular structure, in contrast to sugar. It holds clean up to four-hundredth fewer calories and seventy fifth fewer carbohydrates. The compound isn't light by the bacterium in our biological process systems. Once eaten, the body absorbs and metabolizes xylitol terribly step by step. It doesn't utterly absorb into the blood like plant product sugar and will not cause a similar probably negative facet effects, like intrusive with blood glucose or endocrine production.

SORBITOL

Brand names: Neosorb 60, sorbogen and sorbidex-P.

Sorbitol is utilized as a pill agent in wet granulation or dry compression formulations. It's sometimes employed in cuttable tablets attributable to its sweet style, and it's used as a plasticiser for scleroprotein in capsule formulations[41,42]. It's combined with diuretic drug formulations to decrease the agent price. it's Associate in Nursing optical chemical compound of diuretic drug.

STARCH [37,38]

Brand name: Sta-Rx 1500.

Starch is sometimes used as a pill agent. Starch is obtained from corn, Wheat or potato. The starch that is specially dried encompasses a commonplace wet level of 2-4% however pricey. Sta-Rx 1500 is employed that is free flowing and directly compressible. they're additionally used as agent, disintegrate, binder. USP grade of starch contain wet content between 11-14%. Emdex and Celutab area unit 2 hydrolyzed starches that contain dextroglucose (90-92%) and malt sugar (3-5%). they're employed in cuttable tablets attributable to their sweetness and swish feeling within the mouth.

SUCROSE [1,46,47]

***Brand name*:** Dex-Z

Sucrose is that the sugar of commerce principally created by sugar cane and sugar beets. disaccharide is made is made is made. the 2 monosaccharides area unit control along by a organic compound bond between C1 of α-glucose and C2 of β-fructose. The reducing teams of aldohexose and levulose area unit concerned in organic compound bond, therefore disaccharide could be a non-reducing sugar, and it cannot type osazone. disaccharide is a crucial supply of dietary saccharide. They are convenient for direct compression. they're gettable as sugar tab (90 to ninety three disaccharide &7 to 100% invert sugar), Di political action committee (97% disaccharide & three-d changed dextrin's) and alphabetic character Tab (95% disaccharide & four-dimensional saccharide & bit of corn starch & magnesium-stearate).

MICROCRYSTALLINE CELLULOSE (MCC)

Brand names: Avicel ph, vivacel.

MCC is generally thought-about as a result of the dilutant having the simplest binding properties and is recognized collectively of the favored DC binders. It's used as a binder/ dilutant in oral pill and capsule formulations as well as each wet granulation and direct compression processes.MCC exhibits a high dilution potential, whereas the broad particle size vary provides optimum packing density and coverage of different materials. It additionally has some stuff and disintegrant properties that is useful in direct tableting. tiny amounts of MCC area unit ready to expeditiously bind different materials, particularly poorly pill in a position active pharmaceutical ingredients[48,49]. MCC has been the foremost favorite dilutant among others thanks to its low bulk density. Excipient having low bulk density and enormous particle size distribution can exhibit a high dilution potential on a weight basis, optimum filler density, and coverage of drug and different excipient materials [50].

MCC is commercially gettable in several particle sizes, density, and wetness grades that have totally different property and applications. the foremost wide pronounced grades area unit Avicel pH scale one zero one and Avicel pH scale 102 (FMC Corporation, Princeton, NJ, USA). pH scale stands for the pharmaceutical grade of MCC.Avicel pH scale one zero one is that the original grade of MCC, whereas pH scale 102 is gettable as a partly collective product with a bigger particle size distribution and slightly higher thinness. each grades show no vital distinction within the sponginess. Once employed in wet granulation MCC promotes quicker and even distribution of granulating agent [51].

APPLICATION [52]

- Excipient in pill.
- It is Multifunctional Excipient.
- It is employed as binder /diluent in pill.

DIBASIC CALCIUM PHOSPHATE AND CALCIUM PHOSPHATE

Brand name: PharSQ Active.

Calcium phosphate is unable to be with drug sensitive to alkalescent condition. Dibasic phosphate associate inorganic substance that is out there in each fine type and mixture type.Owing to the security and really prime quality, a number of Budenheim phosphates have recently gone on the far side ancient used as excipients and area unit used as active pharmaceutical ingredients (API) likewise – these API grades (calcium, metallic element and Mg phosphates) area unit registered and offered beneath the family [53]. There area unit varied totally different grades of phosphate based mostly excipient on the market. Budenheim additionally offers totally different types of specialised metal phosphates which may be flexibly employed in differing kinds of pharmaceutical processes [54]. Dibasic phosphate dihydrate (USP/NF), metal H Phosphate dihydrate (Ph.Eur.) - a rough grade DI-CAFOS D a hundred and sixty is that the most typically used product for direct compression as a result of its superb each compaction and flow properties whereas a fine grade DI-CAFOS D fourteen is extremely well-liked product used principally in wet granulation processes.

Anhydrous dibasic phosphate (USP/NF), metal H Phosphate (Ph.Eur.) - directly compressible grade DI-CAFOS A one hundred fifty that have a awfully high binding capability permitting to considerably increase the mechanical strength of tablets even at high drug concentration [55].

SOYABEAN

Soya bean is high in macromolecule and is taken into account resembling animal food in terms of the standard of the macromolecule. It additionally contains 19.5g of fat, 21g of saccharide and provides 432 kcal /100g. It contains 43g of macromolecule per 100g that is that the highest among the pulses. Leguminous plant bean oil is one in all the limited common vegetable oils that contain a major quantity of alpha-linoleic acid, polyunsaturated fatty acid fatty acids and polyunsaturated fatty acid fatty acids. Soy macromolecule is related to vital decrease in humour steroid alcohol, denseness compound protein (LDL) (bad cholesterol) and acylglycerol concentrations [56]. Soy phytoestrogens (isoflavones, genistein and daidzein) adsorbate on to soy macromolecule is recommended because the agent reducing humour steroid alcohol levels. The advantages may probably cut back the danger of hardening of the arteries and different vas diseases [57]. FDA in 1999 allowed the health claim that leguminous plant intake will cut back steroid alcohol and so facilitate guard against polygenic disease and cardiopathy. Each the authority and therefore the AHA recommend 25g of soy macromolecule once incorporated into a diet that's low in steroid alcohol and saturated fat. A soy based mostly dietary supplement reduces plasma concentrations of total and beta-lipoprotein steroid alcohol in statin-treated symptom patients [58].

SOYABEAN NUGGET POWDER [56]

Soyabean nuggets powder as a replacement nutraceutical excipient (diluent) containing simvastatin. The powder is evaluated for parameters like morphology, angle of repose, proportion sponginess, wetness capability and ash price. The ready tablets be evaluated for post compression parameters like hardness, friability, uniformity of content, disintegration check, dissolution profile, weight variation , stability studies and therefore. The marketed leguminous plant bean lump was the formulations convenient to comprehend our goal are determined.

Characterization of the powder

- The marketed soya bean nugget was size reduced and sieved through a mesh (355µm) and dried at 40ºC for 30min.
- The powder is used as the free flowing diluent for simvastatin tablet formulations (100 tablets).
- The powder parameters be evaluated and these were morphology, angle of repose, moisture capacity, percentage compressibility and ash value.

DEXTROSE (D-GLUCOSE) [36]

Brand name: Cerelose.

This dilutant is gettable in 2 forms-hydrates and anhydrous forms. dextroglucose might typically be combined during a formulation to exchange a bit amount of the spray dried disaccharide, which may cut back the darkening tendency of the ensuing pill.

ADVANTAGES OF DILUENTS

LACTOSE [59]

CONVENTIONAL LACTOSE

1. Lactose has no reaction with most of the drugs, whether in hydrous or anhydrous form.
2. Their granulations are readily dried, and the tablet disintegration times of lactose tablets are not strongly sensitive to variations in tablet hardness.
3. Lactose formulations show good release rates.
4. It is a low cost diluent.

SPRAY DRIED LACTOSE [60]

1. It is used for direct compression containing drug, diluent, disintegrant and lubricant.
2. Spray dried lactose also has good flow characteristics.
3. It can usually be combined with as much as 20 to 25% of active ingredients without losing these advantageous features.

DEXTROSE (D–Glucose) [61]

1. Available name Cerelose.
2. Dextrose may sometimes be combined in formulation to replace some of the spray- dried lactose, which may reduce the tendency of the resulting tablets to darken.
3. Available in two forms: as hydrates and anhydrous forms.

MANNITOL [62]

1. Because of the negative heat of solution (cooling sensation in the mouth), its slow solubility, and its pleasant feeling in the mouth, it is broadly used in chewable tablets.
2. It is relatively non-hygroscopic and can be used in vitamin formulations.

SORBITOL [63]

1. It is an optical isomer of mannitol.
2. Sometimes combined with mannitol formulations to reduce the diluent cost.
3. Low calorie content and non-carcinogenic.

SUCROSE [64]

1. They are all used for direct compression.

MICROCRYSTALLINE CELLULOSE (MCC) [65]

1. It acts as diluent and disintegrating agents
2. Chemical Purity / Low Reactivity
3. Excellent Binding Capability
4. It is used as Filler
5. Greater Flow ability
6. Rapid wicking action permits fast addition of granulation fluid
7. Highly Absorbent.

DIBASIC CALCIUM PHOSPHATE AND CALCIUM PHOSPHATE [66]

1. It is superior to anhydrous diluent, which has a moderate to high moisture demand.
2. Possess very low concentration of unbound moisture.
3. Low affinity for atmospheric moisture.
4. Excellent diluents for water-sensitive drugs.
5. Bound water of calcium sulphate is not released below 80ºC.

DISADVANTAGES OF DILUENTS

LACTOSE [67]

Conventional Lactose

1. Lactose reacts with amine drug (aminophylline and amphetamine) in being there of alkaline lubricants e.g. metal stearate, magnesium stearate and gradually discolours (dark brown) with time due to the formation of formaldehyde. This reaction is called Maillard reaction.

Spray Dried Lactose [68]

1. If spray dried lactose is allowed to dry out and the moisture content falls under the usual 3% level, the material loses some of its direct compression characteristics.
2. Spray-dried lactose is particularly level to darkening in the presence of excess moisture, amines, and other compounds owing to Maillard reactions. Hence, a neutral or acid lubricant should be used.

MANNITOL [69]

1. Mannitol has poor flow characteristics and usually requires fairly high lubricant level.
2. Rich.

SORBITOL [70]

1. It is hygroscopic at humidity above 65%.

SUCROSE [71]

1. All are hygroscopic when exposed to elevated humidity.

DIBASIC CALCIUM PHOSPHATE AND CALCIUM PHOSPHATE [72]

1. Tetracycline products made with calcium phosphate diluent had less than half the bioavailability of the standard product.

Divalent cation (Ca++) form insoluble complexes and salts with number of amphoteric or acidic functionality antibiotics, which generally reduces their absorption.

PHARMACEUTICAL DILUENTS AND THEIR UNWANTED EFFECTS

LACTOSE

Lactose area unit mostly attributed to ‘‘lactose intolerance’’, that happens in persons with a deficiency of the enteric accelerator Lactaid. the primary sort of adult sort hypolactasia is AN chromosome recessive condition ensuing from the physiological decline in activity of the Lactaid accelerator in enteric cells when ablactation. The secondary sort of genetic abnormality happens in people with low Lactaid level, any amount of disaccharide that's eaten isn't fully hydrolysed metabolization in gut [73]. Moreover, the unabsorbed disaccharide raises the pressure with within the colon, preventing water re-absorption and inflicting laxative result. These gases cause abdominal and general symptoms together with abdomen cramps, bloating, diarrhoea, flatulence, muscle cramps and headache. In 2 studies, roughly 10-20% of disaccharide intolerant people showed clinical symptoms of intolerance when bodily process of 3-5g of disaccharide [74]. In one in every of these studies, seventy fifth of the topics had symptoms with 12g of disaccharide. In the alternative study, eight out of thirteen people developed diarrhea when the administration of two g of disaccharide, and nine out of thirteen when the administration of 25g. Others contemplate the security limit to be as low as 5g.Most patients with genetic abnormality will ingest upto12g of disaccharide before coverage symptoms. In some cases the bodily process of four hundred mg of disaccharide from oral medications doesn't cause a big distinction in breath or among the severity of duct symptoms compared to placebo [6].

Lactose ingestion causes the following three main side effects as follows

- Nausea
- Flatulence
- Malnutrition

Nausea

Nausea Nausea is that the aspect result of ingesting disaccharide because the body has intolerance for it. From the irritation within the body, the feeling of getting AN urge to vomit, ends up in the nausea [76].

Flatulence

Flatulence if comfortable disaccharide enters the colon, the topic could expertise symptoms of abdominal pain, bloating, excess flatulence, and diarrhea, a condition referred to as genetic abnormality. Malnutrition it happens because the aspect result of disaccharide bodily process [56].

Malnutrition

Deficiency disease is condition that shows impact on each physical and psychological state thanks to the dearth of nutrients necessary to take care of health. Deficiency disease will result in weight loss, fatigue, dizziness, swollen and hemorrhage gums, muscle and bone weakness, and immune deficiency [77].

MANNITOL

Mannitol is additionally loosely used as AN excipient in pharmaceutical preparations. it's often used as a thinner in tender and dispersible tablets. Diuretic is relatively less cariogenic than sugars. In some case hypersensitivity reactions area unit rumored when the endovenous infusion of 100 percent or two hundredth (w/v) diuretic answer [36]. These hypersensitivity reaction reactions appear to be caused by objection of diuretic at hyperosmolar concentrations on mast cells throughout a restricted variety of subjects [78]. When used orally, the absorption of diuretic isn't over two hundredth. Diuretic causes the symptom when the oral administration. Mannitol shows the unwanted effects a bit like the sorbitol and alternative polyalcohol and it ought to additionally show impact on endocrine remotion rate and enteric transit time. variety of adverse reactions to diuretic are rumored, primarily following the therapeutic use of two hundredth w/v binary compound endovenous infusions.

The quantity of diuretic used as excipients is significantly but that used therapeutically and is consequently related to a lower incidence of adverse reactions. However, allergic, supersensitive sort reactions, internal organ injury and necrobiosis in urinary organ and heart could occur once diuretic is employed as excipients [79].

METHYL CELLULOSE [80]

Methylcellulose is that the organic material used as a thinner within the pharmaceutical formulation. it's the polysaccharide spinoff. it's used as a thinner within the pharmaceutical formulation it causes the assorted aspect effects. largely it causes the abdominal fullness. It additionally causes the severe allergies (rash, hives, itching, issue in respiratory, tightness within the chest, swelling of the mouth, face, lips or tongue) pain, issue swallowing, nausea, body part hemorrhage, abdomen pain, and puking.

POLYETHYLENE GLYCOL [81]

Polyethylene glycol used as inactive ingredient within the pharmaceutical trade. At the high doses causes the agent activity which boosts the craniate loss, decrease weight and malformation.

DEXTROSE [83]

Dextrose is common name for the ever-present sugar molecule, glucose. Over use of the dextroglucose may end up in some terribly undesirable aspect effects. Too ton dextroglucose will really result in a incomprehensible result in people while not polygenic disease. If blood glucose raises terribly high and really quick, the exocrine gland secretes terribly massive quantities of hypoglycaemic agent. This signals the cells to require up blood glucose quickly, since symptom is damaging to the tissues. As a results of the duct gland over reaction to terribly high blood glucose, the cell will take up an excessive amount of blood glucose, resulting in symptom. High dextroglucose consumption additionally ends up in symptom, if untreated, will result in tissue harm, coma and death. alternative aspect result of excess dextroglucose consumption is a rise in body fat. to scale back the unwanted effects of the diluents there's a deemed has to establish new flavoring pharmaceutical diluents that area unit inert or give their nutraceutical worth for treating such unwellness.

DICALCIUM PHOSPHATE [84, 85]

Dicalcium phosphate (DCP) could be a combination of charged particles of atomic number 20 and charged particles of gas phosphate that is interchangeable with the phosphate within the body. future use of DCP ends up in upset within the balance of phosphates and alternative chemicals within the body. in keeping with the fabric safety knowledge sheet, the pulverised sort of DCP could irritate skin. Prolonged skin contact could result in dry or roughened skin. People with AN allergic reaction to DCP might develop dermatitis, a particular hypersensitivity characterised by redness, swelling or skin sensation on skin areas that acquire contact with AN irritating substance In severe cases, this hypersensitivity could unfold elsewhere, even to areas that haven't been in direct contact with di-calcium phosphate. Inhalation of di-calcium phosphate powder could irritate the respiratory organ and nasal passage and causes cough and sternutation. High level of this thinner could upset the system. It causes the nausea, vomiting, loss of appetency, constipation, abdomen pain, waterlessness and increase excreting.

CALCIUM CARBONATE [86-88]

It is the principal sort of metallic element establish in bovine milk and blood. it's utilized in the variability of dental product for demineralization and as a dilutant in some medications wherever it provides the pill a gray colourise the absence of colouring agents. It causes the constipation, hypersensitive reaction (rashes, itching, and tightness in chest, swelling of the mouth, face, and lips) confusion, accrued micturition, loss of appetency, mood changes, nausea, abdomen pain, weakness and reflex. Rare cases of carbonate gallstones are according within the medicine. Prolonged bodily function of huge quantity of carbonate leads to the milk alkali syndrome and calcinosis. The milk alkali syndrome is characterised by the triad of hypercalcaemia, alkalosis and nephropathy. Metabolicfacet effects enclosed hypercalcaemia and hypophosphatemia.

CONCLUSION

Diluents are defined as the pharmaceutical excipients which are used in dilution of predominantly solid dosage forms E.g. Lactose, Mannitol, Dextrose, Sorbitol, Sucrose and Xylitol. Diluents being an indispensible component of some dosage forms, they must be evaluated for their safety and stability. The safety assurance of diluents helps the formulator to design an effective and safe dosage form with the use of efficient and safe diluents.

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Table 1.LACTOSE

SI NO	MESH SIZE	GRADE
1	60 to 80	Coarse
2	80 to 100	Regular
3	200 to 450	Impalpable

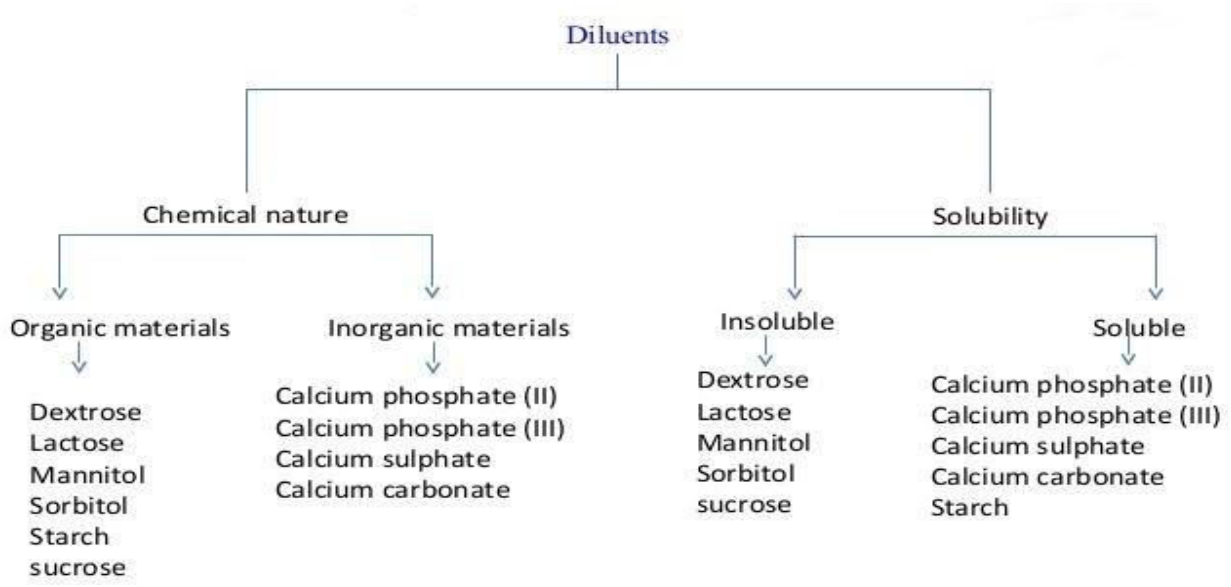

Fig. No: 1 Diluent Classification

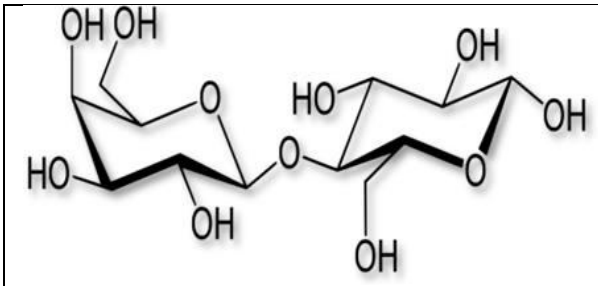

Fig.No:2 Chemical Structure of Lactose

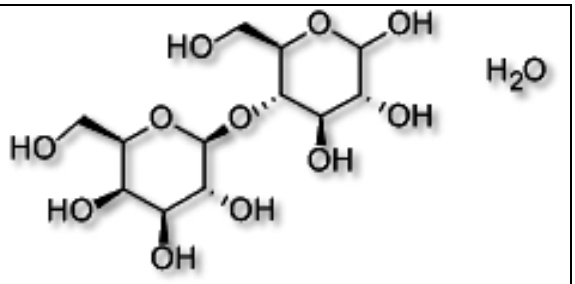

Fig.No:3 Chemical structure of lactose monohydrate

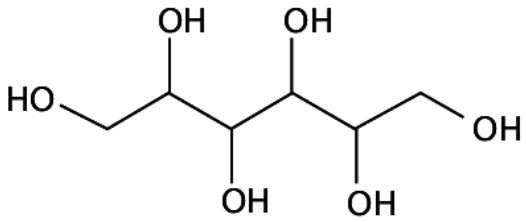

Fig.No:4 Chemical Structure of Mannitol

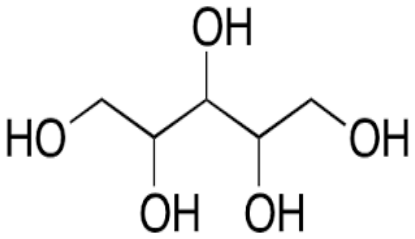

Fig.No:5 Chemical Structure of Xylitol

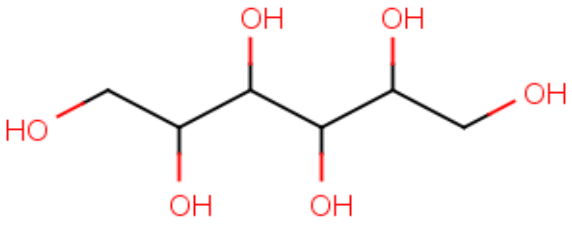

Fig.No:6 Chemical Structure of Sorbitol

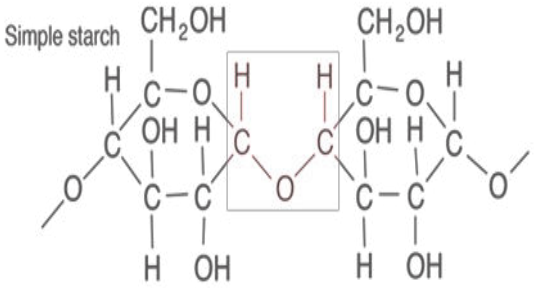

Fig.No:7 Chemical Structure of Starch

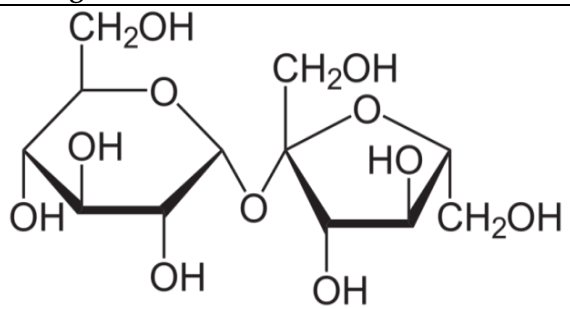

Fig.No:8 Chemical Structure of Sucrose

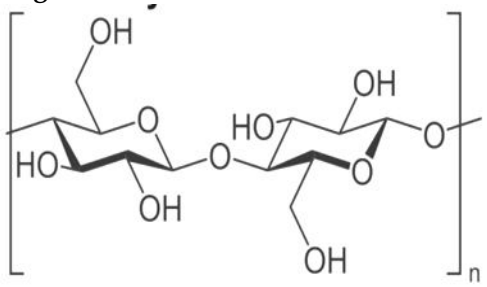

Fig.No:9 Chemical Structure of Microcrystalline cellulose

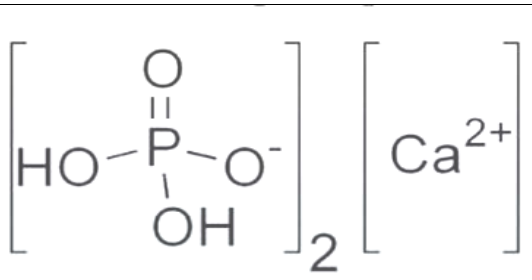	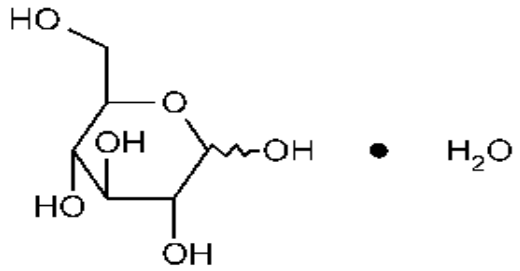
Fig.No:10 Chemical Structure of Calcium phosphate	**Fig.No.11 Chemical Structure of Dextrose**

RESEARCH ARTICLE

Corrosion Resistance by Ethanolic Extract of Pentatropis nivalis (White milkweed) leaves on Carbon Steel in Well-Water

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ABSTRACT

The corrosion resistance of ethanolic extract of *Pentatropis nivalis* (PN) on carbon steel surface in well-water and the effect of adding Zn^{2+} were studied using the weight-loss measurement with variable solution temperatures and different pH levels. When Zn^{2+} ions are added to PN inhibitor system, the inhibition efficiency was increased. The optimum inhibition efficiency of 94% was achieved in 500ppm of PN and 30 ppm of Zn^{2+} for one day immersion system at 303K. When temperature is increases, the inhibition efficiency was reduced. The adsorption of ethanolic extract of PN leaves alone and in combination of Zn^{2+} ions was found to obey Langmuir isotherm at all temperatures studied. The potentiodynamic polarization studies show that PN behave as a mixed-type inhibitor. AC impedance spectra indicate that a protective layer is formed on carbon steel surface. The kinetic [Ea, ΔH] and thermodynamic parameters (ΔG_{ads}, q_{ads}, ΔS_{ads}) have also been calculated to identify the mechanism of corrosion resistance and type of adsorption on carbon steel surface. The nature of the protective layer formed on carbon steel surface has been analyzed by FT-IR spectra and SEM analysis.

Keywords: Corrosion, carbon steel, weight loss, Tafel slope, Nyquist plot, pH levels, FT-IR, SEM, adsorption isotherms.

INTRODUCTION

Corrosion is a spontaneous process that results into conversion of pure metals and their alloys into several stable forms such as their sulphide, oxides, and hydroxides by the chemical and chemical reactions with the surrounding environments [1-3].Carbon steel finds a lot of application in industries like metal finishing. Boiler scale removal, pickling baths etc., it gets rusted when it comes in contact with any aqueous medium [4]. Carbon steel has

remarkable mechanical properties such as great durability, fatigue resistance, high strength and excellent corrosion resistance which make it more commonly used in multistage flash desalination plants than other steel [5-7]. Plant extracts have become important as environmentally acceptable, readily available and renewable source for wide range of inhibitors [8]. The different plant extracts are used [9-15] for corrosion resistance on the metal surface using various corrosion medium. In general, the plant extracts are of inhibitors with high inhibition efficiency and of non-toxicant [16]. Investigation of natural inhibitors is particularly interesting because they are non-expensive ecologically acceptable and possess no threat to the environment [16]. Corrosion inhibitors are used to the prevention of metals against corrosion [4]. The present work is undertaken, to evaluate the inhibition efficiency of ethanolic extract of *Pentatropis nivalis* leaves to prevent the corrosion of carbon steels to analyze the protective layer on carbon steel by FT-IR spectra, to understand the mechanistic aspects of corrosion inhibition by electrochemical methods [17], to study the stability of the protective layer formed on the metal surface by SEM technique, to study nature of corrosion inhibition mechanism and type of adsorption by kinetic and thermodynamic parameters, to study the adsorption of ethanolic extract of PN leaves by various adsorption isotherms. Therefore this work indicates that the ethanolic extract of *Pentatropis nivalis* leaves behave as an effective corrosion inhibitor on carbon steel in well-water.

EXPERIMENTAL METHODS

Preparation for Ethanolic Extract of PN leaves

By refluxing 10g of dried *Pentatropis nivalis* tends to leave in presence of 200ml of ethanol for 3h, the plant extract was prepared and then filtered off using Whatmann No.1filter paper. By using distilled water, these crude extracts were dried and then a dense solid mass was obtained. 1g of Pisonia alba crushed up leaves has been decided to make with a 100ml Standard Measuring Flask with double distilled water up to the mark. Various amounts of leaves extract was decided to make from this solution.

Weight-loss Study

The weight-loss studies are the conventional and simplest of all corrosion monitoring techniques [18]. The method involves the exposing of the specimen of material to a process environment for a given period, then removing the specimen for measurement the basic measurement which is determined from corrosion coupon is weight loss, the weight loss taking place over the period of exposure being expressed as corrosion rate [19] in the weight-loss study carbon steel is completely immersed in 100ml of the test solution of well-water in the absence and presence of ethanolic extract of PN leaves at various temperature. After the immersion period, the specimens were taken out, washed in running water, dried and weighted. From the change in weight of the specimens the corrosion inhibition efficiency and corrosion rates are calculated using the following equations.

$$IE\% = \frac{W_{BLANK} - W_{INHIBITOR}}{W_{BLANK}} \times 100$$

$$\text{Corrosion Rate} = \frac{87.6 \times \text{Weight loss (mg)}}{D \times A \times T}$$

Surface Coverage (θ)

Surface coverage values are calculated from the weight-loss study [20-21] using following equation

$$\theta = \frac{W_{(blank)} - W_{(inhibited)}}{W_{blank}}$$

Electrochemical Measurement

The electrochemical measurements were carried out in three electrode cell assembly, the working electrode was carbon steel, a saturated calomel electrode (SCE) was used as a reference electrode and a platinum electrode was

used as a counter electrode. From the data of Tafel slope and nyquist plot, the inhibition efficiency is calculated using the following equations.

From Tafel slope,

$$IE\% = \frac{I_{corr(blank)} - I_{corr(inhibitor)}}{I_{corr(blank)}} \times 100$$

From Nyquist plot,

$$IE\% = \frac{R_{ct(inhibitor)} - R_{ct(blank)}}{R_{ct(inhibitor)}} \times 100$$

RESULT AND DISCUSSIONS

Effect of Immersion Period on IE and C_R

The values of percentage inhibition efficiency and corrosion rate obtained from weight-loss study at various immersion periods are summarized in Table 2. The maximum inhibition efficiency of 94% was achieved by one day immersion period system. When immersion period is increases, the inhibition efficiency was decreased and also corrosion rate increased [22].The effect of immersion period on inhibition efficiency and corrosion rate is shown in Figure 3.

Effect of pH on IE% and C_R

It is seen from Table 3 that at pH 8, the PN (500ppm)-Zn^{2+} (30ppm) system has 94% inhibition efficiency. When pH is lowered to 4 by addition of HCl the inhibition efficiency decreased from 94% to 71%. This is due to the fact that when the acid is added the protective film is broken by the aggressive H^+ ion present in the acid [23]. When the pH is increased to 12 by addition of diluted sodium hydroxide solution, the inhibition efficiency is increased to 71% to 82%, due to the fact that the phenolic –OH groups would have been ionized to phenolate anion (O^- Na^+). The phenolate anion helped the anchoring of phenolic O^- on the anodic sites of the metal surface effectively and hence inhibition efficiency increased at higher pH values, therefore when the value of pH is increased, the corrosion inhibition efficiency also increased [24]. The results are given in Table 3. The effect pH on the C_R for PN-Zn^{2+} system is plotted in Figure 4.

Effect of Temperature on Inhibition Efficiency and Corrosion Rate

The influence of Temperature on Inhibition efficiency and corrosion rate for an ethanolic extract of PN leaves on carbon steel in well-water are studied by using weight-loss study. When the temperature is increases the corrosion rate was increased with increasing in concentration of inhibitor as well as the inhibition efficiencies are decreased when temperature is increased. This is mainly due to the fact that the adsorbed layer is unstable and easily damaged at higher temperature [25-26].The inhibition efficiency is found to be decreased from 94% to 70% [303K-343K]. This shows that the adsorption of the extract on the carbon steel may be due to physisorption. However, the inhibitor could be effectively used at 303K and the optimum inhibition efficiency of 94% was achieved, the results are given in Table 4. The effect of temperatures on inhibition efficiency is shown in Figure 5.

Potentiodynamic Polarization Study

The polarization studies were used to calculate the corrosion parameters for PN-Zn^{2+} system in well-water on the carbon steel surface. The corrosion parameters are given in Table 5. The polarization curves for PN-Zn^{2+} and well-water system is shown in Figure 6. When carbon steel is immersed in well-water, the corrosion potential (E_{corr}) is 580mV vs SCE. When 500ppm of PN and 30ppm of Zn^{2+} are added to the above system, the corrosion potential value obtained -586mV vs SCE, therefore the corrosion potential shifted to cathodic side. As there is not much change in the corrosion potential value, it is concluded that the inhibitor system perform as a mixed type-inhibitor [27] and this

formation controls the cathodic reaction predominantly [28-29]. The anodic slope value is found to change from 116.23mV/decade to 151.98mV/decade and the cathodic slope value from 110.88mV/decade to 175mV/decade. The corrosion current decreases from 5.5431μA/cm^2 to 0.1255μA/cm^2. The linear polarization resistance (LPR) value was increased from 963Ωcm^2 to 3849Ωcm^2, these results suggest that the formation of protective layer on the metal surface [30-31].

AC Impedance Spectra

Electrochemical impedance study was used to calculate the R_{ct} and C_{dl} value for PN-Zn^{2+} system on carbon steel surface in well-water. When carbon steel immersed in well-water, the R_{ct} value is 391Ωcm^2. When 500ppm of PN and 30ppm of Zn^{2+} was added to the above system, the R_{ct} value is 2815Ωcm^2. Therefore the charge transfer resistance (R_{ct}) value was increases from 391Ωcm^2 to 2815Ωcm^2. This result indicates that the adsorbed extract forms a protective layer which becomes barrier to hinder the mass and charge transfer processes. The C_{dl} value is 1.3137μF/cm^2 when carbon steel is immersed in well-water. C_{dl} value is 0.02655μF/cm^2, when 500ppm of PN and 30ppm of Zn^{2+} is added to the above system. Therefore the C_{dl} value was decreased from 1.3137μF/cm^2 to 0.02655μF/cm^2, due to the thickness of electrical double layer was increased [32-33]. This result suggests that the adsorption of inhibitor molecules take place at metal-solution interface [34-35]. The AC impedance parameters are given in Table 6. The AC impedance spectra are shown in Figure 7.

Analysis of FT-IR Spectra

The FT-IR Spectrum of dried PN extract is shown in Figure 8a. The FT-IR spectrum of the layer formed on carbon steel surface by 500ppm of PN and 30ppm of Zn^{2+} is shown in Figure 8b.The stretching frequency is shifted from 1637cm^{-1} to 1617cm^{-1}. The –OH stretching frequency is shifted from 3420cm^{-1} to 3309cm^{-1}. The C-H stretching frequency appears at 1387cm^{-1}. The C-O peak appears at 1129cm^{-1}. The peak at 628cm^{-1} is due to Zn-O Stretching. From these observations, this results indicate that the presence of $Zn(OH)_2$ formed on the carbon steel surface. Therefore it is concluded that the protective layer consist of Fe^{2+}-ethanolic extract of PN leaves complex and $Zn(OH)_2$ formed on the metal surface [36].

Scanning Electron Microscopy (SEM) Analysis

SEM Study is used to the surface morphology for carbon steel in well-water in absence and presence of optimum concentration of inhibitor. Figure 9(a) indicates the finely polished surface of carbon steel Figure 9(b) for unhibited carbon steel in well-water, this image suggests that the severely corroded with highly damaged and more roughness occur on the carbon steel surface. Figure 9(c) indicates the formation of a protective layer by the inhibitor on the carbon steel surface.

Kinetic Studies on Temperatures

Arrhenius plots give the straight line according to the Arrhenius equation [37] for blank and an optimum concentration of PN leaves extract on carbon steel in well-water at various temperatures, it is suggests that the effect of temperatures on the corrosion process. The plots of $1/Tx10^{-3}K^{-1}$ vs log C_R is shown in Figure 10

$$\mathbf{lnr = A - Ea/RT}$$

Where
R is the corrosion rate
A is the constant frequency factor
E_a is the apparent activation energy

Kinetic and Thermodynamic Parameters

The kinetic and thermodynamic parameters are used to investigate the mechanism of corrosion resistance as well as type of adsorption (physisorption or chemisorption). The high positive value of Ea suggests that the rate of corrosion

is reduced on carbon steel surface using an ethanolic extract of PN leaves, due to physisorption [38]. From the corrosion rate values, the values of activation energy (E_a) are calculated using the following Arrhenius equation

$$E_a = 2.303R\log\left(\frac{C_{RT1}}{C_{RT2}}\right)\left[\frac{T_1T_2}{T_2-T_1}\right]$$

C_{RT1} is the corrosion rate of the lower temperature (T_1)
C_{RT2} is the Corrosion rate at the higher temperature (T_2)
R is gas constant (8.314 J/mol)
The values of enthalpy change (ΔH) are positive in sign, the positive value of enthalpy change (ΔH) indicates that the endothermic nature of the reaction. From the activation energy values (E_a), the enthalpy change (4) is calculated using following equation. The result is given in Table 7

$$\Delta H = E_a - RT$$

The free energy of adsorption (ΔG_{ads}) is calculated using the following equations are given in table 8.

$$\Delta G_{ads=2.303RT\log(55.5K_{ads})}$$

Where, 55.5 is the molar concentration of water in solution,

$$K_{ads} = \frac{\theta}{C(1-\theta)}$$

Where,
θ is surface coverage
C is concentration of inhibitor
The heat of adsorption was calculated using the equation

$$q_{ads=}2.303R\left[\left(\frac{\theta_{T2}}{1-\theta_{T2}}\right)-\log\left(\frac{\theta_{T1}}{1-\theta_{T1}}\right)\left(\frac{T_1T_2}{T_2-T_1}\right)\right]$$

θ_{T1} is the surface coverage at lower temperature (T_1)
θ_{T2} is the surface coverage at higher temperature (T_2)
The entropy of adsorption (ΔS_{ads}) was calculated using the below relationship

$$\Delta S_{ads=}\frac{q_{ads}-\Delta G_{ads}}{T}$$

From the above result ΔG_{ads} and q_{ads} values are negative in sign, the negative values of ΔG_{ads} and q_{ads} indicate that the adsorption of inhibitor system on carbon steel surface is physisorption with a spontaneous process [39-40] as well as K_{ads} value confirm that the physisorption on the carbon steel surface. The thermodynamic parameters are given in Table 8

Adsorption Isotherms

Adsorption isotherms are used to identify the interaction of the adsorbed molecules and the mechanism of corrosion inhibition on the metal surface [41]. The observed inhibitive action of ethanolic extract of PN leaves could be due to the adsorption of its molecules on the carbon steel surface making a barrier for charge and mass transfer between the metal and the environment [42]. The relationship between the surface coverage and the inhibitor concentration forms a basis to the study of the mechanism of adsorption isotherm [42]. Several attempts were made to fit data obtained from degrees of surface coverage at various concentration of the inhibitor into various adsorption isotherms [43]. All these isotherms are represented as follows [43].

$$f(\theta,x)\exp(-2a\theta) = KC$$

Where,

$f(\theta, x)$is the configurational factor,

θis the surface coverage,

C is the concentration of the inhibitor

X is the molecular interaction parameter

K is the equilibrium constant

The Langmuir adsorption isotherm is expressed as follows.

$$\frac{C}{\theta} = \frac{1}{K_{ads}} + C$$

EI-Awady adsorption isotherm is represented by using the following equation

$$\log\left(\frac{\theta}{1-\theta}\right) = \log K + y \log c$$

Where, K_{ads} is equilibrium constant of the adsorption process. It is related to k by

$$K_{ads} = K^{1/y}$$

Flory-Huggins adsorption isotherm is represented by

$$\log\left(\frac{\theta}{C}\right) = \log K + x\log(1-\theta)$$

Where,

X is the size parameter,

Temkin adsorption isotherm is expressed by following equation

$$\theta = \frac{-2.303 \log K_{ads}}{2a} - \frac{2.303 \log C}{2a}$$

Where, a is the lateral interaction parameter. This isotherm graph is drawn by taking Θ in the y axis and log c in the x axis.

When data of regression coefficient (R^2) for Langmuir isotherm is deduced and compared with other adsorption isotherms, Langmuir isotherm is the best suitable for the adsorption processes over the carbon steel using ethanolic extract of PN leaves. The results are given in Table 9. The various isotherm plots for the adsorption of ethanolic extract of PN leaves on carbon steel surface are shown in Figures [Figure 11-14]

CONCLUSION

An ethanolic extract of *Pentatropis nivalis* is considered as a protective and more effective inhibitor for reducing the corrosion on the carbon steel in well water. The inhibition performance was found to increase with increase in immersion period of extract of PN leaves but reduced with increases in temperature. When pH level is increases, the inhibition efficiency was increased and also corrosion rate was decreased. Tafel slope indicates that the ethanolic extract of PN leaves acts a mixed-type inhibitor. Nyquist plots and SEM analysis suggest that the protective layer formed on carbon steel surface by using ethanolic extract of PN leaves. FT-IR spectra confirm that the formation of Fe^{2+}-ethanolic extract of PN leaves complex over the carbon steel surface. The adsorption of process of ethanolic

extracts of PN leaves follows the Langmuir adsorption isotherm. The phenomenon of physisorption was kinetic and thermodynamic parameters obtained, therefore the ethanolic extract of PN leaves can be considered as an eco-friendly and effective natural plant corrosion inhibitor for carbon steel in well-water.

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Table: 1 Taxonomy of *Pentatropis nivalis*

S.No.	Kingdom	Plantae
1	Class	Magnoliopsida
2	Order	Gentianales
3	Family	Apocynaceae
4	CommonName	White milkweed
5	Tamil Name	Malaiyerukku
7	Genus	*Pentatropis*
8	Species	*Pentatropis nivalis*

Table: 2 Effect of immersion period on PN-Zn^{2+}system

Immersion Period (days)	Corrosion Rate		IE%
	Well water (mmpy)	PN-Zn^{2+} (500:30ppm) (mmpy)	
1	0.1809	0.0109	94
3	0.2013	0.0342	83
5	0.2124	0.0510	76
7	0.2158	0.0690	68

Table: 3 Influence of pH on IE and CR for PN-Zn^{2+}inhibitor system (Period of Immersion: one day)

System	pH		
	3	8	12
Well-water CR (mmpy)	0.2067	0.1809	0.1912
PN-Zn^{2+}(500ppm-30ppm) CR (mmpy)	0.0599	0.0109	0.0344
Inhibition efficiency (%)	71.00	94.00	82.00

Table: 4 Effect of temperatures on IE and C_R for combined inhibitor systems

Concentration of combined inhibitor system(ppm)	303K		313K		323K		333K		343K	
	IE%	CR	IE%	CR	IE%	CR	IE%	CR	IE%	CR
Blank	-	0.1809	-	0.2248	-	0.2437	-	0.2728	-	0.3102
100	49	0.0923	45	0.1849	40	0.2007	36	0.2329	30	0.2801
200	62	0.0687	58	0.1686	52	0.1842	48	0.2119	41	0.2311
300	74	0.0470	70	0.1406	65	0.1642	60	0.1902	53	0.2031
400	86	0.0253	81	0.1265	76	0.1492	70	0.1792	63	0.1802
500	94	0.0109	90	0.1126	84	0.1342	77	0.1652	70	0.1698

Table: 5 Polarization parameters for PN-Zn^{2+}system

System	E_{corr} (mV) vs SCE	b_a [mV/decade]	b_c [mV/decade]	LPR [Ω cm^2]	I_{corr} [µA/cm^2]	IE%
Well water (Blank)	-580	116.23	110.88	963	5.5431	-
PN-Zn^{2+} (500:30ppm)	-586	151.98	175.23	3849	0.1255	97.74

Table: 6 AC impedance parameters of wellwater and PN-Zn^{2+}system

System	R_{ct} (Ω cm^2)	C_{dl} (µF/cm^2)	IE%
Well water (Blank)	391	1.3137	-
PN-Zn^{2+} (500:30ppm)	2815	0.02655	86.11

Table: 7 Kinetic parameters

Concentration of combined inhibitors	Ea KJ/mol	ΔH KJ/mol
Blank	17.1	14.6
100	54.8	52.2
200	70.8	68.2
300	86.4	83.9
400	126.9	124.4
500	184.1	181.6

Table: 8 Thermodynamic parameters

Temperatures (K)	K_{ads}	ΔG_{ads} KJ/mol	q_{ads} KJ/mol	ΔS_{ads} KJ/mol
303	31.3	-18.8	-43.7	-0.206
313	18.0	-17.9	-45.32	-0.202
323	10.5	-17.1	-40.3	-0.178
333	6.7	-16.4	-34.3	-0.152

Table: 9 R^2 values for various isotherms

Various isotherm of combined inhibitor system	R^2
Langmuir	0.995
Flory-Huggins	0.942
El-Awady	0.975
Temkin	0.993

Figure: 1 appearance of *Pentatropis nivalis*

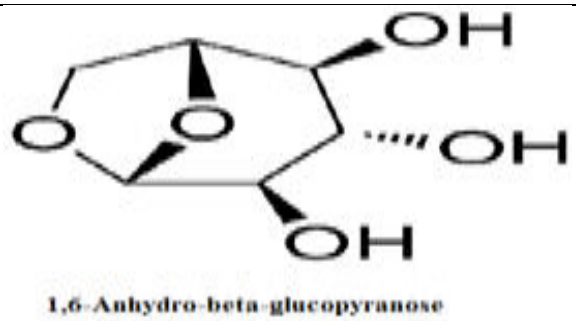

Figure: 2 Major active constituent observed in ethanolic extract of PN leaves

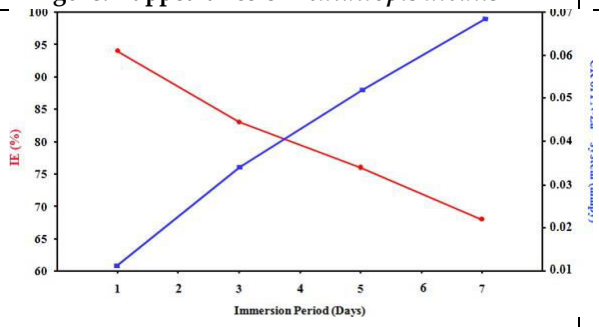

Figure: 3 Influence of immersion period on the IE and CR for PN-Zn^{2+}system

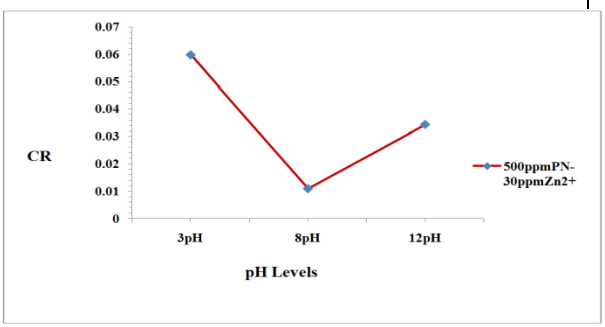

Figure: 4 Effect of pH on corrosion rates at 500ppm of PN and 30ppm of Zn^{2+} system

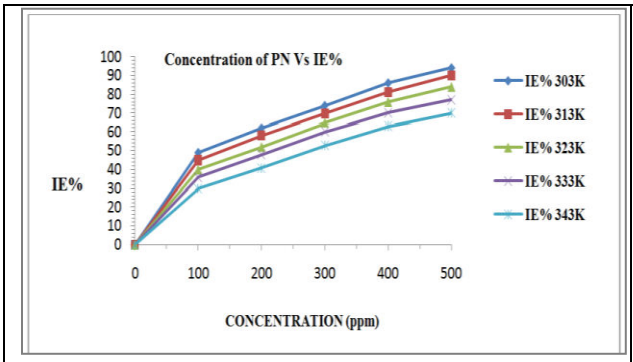

Figure: 5 Effect of temperatures on IE for PN combined inhibitor systems

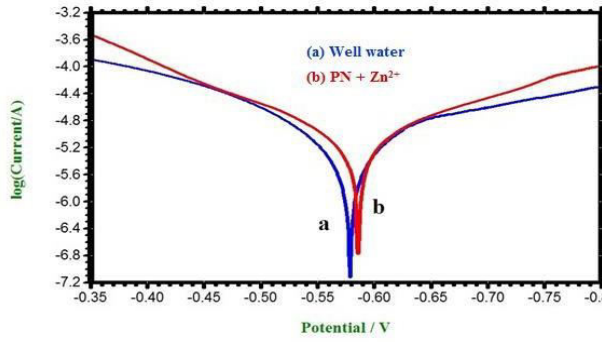

Figure: 6 Tafel curves in well-water (a) and PN-Zn^{2+}system (b)

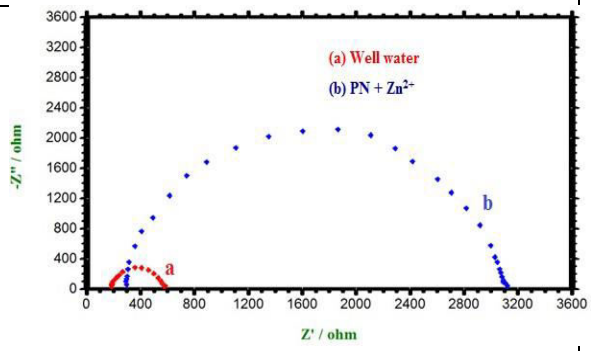

Figure: 7 AC impedance spectra of (a) well-water and (b) PN-Zn^{2+} system

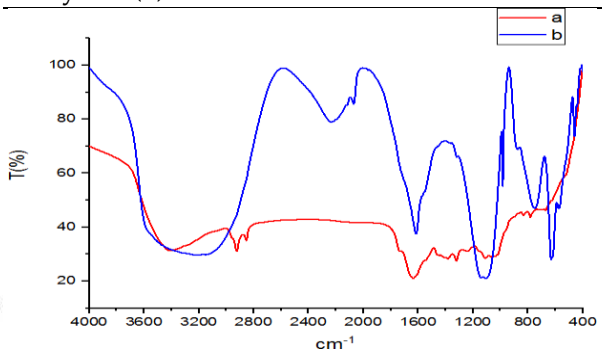

Figure: 8 FT-IR spectra of (a) Dried PN extract and (b) PN-Zn^{2+} (500:30ppm) system

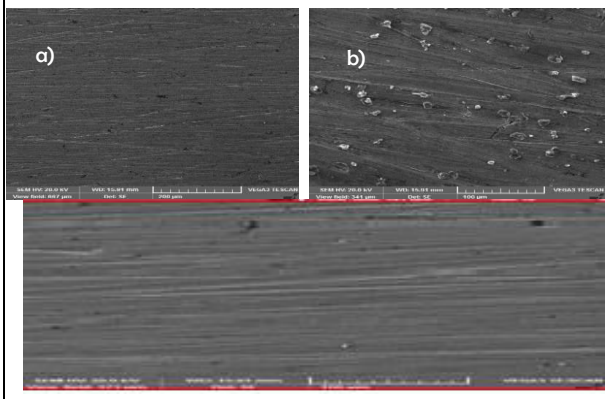

Figure: 9 SEM images for polished carbon steel (a), well-water (b), and PN-Zn^{2+} system (c)

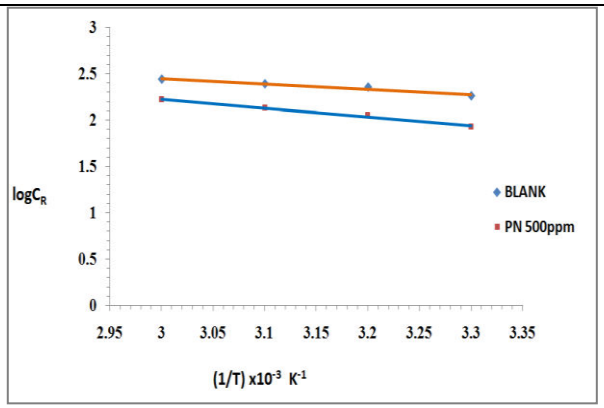

Figure: 10 Arrhenius plots for blank and 500ppm of PN

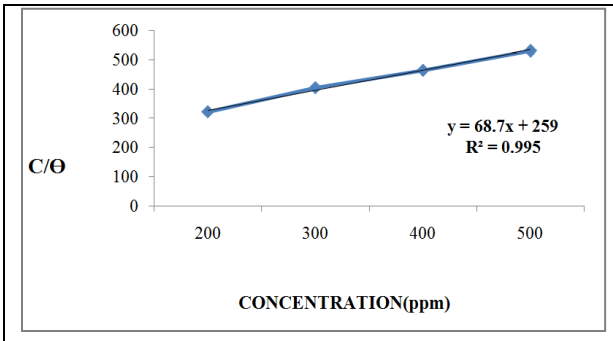

Figure: 11 Langmuir adsorption isotherm of PN inhibitor system at 303K

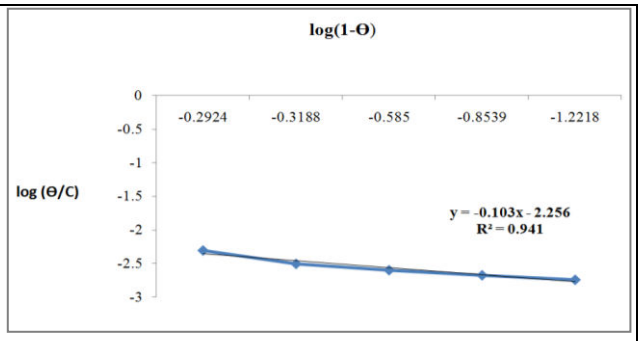

Figure: 12 Flory – Huggins adsorption isotherm of PN inhibitor system at 303K

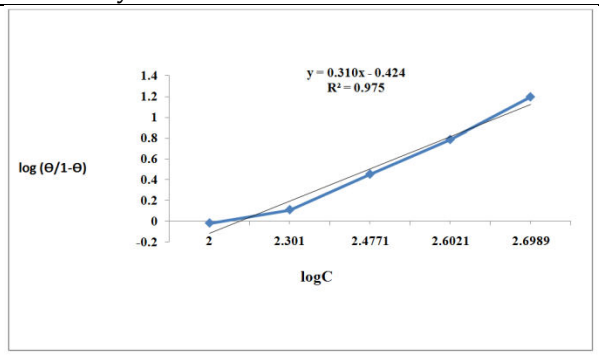

Figure: 13 El-Awady adsorption isotherm of PN inhibitor system at 303K

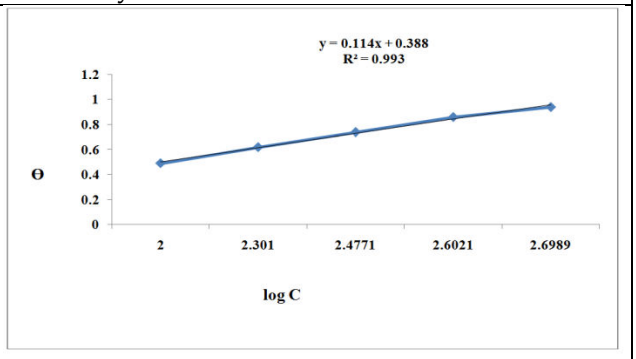

Figure: 14 Temkin adsorption isotherm of PN inhibitor system at 303K

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RESEARCH ARTICLE

Scintillators for an Imaging system

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ABSTRACT

When anyone visits medical for checkup, doctors immediately refer him/her for diagnosis. Out of many diagnosis medical imaging is one important one. This imaging can be done with the help of special gamma camera and special electronics. The main part of these cameras are the scintillators. In this paper various types of scintillators has been discussed which are used for the imaging system.

Keywords: CT ,MRI, X-Ray.

INTRODUCTION

To describe the performance of an imaging system for diagnostic the most and the important part is the detection unit which detects the gamma emitted by the different parts of the body. [1-4] These detectors are called as the scintillators. A complete review of these scintillators has been discussed bellow. .

Scintillators

The various types of scintillators the major one are described bellow [5-8] .Major scintillators with their properties. CsI(Tl) - The Thallium doped Cesium Iodide (whose density is 4.51 g/cm^3) is the scintillator used in many places having a high scintillation efficiency of about 54 photons per keV. Its peak emission (550 nm) is not optimal for the coupling with the photocathodes, however, it is possible to use it with photodiodes and considering the Silicon Drift Detectors (SDDs), this material is a good choice . It is only slightly hygroscopic and therefore there is not the necessity to encapsulate it. The main limitation of this material is the primary decay time, approximately 1 μs, which sets a limit to the high count rate capability of the detector. CsI(Na). The Sodium doped Cesium Iodide has the same density of the CsI(Tl), however is light yield is minor and equal to about 39 photons per keV. Its emission peak (420 nm) allows its coupling with the spectral response of most photocathodes on the market, with an overall behavior similar to that of NaI(Tl), compared to which, however, is much less hygroscopic, to the extent that for many

applications does not need mechanical encapsulation. Its primary decay time is equal to about 630 ns. Finally, because the CsI crystals operate well at high temperatures and are quite rugged, they are both used in space research or other applications where severe shock conditions are encountered.

LaBr3(Ce) - The Cerium doped Lanthanum Bromide also called BrilLanCe 380, may be used as an alternative to CsI(Tl) with the SDDs photodetectors, however its emission peaks at a wavelength of 380 nm does not make it perfectly compatible with them, but more suitable for photomultiplier tubes. It has a very fast primary decay time of only 16ns, a high light yield of about 63 photons per keV and offers the best energy resolution among the various scintillators. Its density is equal to 5.08 g/cm^3 and, differently from the CsI, is hygroscopic so it needs to be encapsulated.

NaI(Tl) - The Thallium doped Sodium Iodide is the most popular and extensively used scintillator. It has a high light yield of about 38 photons per keV and excellent coupling with the spectral response of the photomultiplier tubes (wavelength of maximum emission at 415 nm). Its main problem is that it is strongly hygroscopic, tending rapidly to form a layer of sodium hydroxide if exposed to air, decreasing its performance. It is therefore necessary to encapsulate it, with a consequent increment in the production cost. It is also not easy to work and is difficult to build arrays of single crystals. Finally, another problem is that it is susceptible to damage from radiation and prolonged periods of exposure will ruin its performance. Its density is 3.67 g/cm^3 and its primary decay time is about 250ns.

BGO - The Bismuth Germanate (whose complete formula is $Bi_4Ge_3O_{12}$) is a very dense scintillator (7.13 g/cm3) and therefore shows a high stopping power. It has a primary decay time of about 300 ns without appreciable effects of phosphorescence. The wavelength of the emission peak (480 nm) couples particularly well with the spectral response of the photodiodes rather than with the majority of the photocathodes, although both may be employed. It is not hygroscopic and shows good characteristics of mechanical and chemical stability in comparison with the previous types, however its scarce emission of light (8-10 photons per keV) makes it more suitable for the detection of high energy particles, or photons of more than a few MeV [9-10]. LYSO - The Cerium doped Lutetium (whose complete formula is $Lu_{1.8}Y_{0.2}SiO_5$:Ce and is also called PreLude 420) is another very dense scintillator (7.1 g/cm3) which is used in the same fields as the BGO. It has a short decay time (41 ns) and its wavelength of the emission peak (420 nm) matches well with the sensitivity spectrum of most photomultiplier tubes. It is not hygroscopic and its light yield (32 photons per keV) is about 4

SUMMARY AND CONCLUSION

A detail description of the scintillators has been presented including the properties. It is very important for the medical imaging and image analysis including a good image. Good image with high resolution is always important in medical where these scintillations play a very important role.

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RESEARCH ARTICLE

Concomitant Administration of *Syzygium jambolanum* Leaf Extract with Oral Antihyperglycemic Agents in Type 2 Diabetes Mellitus

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ABSTRACT

The incidence of diabetes which is characterized by the elevated blood glucose level is raising at an alarming rate in the past few decades and the underlying factors are many including lifestyle change and the presence of related ailments. Added to this is the complication encompassing diabetic ketoacidosis, diabeticretinopathy, diabetic nephropathy and diabetic neuropathy. In such a scenario; the striking antidiabetic effects from the plant sources have acquired attention and study in the recent times. A strong source which has shown to exhibit such hypoglycemic effects have been observed in the methanolic leaf extract of *Syzygium jambolanum* [1].Due to this reason it is often employed in the homeopathic system of medicine for the treatment and control of type 2 diabetes mellitus[2]. This case report is aimed at observing the potential hypoglycemic effect exhibited by the leaf extract of *Syzygium jambolanum* in concomitant administration with antihyperglycemic agents in uncontrolled diabetes state.

Keywords: Diabetes mellitus, *Syzygium jambolanum,* blood glucose, hyperglycemia, hypoglycemia

INTRODUCTION

Diabetes mellitus is associated with the inability of cells to transport glucose from bloodstream into adipose tissue due to defect in insulin action. Insulin is a pancreatic hormone that regulates carbohydrate metabolism, reduce blood glucose level, promote the storage of fuel molecules in liver and skeletal muscle. *Syzygium jambolanum* is a usually utilized therapeutic plant for the treatment of different issues, particularly diabetes mellitus and its intricacies. Numerous studies have demonstrated that various species of the *Syzygium jambolanum* plant are known to have a wide scope of restorative properties, powerful in bringing down blood glucose levels just as countering the effects of hyperglycemia. A few in-vitro considers have been done in the past to distinguish the hypoglycemic properties of

Syzygium jambolanum [3]. The fruit and seeds of *Syzygium jambolanum* (family: myrataceae) found in Brazil, India and Pakistan have been used to treat diabetes mellitus .The phytochemical constituents of the plant are anthocyanins, ellagicacid, myricetin, kaemferol, glycoside, and the seed are rich in alkaloid, jambosine , antimellin which are involved in the mediating the inhibition of the process where the starch in the body are converted to sugar and thereby increase the glycemic content in blood . In any case, not many considers have been done in people and recent advances and the application after the establishment of the safety profiles in the field of homeopathic therapy has shown incredible blood sugar lowering effects.

Hormones such as glucagon and epinephrine which convert glycogen and triglycerides into glycerol and the constituents of *Syzygium jambolanum* elicit an opposite effect to these hormone actions. The *Syzygium jambolanum* methanolic leaf extract has insulin-like properties and may be useful as potential therapeutic agent in the management of hyperglycemia [4,5].Diabetes causes long-term damage, dysfunction, and failure of various organ systems (heart, blood vessels, eyes, kidneys, and nerves), leading to disability and premature death. The seriousness of harm activated by hyperglycemia on the particular organ frameworks might be identified with how long the illness was present and how well it has been controlled. A few indications, for example, thirst, polyuria, obscuring of vision, and weight reduction likewise go with diabetes. T2DM results from the body's ineffectual utilization of insulin and hyperglycemia and represents most by far of individuals with diabetes around the globe. Insulin resistance is because of a decreased responsiveness of target tissues to typical circling levels of insulin. Ethnicity, family ancestry of diabetes, and past gestational diabetes, age, overweight and stoutness, eating regimen, physical latency, and smoking increases the chances of being affected by diabetes [2]. Most people with diabetes are affected by T2DM diabetes (90%), usually occur nearly entirely among adults but, in these days, is increasing in children. From the various sources, the hypoglycemic effects of *Syzygium jambolanum* has been recorded and the significant control in the glycemic levels along with the administration of other oral antihyperglycemic agents. [6,7,8] So, this case presented is based on the observation and application existing manuscripts for the expected effects.

Case presentation

A 54-year-old man with no significant medical history, no toxic habits and an active lifestyle was diagnosed with type 2 diabetes mellitus at the primary care consultation after displaying symptoms like polyuria and polydipsia for several weeks. High analytical levels of serum glycosylated hemoglobin (HbA1c) confirmed the diagnosis. The primary care physician started treatment with metformin. Three months later, patient increased the levels of glycosylated hemoglobin [HbA1c]. Ten months after the diagnosis, poor glucose controls and high levels of glycosylated hemoglobin persisted [HbA1c] so his physician recommended insulin therapy and referred him to the diabetes mellitus type 2 specialist consultation at the hospital.

Doctor advised him to meet a homeospecialist to take *Syzygium jambolanum,* and the in the follow-up consultation the co administration of *Syzygium jambolanum* showed significant reduction in the blood sugar levels**.** Doctor adviced him to take *Syzygium jambolanum* because metformin studies showed the presence of N-nitrosodimethylamine (NDMA)**,** which potentiate cancer. EMA advised patients to continue to take metformin medication as the risks from not treating diabetes far outweigh any possible effects of the low levels of NDMA seen in tests.6 December 2019, EMA confirmed that trace amounts of NDMA had been found in a small number of metformin-containing medicines.

DISCUSSION

From the data received, the hypoglycemic effects of *Syzygium jambolanum* is clearly observed where the blood glucose levels have dropped from 190 mg/dl to 126 mg/dl in the fasting state and the post prandial blood sugar level reduced by 30 mg/dl units within in 3 months. *Syzygium jambolanum* as per the mechanism involved an alternative to insulin. Insulin is known to inhibit lipolysis induced by epinephrine as well as promote lipogenesis and glucose uptake adipocytes. Methanolic leaf extract of *Syzgium jambolanum* induced significant lipogenesis at dose (0.1 to 10

mg/ml). They also inhibit epinephrine induced lipolysis. It did not enhance the antilipolytic action of propranolol. whereas this extract inhibited isoproterenol thus induce lipolysis, finally understood that they have binding with beta adrenergic receptors.

Detection of compliance

The regimen required strict patient compliance to bring out the desired therapeutic effect. The compliance was evaluated by measurement of the blood glucose levels in the patient blood sample and was testified by the patient self-report and interview. The medication adherence was crucial in this case as it involved the maintenance of the pharmacological activity of a agent with hypoglycemic effects. The observed extend of effect was possible only because of the stringent compliance of the patient to the medication regimen.

CONCLUSION

On the basis of the current case and reported studies *Syzygium jambolanum* have proved to, bring down the blood glucose levels where the active ingredients present exhibit insulin like properties. The concomitant administration of *Syzygium jambolanum* along with the hypoglycemic agents can potentially control hyperglycemia. Hence, it can be considered as an efficient treatment option. Advances in traditional medicine research have significantly fueled the drug development of novel entities for diabetes. It is worth noting that only a few medicinal plants have been studied for efficacy in humans. The majority of the reports failed to provide the authority's name of herbs, the composition of the formulation, and preparation procedures. Most methods used for clinical trials were poorly designed, leading mostly to inconclusive findings. Therefore, more efficient clinical studies are warranted for further validation. Moreover, as future perspectives, the medicinal plants described may be useful in the design of new functional nutraceuticals with antidiabetic properties or for avoiding hyperglycemic effects of some foods like those rich in simple carbohydrates.

CONFLICT OF INTEREST

There is no conflict of interest to declare

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Table 1: The recording of the fasting and post prandial blood sugar level in the patient who without concomitant administration of *Syzygium jambolanum*.

Month (2019)	Fasting blood sugar	Normal value (mg/dl)	Post prandial blood sugar	Normal value (mg/dl)
June	163mg/dl	(70-110)	215mg/dl	(70-140)
July	175 mg/dl	(70-110)	203mg/dl	(70-140)
August	168 mg/dl	(70-110)	229mg/dl	(70-140)
September	190 mg/dl	(70-110)	209mg/dl	(70-140)

Table 2: The recording betterment of the fasting and post prandial blood sugar level in the patient who with concomitant administration of *Syzygium jambolanum*.

Month (2019)	Fasting blood sugar	Normal value (mg/dl)	Post prandial blood sugar	Normal value (mg/dl)
October	150mg/dl	(70-140)	180mg/dl	(70-140)
November	135mg/dl	(70-140)	176mg/dl	(70-140)
December	126mg/dl	(70-140)	177mg/dl	(70-140)

Hence, Syzygium jambolanum exhibited potential hypoglymeic properties in this case.

REVIEW ARTICLE

Review Study on Natural and Synthetic Coating Materials used for Tablet Dosage Forms

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ABSTRACT

Tablet coating is a common pharmaceutical technique of applying a thin polymer- based film to the tablet or granule which contains a active pharmaceutical ingredients (APIs). The primary components of tablet coating and its properties will decide a perfect making and friability to it flow. There are various designs, process, control, compositions and equipments are in the coating of tablets. The coating has its own benefits as well as short comings based on its effectiveness. The history and the traditional techniques in coating such as sugar, enteric, film find its significant role in intake of tablets. The tablet coating involves the recent trends and techniques for innovative preparation of coating in tablets. Coating involves various defects in its size, shape and colour during its manufacturing. The coating involves the natural and synthetic polymers which own its importance in the tablet coating. Finally, the coated tablets are kept for the evaluation purpose.

Keywords: Coating, tablet, Film coating, Cell coating technology, Dry powder coating.

INTRODUCTION

Coating is a technique by which, tablet is covered by a material in its outer surface, in order to get specific benefits like protection of dosage form and controlling drug release from it. Coating can be applied in different dosage form, including tablets, capsules etc [1]. One can direct 0.01mg-1gm of medication portion by oral course of the organization by defining as a tablet. Before the tablet surface dries, the applied covering changes from a tacky fluid to cheap semisolid and in the end to a non-tacky dry surface container. The covered tablet will deliver the medicament bit by bit and accessible for absorption. The covering cycle can be uncommonly planned to control how quick the tablet disintegrates and where the dynamic medications are to be assimilated into the body after ingestion [2].

Primary components involved in tablet coating [2]

1) Tablet properties
2) Coating interaction, plan, and control, coating sorts of hardware
- Parameters of the covering cycle
- Facility and subordinate kinds of gear
- Automation in covering measures

Tablet properties

The tablet should be impervious to and chips. The ideal state of the tablet covering is a circle. The hardness of the tablet ought not be under 5 kg/cm^2. it should have great stream properties and friability[3].

Coating process design and control

The essential rule of tablet covering is straightforward. Tablet covering is the use of covering synthesis to a moving bed of tablets with the concurrent utilization of warmed air to encourage vanishing of the dissolvable. The dissemination of covering is cultivated by the development of the tablet either opposite (covering skillet) or vertical (air suspension). Development of configuration space can assist with understanding the impacts of a blend interaction of boundaries to get the ideal reaction and carry out a control system to screen the item in its life cycle [4,5]. A new advancement in drug fabricating has aided the utilization of pat (measure insightful innovation) a lot simpler for different cycles. for the tablet covering measure, pat might be executed utilizing different spectroscopic and imaging procedures to screen the covering consistency and covering thickness [6,7]. One exploratory examination broke down the CPPS (basic cycle boundaries) bury tablet covering consistency in a functioning skillet covering measure utilizing terahertz beat imaging [8]. In this work, the covering consistency was estimated by ascertaining the coefficient of variety (CV) of covering thickness [9].

Coating composition [10]

Tablet is in the lesser cost for the creation, unobtrusive for organization and taste [10].the organization of tablet made of,

- Polymers
- Solvents
- Plasticizers
- Colorants

Coating equipments [12]

A modern tablet coating system combines several components:

- A spraying system
- A coating pan
- A dust collector
- An air handling unit

Benefits of tablet coating [13-16]

The covering of tablets covers the taste, smell, or shade of the medication.

1) The pace of medication delivery can be changed and controlled as in rehashed activity, postponed discharge, enteric-covered and supported delivery items.
2) The timeframe of realistic usability of the medication can be delayed by tablet covering.
3) To improve the simplicity of gulping huge portion structures.
4) Increases the mechanical strength of the dose structure.

5) To consolidate incongruent medications together in a solitary dose structure.
6) The pace of medication delivery can be changed and controlled as in rehashed activity, postponed discharge, enteric-covered and supported delivery items.
7) The timeframe of realistic usability of the medication can be delayed by tablet covering.
8) To improve the simplicity of gulping huge portion structures.
9) Increases the mechanical strength of the dose structure.
10) To consolidate incongruent medications together in a solitary dose structure.
11) It gives physical and substance insurance and shields the medication from the gastric climate of the stomach (corrosive safe enteric covering).
12) Tablet covering improves the actual dependability of long stockpiling.

Drawbacks of tablet coating

Sugarcoating brings relatively high cost, long coating time and high bulk density due to the use of other coating materials. it is tiresome, time-consuming and requires the expertise of the highly skilled technician[17].

History of coating technique

"Panning" was the imaginative word for the way toward adding a covering to a tablet. The word panning is as yet a typical term that is utilized in the dessert shop business. In past years covering was performed essentially utilizing a pivoting drum (dish) on a stand. A covering arrangement was added, while the pivot of the container appropriated the arrangement all through the bed of tablets. The primary burden of this innovation was moderate, trusting that the covering arrangement will dry; and the stunt was to get it to dry uniform. With the appearance of film covering a film or layer, as a rule, addressing 1-3% of the complete tablet weight was splashed on utilizing a punctured dish. To diminish the general interaction time, openings were made through the dish so that treated air (hot or cold) could be gotten through the skillet, similar to a garments dryer, permitting the tablets to dry all the more rapidly. With this start of improved drying came the capacity to switch the film covering arrangement from a dissolvable based answer for a water-based arrangement [18].

Traditional coating techniques

Generally, three methods are used for tablet coating,

1. Sugarcoating
2. Film coating
3. Enteric coating

Sugar coating

The packed tablets having a glossing over are designated "glossed over tablets". The glossing over measure includes five separate tasks

a) Sealing/water proofing

Gives a dampness hindrance and solidify the tablet surface [19].

b) Sub coating

Causes a fast development the tablet size and to adjust the tablet edges [20].

c) Colouring

Gives the tablet its tone and completed Size [21].

d) Grossing/smoothing

Smooth out the sub-covered surface and expands the tablet size to foreordain measurement [21].

e) Polishing

Produces the qualities gleam[22].

- Ferrous sulphate-200mg (anaemia)

Example

- **Advil (ibuprofen)-200mg (arthritis, menstrual cramps, dental pain)**

Film coating [23,24]

This cycle includes splashing of an answer of polymer, colors and plasticizes onto a pivoting tablet bed to frame a slight, uniform film on the tablet surface. The decision of the polymer mostly relies upon wanted site of medication discharge in stomach/digestive tract or on the ideal delivery rate .if the accompanying inquiries are addressed associatively then one can go for film covering.

Ideal requirements of film coating materials [25]

a) Solubility in dissolvable of decision for covering planning
b) Solubility necessity for the expected use e.g. free water-dissolvability, moderate water solvency or ph - subordinate solvency
c) No natural tone, taste or scent
d) High strength against heat, light, dampness, air.
e) Compatible to printing strategy
f) Nontoxic with no pharmacological action
g) Film previous ought not give crossing over or filling of the embellished tablet
h) High similarity with other covering arrangement added substances
i) Capacity to deliver a rich looking item
j) High protection from breaking

example

- valsartan-320mg(heart failure, high BP)
- diclofenacpotassium-100mg(non steroidal anti-inflammatory drug

Enteric coating [26]

An enteric coating is a polymerthatperm its transit through the stomach the small intestine (enteric) be for the medicament is released.

Ideal properties of enteric coating materials,

a) Nontoxic, modest and simplicity of use.
b) Resistance to gastric liquids.
c) Compatibility with most covering arrangement parts and the medication substrate.
d) To preclude gastric misery or sickness because of disturbance from a medication
e) Formation of consistent film.
f) Susceptible/penetrable to intestinal liquid.
g) Ability to be promptly printed.

Polymers used for enteric coating are as follows [27]

- Cellulose acetic acid derivation phthalate (cap)
- Acrylate polymers
- Hydroxypropyl methyl cellulose phthalate
- Polyvinyl acetic acid derivation phthalate

example

- Aspirin-81mg(fever, muscle pain)
- Erythromycin-500mg(infection, bronchitis, pneumonia

Tablet coating techniques

Magnetically assisted impaction coating(maic)[28]

A method is set up for assessing the covering time in an attractively helped pixie activity covering (maic) gadget. the combination of the host visitor and attractive particles is expected to remain in a liquidized state where the dissemination of speeds is a maxwell–boltzmann type. it is made-up that the impact happens among the particles are huge for impinging the visitor particles onto the outside of host particles, and in this way making a semi-perpetual covering on the outside of host particles. The covering time relies upon numerous boundaries, including the number thickness of host particles, the distance across proportion of the host and visitor particles, the tallness of the liquidized molecule bed and the material properties of the host and visitor particles. there is an ideal estimation of the bed stature for which the covering time is a base. the covering time rises strongly when bed stature is more modest or bigger than the ideal worth, likewise when the distance across of host particles is improved.

Mechanism of coating in the maic. there are few stages in the mechanism of coating of maic process they are,

Stage-I : magnetic particles excitation.
Stage-II : coating material de-agglomeration.
Stage-III : shearing and spreading of coating material on the surface of the host particles (material to be coated).
Stage-IV : magnetic-host-host particle interaction.
Stage-V : magnetic–host–wall interaction.
Stage-VI : coated products synthesis

In one examination study, try was led to assess the viability of the maic gadget in adjusting the surface properties of cornstarch and cellulose (have particles) when they are covered with silica (visitor particles). it was seen that gigantic agglomerates of silica were separated into more modest essential sizes (de-agglomeration) during the maic interaction and delicate natural materials (cornstarch and cellulose) get covered maintaining nearly their unique shape and size.

Electrostatic dry coating [30]

Interestingly establishment of an electrostatic dry powder covering measure for tablets was performed by electrostatic dry powder covering in a dish coater framework. Electrostatic covering is a fit technique for applying covering to conductive substances. For fluid or dis-solvable based covering cycle of drug items, novel electrostatic dry powder covering strategy is considered as another option.

Uses of electrostatic-coating

The electrostatic covering measure is broadly helpful in

1. Paint innovation
2. Food innovation
3. Coating of living cells
4. Metal coatings
5. Coating of tablets just as cases.

Principle

The standard of electrostatic powder covering states that showering of a combination of finely grounded particles and polymers onto a substrate surface without utilizing any dis-solvable and afterward warming the substrate for

relieving on broiler until the powder blend is melded into film in this ionic charge is accounted for profoundly and a contrary charge to the covering material. Electrostatic dry covering affirms dainty, persistent and electronically punctured film to the surface. as per the charging system, there are two sorts of splashing units,

Mechanism of corona charging[30]

Instrument involves the electrical breakdown and ionization of air by striking high voltage on a sharp pointed needle like anode (for example charging pin) at the power source of the firearm. The negative particles are picked to the powder particles on their way from the weapon to the substrate. The development of particles between the substrate and the charging weapon is finished by the blend of electrical and mechanical powers. The powder passes up mechanical powers from the shower firearm. The electrical powers are gotten from the electrical field between the earthen substance and the charging tip of the shower firearm, and from the unpleasant powers between the charged particles. The electrical field can be changed in accordance with direct the powder's stream, control design size, shape, and powder thickness as it is delivered from the weapon.

Mechanism of tribo charging [30]

Tribe charging mechanism utilizes the rule of grinding accusing related of the dielectric properties of strong materials so that there will be no free particles and electrical present between splash firearm and grounded substance. Tribo charging firearms, just respected to the frightful powers and electrical powers between the charged particles. Subsequent to showering, charged particles come into the space close by to the substrate and the fascination powers between the grounded substrate and the charged particles puts aside the molecule to installment on the substrate. By mechanical powers and electrostatic fascination, the charged particles are showered to the earthen substrate. The particles store on the substrate before the aversion power of the kept particles against changed particles with rise and surpass of electrostatic fascination. When the shock power gets identical to the fascination power, particles can't see to the substrate any longer, and the covering thickness do no increment any more. Electrostatic dry covering of electrical non-directing substrates and drug tablet center is more troublesome. Different properties of powder, for example, molecule size dissemination, substance piece, tribe charging and crown charging attributes, electrical resistivity, arthroscopic, ease and shape appropriation assume a critical part on the presentation of powder covering, for example, move proficiency, film thickness, attachment and appearance.

Aqueous film coating technology [31]

The glossing over measure is tedious and it is relying upon the abilities of covering administrator, subsequently these strategy has been supplanted by film covering innovation. this procedure was begun with the utilization of natural solvents like m ethylene chloride however now has been supplanted with watery film covering because of ecological and administrative contemplation. more over the expense of any natural dissoluble is undeniably more than the expense of purged water hence, this innovation is financially high and at first it might require somewhat more venture to redesign the covering office. the need of this up-gradation emerges because of the need of higher drying limit (the inactive warmth of water is 2200 ks when contrasted with 550 ks for m ethylene chloride which suggests that to vanish water one will require multiple times more energy when contrasted with m ethylene chloride). The issues related with natural dissolvable based film covering and the benefits of watery based frameworks have for some time been perceived. the advancement researcher needs to consider three central point which can influence the film quality - rigidity of the film covering plan (predominantly dependant on polymer properties), versatility of the resultant film (mostly dependant on properties and amount of plasticizer utilized) and the film-tablet surface connection (every single fixing utilized in the covering definition can influence this cooperation and can change the bond properties of the film on the tablet surface). Because of these fundamental components, it turns out to be exceptionally major to utilize the most upgraded covering details to get the best outcomes.

Supercell coating technology [32,33]

Super-cell coating technology is a progressive tablet covering that precisely credits controlled measures of covering materials on tablets—regardless of whether they are incredibly hygroscopic or friable. Conflicting and defective condition, this "standard" practice of tablet covering regularly conveys a non-homogeneous item. since the tablets are

stacked in huge pivoting dish and vented for hot air drying, edges of tablets can get grounded off, can get filled in by covering material, and edges and corners may not be covered with the equivalent thickness as the tablet faces. The error in testimony of covering material restricts the utilization adjusted delivery coatings. In a research center, it is important to cover a few kilograms of tablets all at once, making R&D of a tablet measurements structure expensive and troublesome. super-cell coating technology additionally, hygroscopic tablets can't be covered with current innovation, nor can level or other odd shapes be continually covered. To forestall "twinning," (where at least two tablets remain together) the cycle should be run delicately.

Tablets may likewise be covered in a wurst-type covering mechanical assembly, yet tablet disintegration by and large keeps everything except the hardest tablets from being covered thus. The motivation behind this examination is to explore the idea of super-cell covering, an on-line tablet coater that utilized a special example of wind current. tablets covered at various splash rates (4, 6, 8, 10, and 12 ml/min) are inspected to explore the impact of various wetting conditions on nature of coats planned. At a shower pace of 6 ml/min, surface harshness is discovered to be lower than at the other splash rates, and the coat shows up smoothest, whereby beads appears to be appended together. at higher shower rates, the beads show up as fanning arms and scale-like designs.

Supercell (TM) Coating Technology [34]

(SCT) is a creation of niro-pharma systems viably takes care of these issues utilizing a minor, measured plan. Handling of coating technology sct's consistent little group proficient covering measure is unsurprising and effective. in sct, the tablets are covered in bunches going from 30 to 120 grams, which straightly scale up to creation limits. The tablets are covered with the covering shower the comparable way as the drying gas, which results a more proficient interaction. Because of sct's interesting air dispersion plate plan, the tablets travel exceptionally quick and presumably through the shower zone, getting just a modest quantity of covering per pass, in this manner arriving at higher Covering exactness. The interaction time is short, in a moment or two or in minutes instead of hours, and in this way gentler on the tablets. Niro-company claims that customary strategies for tablet covering have sporadic and imperfect outcomes, which prompts lopsided outcome that can influence the conduct of the tablet. This outcome can changeability that advance in importance if a little run of tablets is being shaped for clinical preliminaries. in traditional coasters, covering tablets are stacked in enormous turning skillet and vented for hot air drying, yet this implies tablet edges can get ground off, initialization examine get involved in by covering material and edges and corners may not be covered with a similar thickness as the tablet faces. These kinds of mistakes limit the utilization of adjusted delivery coatings.

Super cell coating technology may likewise use for covering of friable tablets, just as even or incredibly elliptical tablet shapes. In this interaction, drying is exceptionally firm, making it conceivable to cover amazingly hygroscopic tablets. The precision of statement is profoundly sufficient that active pharmaceutical ingredients can be layered onto tablets, and uniform layers of taste veiling or changed delivery coatings can be applied successively inside a solitary consistent clump.

Unique features of super cell coating technology [35]

a) No scale-up to boundaries
b) Continuous covering
c) Flexible measured plan
d) Short preparing time
e) Multilayer covering
f) Production limit of 6 cells coats 200k tph of 120 mg tablets
g) R&D clump size (minimum group size of 30 grams)
h) Technology Enchancing
i) Difficult-to-cover shapes
j) Tablet friability

k) "Low moistness measure" appropriate for dampness touchy materials.
l) Accuracy of covering RSD under 1% illustrated.
m) Enabling innovation.

Plunge coating [36]
Plunge covering is notable method of making meager movies for research capacities. Uniform movies might be executed on to level or barrel shaped substances. For business systems, turn covering is utilized better. the plunge covering interaction can be isolated into five phases:

a) ***Immersion :*** The substrate is drenched inside the arrangement of the covering material at a consistent speed.
b) ***Start-up :*** The substrate has stayed inside the answer for some measure of time and afterward pulled up.
c) ***Deposition :*** The dainty layer stores itself at the substrate even as it is pulled up. the speed decides The thickness of the covering.
d) ***Drainage :***Additional fluid will deplete from the surface.
e) ***Evaporation :***After that the dissolvable vanishes from the fluid, framing a meager layer.

Tablet coating defects [37]

An ideal tablet ought to be liberated from any visual deformity or utilitarian imperfection. the progressions and developments in tablet make have not diminished the issues, regularly experienced in the creation, rather have expanded the issues, fundamentally in view of the intricacies of tablet presses; and additionally the more prominent requests of value. Larger part of visual deformities are because of lacking fines or deficient dampness in the granules prepared for pressure or because of broken machine setting. useful deformities are because of blemished detailing.

Twinning [37]
Sticking of two tablets together is known as twinning and it is a common defect with Capsules and tablets.

Blushing[37]
It is where the film becomes chipped and dented, usually at the edges of the tablet.

Picking and sticking[37]
This is the point at which the covering eliminates a piece of the tablet from the center. Over wetting or inordinate film crudeness makes tablets adhere to one another or to the covering dish. On drying, at the resource, a piece of the film may remain clung to the container or to another tablet, giving a "picked" appearance to the tablet surface and bringing about a little uncovered territory of the center

Remedies
1. Reduction in fluid application rate.
2. Increase in drying temperature and air volume

Mottled colour [38]
This can happen when the covering arrangement is inappropriately arranged, the real shower rate varies from target rate, tablet centers are cold, or the drying rate is out of specification.

Bridging [39]
This happens when the covering fills in the lettering or logo on the tablet and is ordinarily brought about by inappropriate use of the arrangement, helpless plan of the tablet embellishing, high covering consistency, high level of solids in the arrangement, or ill-advised minimization pressure.

Remedies

1. Increase in plasticizes content.
2. Change in plasticized.

Erosion[40]

This can be the consequence of delicate tablets, an over-netted tablet surface, deficient drying, or absence of tablet surface strength.

Capping and lamination [42]

It is defined as when the lower or upper portion of the tablet separates horizontally i.e. either partially or completely from the main body of a tablet and comes off as a cap, during ejection of the tablet press or during subsequent handling. Division of the tablet into at least two separate layers is characterized as cover. it occurs because of air entanglement during pressure cycle or in view of development of the tablet during discharge.

Peeling and frosting [43,44]

This is a defect where the covering strips from the tablet surface in a sheet. Stripping shows that the covering arrangement didn't secure in the tablet surface. This could be because of an issue in the covering arrangement, over-wetting, or high dampness content in the tablet center.

Chipping [45]

In this, the film gets chipped, for the most part at the edges of the tablet [45].
This is the consequence of high dish speed, a friable tablet center, or a covering arrangement that comes up short on a decent plasticizer.

Orange peel [46,47]

This alludes to a coating surface that takes after the outside of an orange (excessive unpleasantness). it is imperfection where the film gets chipped and imprinted, ordinarily at the edges of the tablet. It is generally the after effect of high atomization pressure in mix with shower rates that are excessively high.

Remedies

1. Thinning of covering arrangement with extra solvents may address the issue.
2. Adjustment of speed of covering skillet

Blooming [48]

In this covering becomes dull immediately or after prolonged stretch of time.

Filling [49]

Applying to much arrangement bringing about a thick film that fills and tight the monogram or separates. furthermore, if arrangement applied too quick, over wetting may make the fluid rapidly fill and be held in the monogram.

Remedies

1. Judicious observing of the liquid application rate.
2. Thorough blending of tablets in the skillet forestall filling

Blistering [50]

Vanishing of the solvents from the center in the broiler. furthermore, impact of high temperature on the strength, flexibility and bond of the film may bring about rankling.

Remedies
Controlled milder drying conditions.

Natural coating of tablets
The natural coating is made by natural polymers without using chemicals inits preparation.

Natural polymers[51-60]
Recipients assume a significant part to change over the dynamic drugs fixing (api) in to measurement structure by guaranteeing its well-being and viability with the goal that organization can be appropriate for the patients[51]. The utilization of common polymeric excipients in drug areas is expanding day by over semi-engineered or manufactured excipients[52]. Low harmfulness, accessibility, cost adequacy, mitigating activity, non-aggravation nature are the primary reasons which make them unrivaled from others sources[53-56]. Regular polymeric excipients can be used in different definitions like solid, liquid and semisolid estimations structures where the go about as, break down, framework former, covers, film former, release modifiers, suspending expert thickeners, stabilizers, emulsifiers, sugar, and muco-stick expert [57]. Strong solid framework, films, dots, miniature particles, nano particles, inserts, inhalation and inject-able frameworks, different fluids can be detailed and made by the assistance of the characteristic polymeric excipients

Sources of natural polymers
Natural polymers are obtained from one of the three sources. these are plants, microbes and animals. from these sources, plants have the chief amount of polymeric substances as well as the varieties. some polymeric substances are obtained from animal sources and very few are obtained from the microbes [61].

Examples of natural polymers and their applications

a) Starch used as binder, disintegrant, aiding drug delivery, film coating material [62,63].
b) Guar gum is used as a binding agent. in addition, the pharmaceutical field involves the study about guar gum based on hydrogel, microparticle, and nano particle formulations.
c) Inulin in colon specific drug delivery[65].
d) Rosin in microencapsulation, film former, coating material, sustained release property, nano particle drug delivery[66-69].
e) Pectin in colon specific drug delivery, controlled release drug delivery, patch and transdermal drug delivery, nano particle drug formulation [70-73].
f) Dextran in colon specific drug delivery[74-76].
g) Neem gum in aqueous film coating [77].
h) Bhara gum in microencapsulation [78].
i) k. yaha gum as a binder [79].
j) Tamarind gum used as binder, emulsifier, suspending and sustaining agent, muco adhesive drug delivery[80-82].
k) Mimosa pudica as binder and disintegrating agent[83,84].
l) Cordia gum[85].
m) Tragacanth gum as suspending agent, emulsifier, demulcent [86].
n) Moringa oleifer gum as tablet physical characteristic enhancer[87].
o) Cashew gum as suspending agent[88].
p) Xanthum gum as suspending agent emulsifier, stabilizer, sustained release agent ,pellets[89-91].
q) Cellulose as a binder, filler, diluents, compressibility enhancer [92].
r) Hemicellulose as stabilizer of the gel phase of tablet and release modifier [93]

Examples of semi-natural polymers
✓ Chemically modified starch

- ✓ Hydroxypropyl methylcellulose(HPMC)
- ✓ Hydroxy ethyl methylcellulose
- ✓ Hydroxy ethyl cellulose

Natural polymers used in fast dissolving tablets [94]

- ✓ Chitin and chitosan
- ✓ Mango peel pectin
- ✓ Fenugreek seed mucilage
- ✓ Agar and treated agar
- ✓ Dehydrated banana powder (DBP)

Synthetic polymers

Synthetic polymers are polymer compounds that are produced artificially by humans. They do not occur naturally. these polymers are produced from chemical processes. Most polymers are hard to degrade naturally by biological processes.

Examples of synthetic polymers

- ✓ Polyvinyl liquor
- ✓ Polyvinyl liquor esters.

Examples of opacifiers

- ✓ Titanium dioxide
- ✓ Zinc oxide
- ✓ Ferric oxide
- ✓ Calcium carbonate.

Examples of plasticizers

- ✓ Polyethylene glycol
- ✓ Polysorbate glycerin
- ✓ Medium chain fatty oils
- ✓ Food oils and different lipids with low softening focuses
- ✓ Triethyl citrate

Examples of colorants[95-97]

- ✓ Tartrazine
- ✓ Quinoline yellow
- ✓ Carminic acid
- ✓ Allura red
- ✓ Patent blue
- ✓ Amaranth
- ✓ Erythrosine

Tablets examples of stabilizers and bulk agents

- ✓ Maltodextrin
- ✓ Talc

Application of synthetic polymers in clinical medicine [98]

It has been tracked down that biomedical polymers include mass materials, yet additionally coatings and drug nano-transporters for drugs.

Synthetic polymers functionalized by carbohydrates [99]
Functionalization of polymers has emerged as another important area of polymer science and technology. Chemically linking sugar moieties on to synthetic polymers is a unique method of functionalization of synthetic polymer, whereby not only is the polymer functionalized, but it can also get other desirable properties such as biodegradability a property much debated and researched in modern times.

A versatile applications of blends and composites of pullulan with natural and synthetic polymers [100]
Pullulan is a non ionic, linear, water soluble and a neutral polysaccharide. It shows non-immunogenic, non-toxic, non-carcinogenic, and non-mutagenic properties. it is used in food edible coatings, films, as flocculant, foaming agent and adhesive.

Evaluation of coated Tablets
Outward presentation, size and shape, one of a kind id making, organoleptic properties, hardness and variability, weight variety test, crumbling test, disintegration test, and so on.

Tests for coated tablets
1. Adhesion test with rigidity.
2. Diametric smashing strength.
3. Disintegration test.
4. Dissolution trial of covered tablets.
5. Temperature and stickiness changes.

CONCLUSION

In recent years, coating of pharmaceutical formulation in tablet coating gains remarkable development, efforts are there to ensure and enhance the quality of tablet dosage form. Significant development and improvement of this technology regarding energy consumption, distribution of film, drying efficiency, has taken place. Still there is a lot of scope for betterment of coating technique in future. More work can be done to get better coating solvent, drying technique and spraying methods. the natural and synthetic polymers are also plays a vital role in coating technology.

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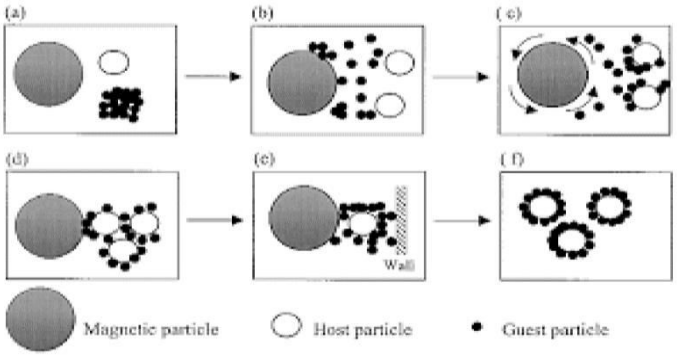

Fig: 1 The process of MAIC

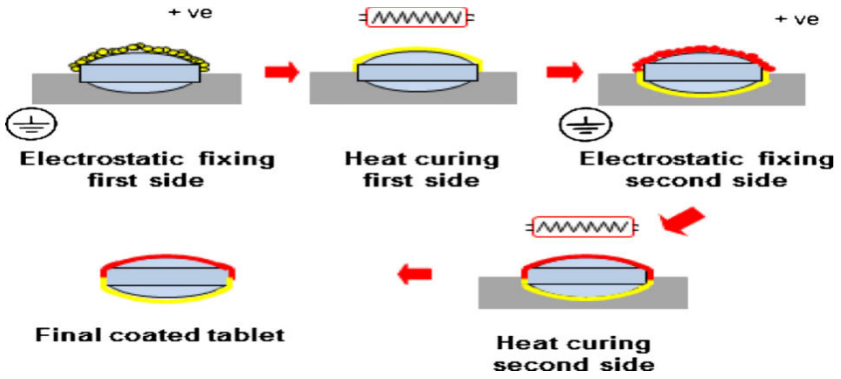

Fig: 2. Electrostatic dry coating

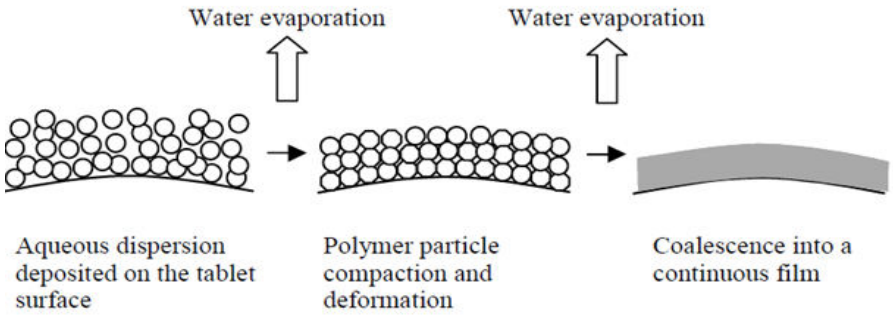

Fig: 3 Aqueous film coating of tablets

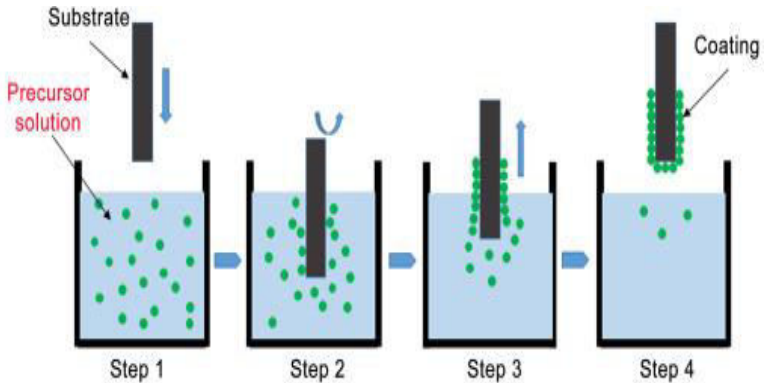

Fig: 4 Representation of dip coating

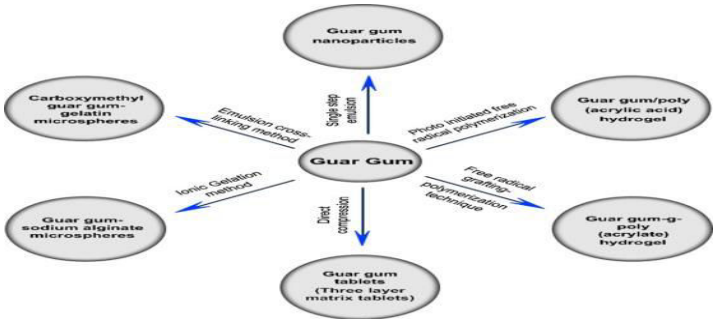

Fig: 5 Represents a chemical modification of guar gum for micro

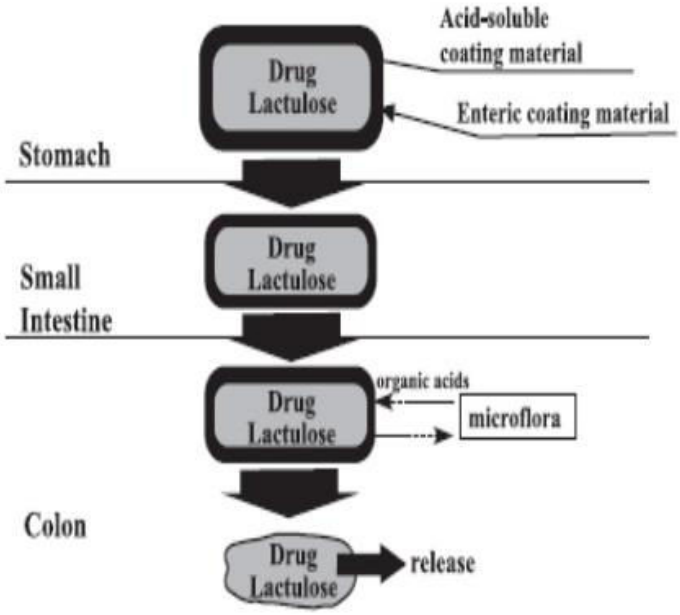

Fig: 6 Colon specific drug delivery system by polymers

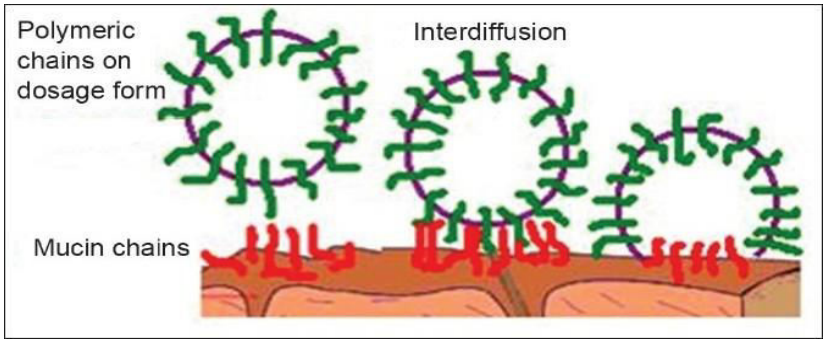

Fig: 7 Muco adhesive drug delivery system by polymers

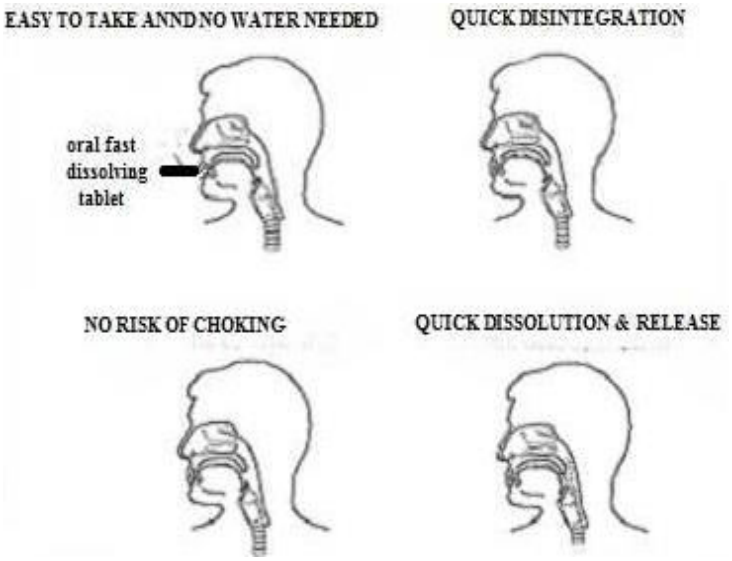

Fig: 8 Advantage of fast dissolving tablets

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RESEARCH ARTICLE

Recent Trends in Sensor and its Applications

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ABSTRACT

To meet demands in a variety of disciplines, the next generation of sensing devices will require significant improvements in sensitivity and selectivity. To meet these requirements, metal-oxide sensors based on NWs take advantage of fundamental nanoeffects. NWs are innovative, low-dimensional, lightweight materials with outstanding mechanical, electrical, thermal, and multifunctional capabilities. Electrical sensors benefit greatly from their tiny size and high aspect ratio. Different features of metal-oxide NW-based gas sensors were discussed in this instructional article, including their synthesis techniques and sensing characteristics and mechanisms. For identifying dangerous chemicals in the environment, gas sensors are essential. The morphology of a gas sensor has a big impact on its sensing ability One-dimensional nanowires (NWs) have a number of benefits over other topologies, including a large surface area, compact dimensions, high charge-carrier concentrations, easy production, high crystallinity, and stability.

Keywords: Gas sensors , lightweight, sensing devices , nanowires.

INTRODUCTION

Gas molecules are adsorbed on the surface of the substrate nano material, which is the detecting principle of the gas sensor. The gas molecule then transfers its charge to the substrate material, changing the resistivity of the substrate nanomaterial. Characteristics of gas, such as qualities and concentration, can be determined by evaluating the resistivity of the substrate nanomaterial. When it comes to substrate nanomaterials, you can choose between 0-D quantum dots, 1-D quantum wires, and 2-D quantum surfaces. In comparison to 0-D and 1-D nanomaterials, 2-D nanomaterials have a higher surface area, according to numerous studies. The ability to absorb gas molecules is enhanced by a special membranous or lamellar structure.

Literature survey

Most living organisms require a constant supply of air, which is a mixture of O2, N2, Ar, and other gases. Moreover, several gases are used in business and for personal usage. Liquefied petroleum gas (LPG), for example, is widely used for cooking and heating, as well as in a variety of industrial applications.1LPG is harmless, however it is quite explosive. Although it is highly explosive, H2 gas is viewed as the next "green fuel" and is currently employed in fuel cells. In addition to explosive gases, the number of toxic and hazardous gases has expanded dramatically in recent years as a result of increased automobile use and rapid industrialization, resulting in severe indoor and outdoor pollution as well as a variety of negative health impacts.5Toxic gases can cause injury at low concentrations over time (chronic exposure) or at higher quantities over time (acute exposure) (acute exposure).

The greatest concentration of a gas allowed for repeated exposure throughout an 8-hour working day without causing detrimental health effects is known as the threshold limit value (TLV).Carbon monoxide (CO), nitrogen dioxide (NO2), and hydrogen sulphide (H2S) gases, for example, have TLVs of 50, 3, and 10 ppm, respectively.

Measurement Systems

Dynamic and static systems are the two basic types of gas-sensing measurement devices. Gas valves and gas-flow controllers are required for the injection of the target gas into the gas chamber, which has a gas input and outlet, regardless of the kind of measuring system. The detecting temperature should be adjustable, and a gas chamber with a small volume is usually recommended to avoid long response times. Finally, the measuring equipment should be connected to a computer so that the sensor's resistance may be continually recorded in various environments. Predetermined gas concentrations with constant flow rates are delivered to the gas chamber through tubes in a dynamic system, and the flow is controlled by mass flow controllers. The sensors inside the gas chamber are linked to a measurement device, which continually records the resistance variation. The resistances of the sensor in air and in the presence of various quantities of the target gas at various temperatures are recorded during gas sensing testing.

Detector of gas

The MQ-2 gas sensor's sensitive substance is SnO2, which has a reduced conductivity in clean air. When the target flammable gas is present, the sensor's conductivity increases as the gas concentration increases. Please utilise a basic electro circuit to convert changes in conductivity to a gas concentration output signal. The MQ-2 gas sensor has a high sensitivity to LPG, Propane, and Hydrogen, and it may also be used for Methane and other combustible steam. It is inexpensive and suited for a variety of applications.

Characters

- High sensitivity to LPG, Propane, and Hydrogen
- Long life and inexpensive cost
- Simple drive circuit
- Good sensitivity to combustible gas in a wide range

Applications: Domestic gas leakage detectors, industrial combustible gas detectors, portable gas detectors. The sensor's basic test circuit is shown above. The sensor requires two voltages: a heater voltage (VH) and a test voltage (VC). The heater voltage (VH) is needed to supply the sensor with an approved working temperature, while the test voltage (VC) is required to detect voltage (VRL) on the load resistance (RL) in series with the sensor. Vc requires DC power since the sensor has light polarity. To ensure sensor performance, VC and VH could use the same power circuit with preconditioning. A sufficient RL value is required in order to improve the sensor's performance: Sensitivity Body Power (Ps):

$$Ps=Vc^2\times Rs/(Rs+RL)^2$$

The following situations must be avoided.

Organic silicon steam exposure

Sensors must be protected from organic silicon steam by avoiding contact with silicon bond, fixature, silicon latex, putty, or plastic that contains silicon.

Gas with a High Corrosive Potential

When sensors are subjected to high concentrations of corrosive gas (such as H2Sz, SOX, Cl2, HCl, and so on), not only will the sensors' structure corrode, but it will also cause significant sensitivity reduction.

Halogen contamination, alkali, alkali metals salt

If sensors are sprayed with alkali metals salts, particularly brine, or exposed to halogens such as fluorin, their performance will be adversely affected.

Put your hand in the water

When the sensors are spattered or dipped in water, their sensitivity is diminished.

Defrosting

If there is icing on the sensor's surface, the sensor will lose sensitivity.

Increased applied voltage

The applied voltage on the sensor should not exceed the specified value; otherwise, it will damage the down-line or heater, causing the sensors' sensitivity characteristics to vary dramatically.

volts on the incorrect pins

If you provide voltage to 1,3 pins or 46 pins on a 6 pin sensor, the lead will break, and if you provide voltage to 2,4 pins, the signal will be lost.

The conditions listed below must be avoided.

Condensation of Water

Indoors, small water condensation will have a minor impact on sensor function. However, if water condenses on the sensor's surface for an extended period of time, the sensor's sensitivity will be reduced.

Used when there is a lot of gas.

If a sensor is exposed to a high gas concentration for an extended period of time, regardless of whether it is electrified or not, the sensor's characteristics will be affected.

Storage for a long time

When a sensor is held for an extended period of time without being charged, it develops reversible drift; this drift is dependent to storage circumstances.

Sensors should be stored in an airtight, non-silicone gel bag with plenty of fresh air.
Sensors with a lengthy storage life but no electrification require a considerable ageing time for stbility before being used.

Prolonged exposure to a hostile environment
Whether the sensors are electrified or not, if they are exposed to an adverse environment over an extended period of time, such as high humidity, high temperature, or high pollution, the sensors' performance will suffer.

Vibration
Constant vibration will cause the sensor to down-lead and then repture.
This vibration can be caused by a pneumatic screwdriver/ultrasonic welding equipment in a transportation or assembly line.

Sensors and how they're used
Features of the Mq-3 Gas Sensor include:
- High sensitivity to alcohol and low sensitivity to benzine.
- Fast reaction and high sensitivity.
- Stable and extended life

Utilization
They can be used with an alcohol checker or a Breathalyser.
Mq-135 is a type of microcomputer.
Features of Gas Sensors
Detection range is broad
High sensitivity and quick response
Longevity and stabilitya basic driving circuit

Applications
They are suitable for detecting NH3,NOx, alcohol, Benzene, smoke, CO2, and other gases in air quality monitoring systems for buildings/offices.
Detailed specifications
A. Normal working conditions
Tc100n Gas Detector (Fixed)
The TC100N is a fixed gas detector that measures oxygen, poisonous gas, and combustible gas in areas where there is a potential gas hazardIt is suitable for use in explosive environments because it has received ATEX clearance.It connects to the control panel through a 4-20 mA analogue output or an RS485 digital signal.

Characteristics
4-20mA analogue or RS485 digital outputs are ATEX certified. For 4-20mA type, there are two relay outputs.
Sensor module design that is simple to replace.
Steelworks, petrochemical factories, shipyards, water treatment plants, mines, power plants, and the food sector are all examples of applications.

CONCLUSION

If sensors are subjected to severe concussion, the lead wire may become detached. These advantages enable the creation of tiny, versatile sensors. Increasingly sensitive, selective, and stable gas sensors with metal oxide-based NW

structures are expected to be produced in the near future, and such NW sensors will become more common in research and development.

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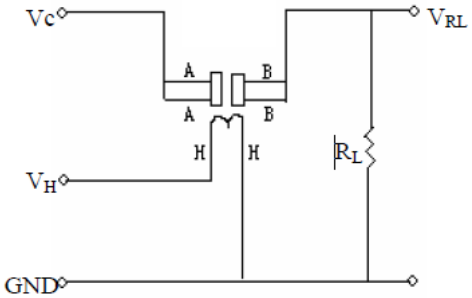

Fig.1. Circuit diagram

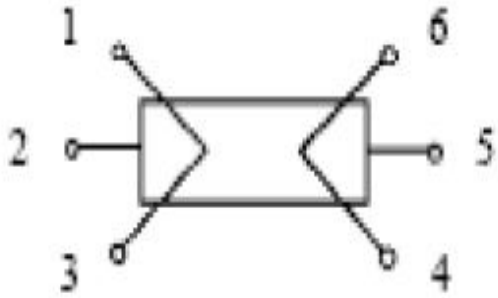

Fig.2. Pin diagram

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RESEARCH ARTICLE

Radon and Thoron Exhalation Measurement of Coal and Fly Ash Samples Using a Scintillation Detector

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ABSTRACT

Flyash, a by-product of burning coal, is one of the necessary sources of technologically increased exposure of human beings to natural radio nuclides. This study shows the results of the measured value of radon/ thoron exhalation rate. Radon (^{222}Rn) mass exhalation from fly ash samples from dumping areas was carried out using Smart Radon Monitor (SRM). Thoron (^{220}Rn) surface exhalation measurements were also made for the above samples using Scintillation-based Smart Thoron Monitor (STM). To the most effective of our data, Thoron exhalation measure is that the initial of its kind in the Asian country. during this study, a complete of twelve samples were collected from Guru Nanak Dev Thermal Plant (GNDTP), Bhatinda, Punjab, India. From measurements, the value of radon exhalation varies from 36.3mBq/Kg/h to 383.5 mBq/Kg/h with an average of 102.1 mBq/Kg/h. Thoron surface exhalation rates varied from 514.0 mBq/m^2/h to 1331.6mBq/m^2/h with an average 870.7mBq/m^2/h. This study aimed to be aware of the safety aspects of radiation point of view on coal-based thermal power stations and concludes that radiation from fly ash residues and chimney emissions built up around coal power plants. Smart radon monitoring techniques account for the effect of back diffusion and possible leakage in the process of the exponential fitting model, and there is no thorn interference during radon monitoring using smart radon monitor techniques.

Keywords: Radon and Thoron, Coal, Flyash, Exhalation, SRM, and STM

INTRODUCTION

Coal is a very important source of power generation in India. The country has at present 90,000 MW of electricity generation, of that coal combustion contributes to larger than 70% of the power generation (1). Flyash that is the

combustion of coal leads to the generation of enormous amounts of ash, which could be a major environmental problem. This problem is especially important for Indian power plants since most of the power plants use poor quality coal with 55–60% ash content. This leads to a median production of 100 million tons of ash each year(2).

Human beings have continuously been exposed to ionizing radiation from varied natural sources of radiation, and one of the main routes of internal exposure is through inhalation of radioactivity present in the atmosphere. Radon elements and their progenies are proved to be a health hazard, and their contribution is nearly about 50% to the total radiation population exposure, whereas the contribution of thoron and its decay products to the annual effective dose of radon is about 8%. It's essential to assess the emission potential of radon and thoron for the study of possible risk effects (3). Radiogenic lung cancer is the oldest type of known radiation-induced malignancy disease. It is now a well-established fact that radon, when inhaled in a large quantity, causes lung disorders and is the second major cause of lung cancer after smoking (4-5). The exposure of the population to high concentrations of radon and its daughters for a long period leads to pathological effects like respiratory functional changes and the occurrence of lung cancer. During recent years, radon monitoring has become a global phenomenon due to its health hazard effects on the population (Radiation workers and the general public). Health effects of radon are noticed in human beings as lung cancer which has been investigated from a previous couple of decades (6-7).

MATERIALS AND METHODS

In this study, samples were collected from different units of the power plant from different locations of the Guru Nanak Dev Thermal Plant. Measurement of radon exhalation from a coal-fired thermal power plant has been done. It is located at Bhatinda, Punjab, and using primary fuel as coal in the present active state and is operated by Punjab Government Power Corporation. A total of 12 samples have been collected, of which 6 from coal and 6 samples from fly ash. Collected samples from the different areas are different types in nature like coal, stone, sand, and soil type. After collection, all samples were crushed into a form of fine powder by using mortar and pestle. A fine quality of the sample was obtained by using a scientific sieve of the 150-micron mesh size. Before measurement, the samples were oven-dried at 110°c for 24 h and the samples were then packed and sealed in an impermeable airtight PVC container to prevent the escape of radiogenic gases radon and thoron. An amount of 500 grams was taken as samples for SRM and STM-based technique for measurement of radon exhalation rate and thoron exhalation rate.

The accumulation chamber technique was used to measure the radon and thoron exhalation rates. Radon mass exhalation and Thoron surface exhalation measurements were performed using BARC developed Smart Radon as shown in Fig.1 and Thoron Monitor as shown in Fig.2, respectively. About 500 grams of sample was taken in the accumulation chamber for carrying out measurements. For Radon mass exhalation rate measurement, radon built up in the accumulation chamber is sampled into the scintillation cell (150cc) of the Smart Radon Monitor through a "progeny filter" and "thoron discriminator" eliminating radon progenies and thoron. The thoron discriminator based on "diffusion time delay" does not allow the short-lived thoron ^{220}Rn (half-life 55.6 sec) to pass through. The alpha scintillations of radon and its decay products formed inside the cell are continuously counted for a user-programmable counting period by the PMT and the associated counting electronics. The alpha counts obtained are processed by a microprocessor unit as per a look-back algorithm to display the concentration of radon. The build-up radon concentration was measured at time intervals of 1 hour to attain the saturation of radon concentration. On the other hand, thoron concentration was measured at a regular time interval of 15 minutes until equilibrium is reached for thoron concentration.

CALCULATION METHODOLOGY

The radon concentration C (Bq m^{-3})at time t inside the chamber can be written as

$$C(t)= \frac{J_m M}{V\lambda_e}\left[1-e^{-\lambda_e t}\right]+C_0 e^{-\lambda_e t} \quad (1)$$

Where J_m is the ^{222}Rn mass exhalation rate (mBq kg^{-1} h^{-1}), V is the effective volume (m^3), i.e., the volume of the container + volume of the detector – a volume of sample, C is the radon concentration per unit volume of air (Bq m^{-3}), C_0 is the ^{222}Rn concentration (Bq m^{-3}) present in the chamber volume at $t = 0$. M is the mass of the sample (kg), λ_e is the effective decay constant for ^{222}Rn, which is the sum of the leak rate (if existing) and the radioactive decay constant of ^{222}Rn (h^{-1}).

Upon least square fitting the experimentally measured radon build-up data to the exponential growth equation available in the software origin

$$Y(x)= Y_0 + A_1 e^{-\frac{x}{t_1}}, \quad (2)$$

we get fitting parameters Y_0, A_1, and t_1. Comparing Eq (1) and Eq(2), we can get radon mass exhalation rate $J_m = Y_0 V\lambda_e / M$and effective decay constant $\lambda_e = 1/t_1$. A typical plot of radon build-up inside the closed chamber is given in Fig .2.

The thoron (^{220}Rn) concentration in the chamber will reach equilibrium within a short period. Then equilibrium thoron concentration (C_T) is given by the formula

$$J_T = C_T V \lambda / A \quad (3)$$

where V is the residual air volume of the set up (m^3). A is the surface area of the sample (m^2).λ is the ^{220}Rn decay constant (0.0126 s^{-1}). Hence by knowing the value of equilibrium thoron concentration, the thoron surface exhalation rate can be estimated using Eq.(3).

RESULT AND DISCUSSION

Radon mass exhalation and thoron surface exhalation rates using active techniques (SRM based) are summarized in Table.1. Histogram for the radon mass exhalation rates and thoron surface exhalation rates from coal and fly ash samples from Guru NanakDevThermal Plantpower plants shown in fig.3are and fig.4.

From the data listed in Table-1, Radon mass exhalation rate varied from 14.7mBq/kg/h to 383.5mBq/kg/h with an average of 102.1mBq/kg/h. Thoron exhalation rate varies from 514Bq/m^2/h to 1331.6 Bq/m^2/h with an average of 870.6 Bq/m^2/h. All samples have been taken from Guru Nanak Dev Thermal Plant, Bhatinda, Punjab, and the measurement technique is scintillation based in active mode.

The radon exhalation rates of the coal and fly ash samples from Panipat Thermal Power Station (PTPS) are under the limit prescribed by Radiation Protection Agencies. Effects on nearby localities around the thermal power plants can be neglect as the value obtained are under the limits prescribed by the regulatory board. Thus, fly ash appears to be safe, and bricks made from fly ash can use as building materials without imposing significant radiological hazards on the human being.

ACKNOWLEDGMENT

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Table -1. Radon/Thoron Exhalation Rate using Active Technique in samples of Guru Nanak DevThermal Plant, Bhatinda, Punjab

S. No.	Sample code	Type of sample	Weight of sample (in gram)	Radon Mass Exhalation Rate (using SRM) in mBq/kg/h	Thoron Surface Exhalation Rate (using STM) in Bq/m^2/h
1	GNDTPCA1	COAL	500	69.3	1202.0
2	GNDTPCA2	COAL	500	97.6	1159.5
3	GNDTPCA3	COAL	500	86.0	1331.6
4	GNDTPCA4	COAL	500	87.8	985.5
5	GNDTPCA5	COAL	500	147.1	1102.9
6	GNDTPCA6	COAL	500	383.5	1139.3
7	GNDTPFA1	FLYASH	500	81.5	655.6
8	GNDTPFA2	FLYASH	500	14.7	576.7
9	GNDTPFA3	FLYASH	500	56.2	514.0
10	GNDTPFA4	FLYASH	500	36.3	544.3
11	GNDTPFA5	FLYASH	500	69.8	633.4
12	GNDTPFA6	FLYASH	500	95.6	603.0
AVERAGE				102.1	870.6

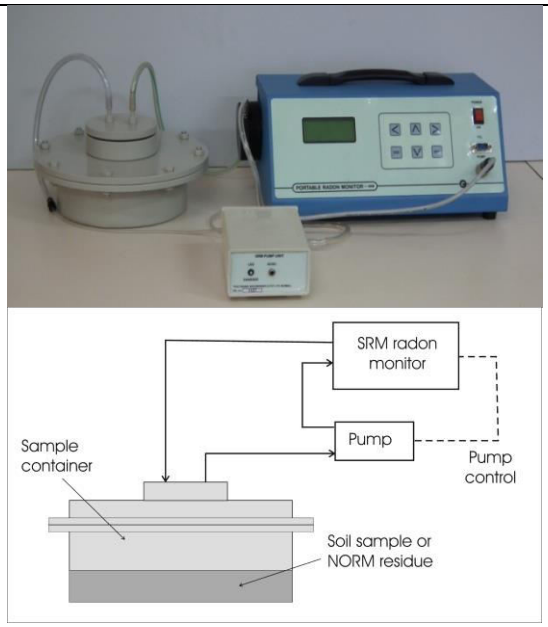

Fig.1: Photograph and schematic diagram of the radon/thoron exhalation measurement set up

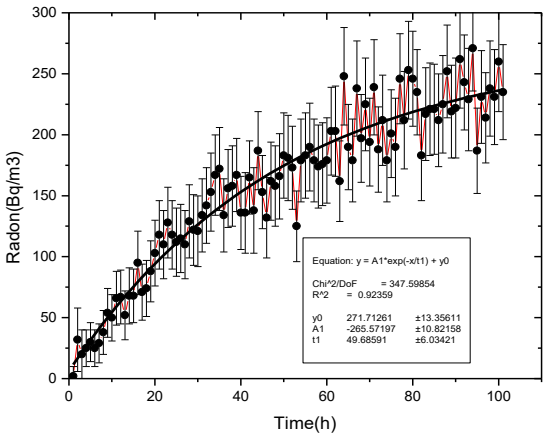

Fig.2:Least square fitting of Eq. (2) to data plotted between radon concentrations in the chamber with time.

Equations (2) and (3) were used for calculating radon exhalation rates and thoron exhalation rates for coal and fly ash samples (8-9).

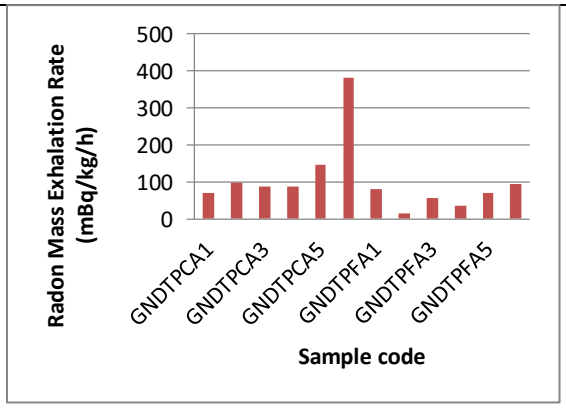

Fig.3: Bar diagram of Radon mass exhalation rate

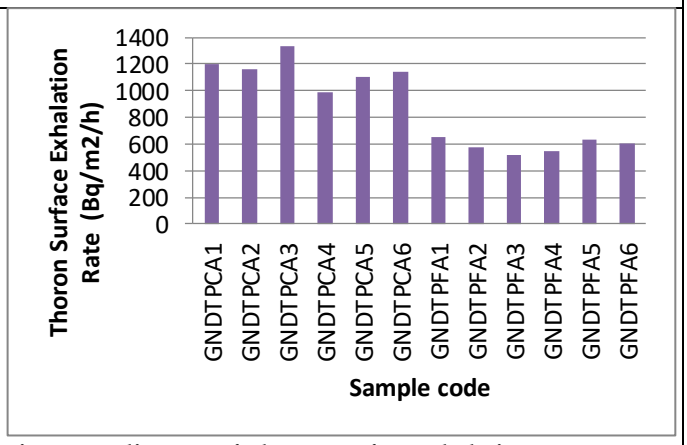

Fig.4 : Bar diagram of Thoron surface exhalation rate

RESEARCH ARTICLE

Collimators for an Imaging system

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ABSTRACT

When anyone visits medical for checkup, doctors immediately refer him/her for diagnosis. Out of many diagnosis medical imaging is one important one. This imaging can be done with the help of special gamma camera and special electronics. Out of many important components are there in gamma camera Collimators are one of the main components which helps to take better image with good contrast. The details of the collimators has been presented.

Key words: CT ,MRI, X-Ray.

INTRODUCTION

To describe the performance of an imaging system for diagnostic one of the most important part is the collimators which collimated the light including the detection unit which detects the gamma emitted by the different parts of the body [1-4] . The details of the collimators has been explained Bellow.

Collimator

Ideally, the collimator must prevent that each gamma ray coming from a direction not perpendicular to the photodetectors matrix reaches the scintillator. To obtain this result, a thick layer of a material with a high stopping power, i.e. with a high atomic number Z and a high density (typically metals such as lead (Z=82) or tungsten (Z=74)) is positioned between the gamma ray source and the crystal. In fact, the probability of photoelectric absorption of the gamma ray is proportional to the atomic number of the crossed material and hence higher it is, more easily the incident photon will be absorbed. In the collimator are then present holes which allow to propagate only the gamma rays coming from the desired direction [5-9].

The collimation done is therefore different from the one of optical lenses, which varies the photons direction to make them converge in a single focal point, but is a collimation for absorption: the collimator does not change the direction of motion of the gamma rays but merely eliminate those traveling in "unwanted directions". Moreover, it is important to note that the gamma photon would pass through optical lens because of its strong penetrating power and, having no charge, could not be deflected by electric or magnetic fields. The only gamma rays that pass through the collimator are those whose trajectories pass through the focal point and are also reduced of a percentage which depends on the holes' diameter (an example is shown in Fig. 1). Furthermore, the collimator is characterized by an unwanted transmissions of gamma photons, due primarily to three different mechanisms:

a) Photons whose trajectories are at an angle from the normal that allows them to pass through the holes without interacting with the collimator surfaces.
b) Photons which are not blocked while passing through the collimator
c) Photons which have acquired the right direction after a Compton scattering on their way from the source to the collimator

In general, the greater is the accuracy in the selection of the incident gamma rays, the more accurate is the image reconstructed, i.e. a better spatial resolution is obtained. However, at the same time, the number of photons detected is lowered proportionally, decreasing the efficiency of the system. It is therefore necessary to choose a compromise between the holes size and the distance between the source and the collimator in such a way to optimize these two conflicting requirements: to have a large number of gamma photons interacting with the crystal and to block those whose trajectories are very different compared to the direction normal to the scintillator top surface. The holes can have different shapes (cylindrical, squared, hexagonal ...) and, on one hand, increasing their diameter decreases the collimator blocking capability, because the solid angle that allows a photon to pass through a hole is greater. On the other, decreasing it can cause a higher absorption by the collimator and, consequently, lower the gamma camera efficiency. The collimator holes size determines moreover the minimum spatial resolution which is possible to obtain: each gamma photon which passes through the collimator arrives in the crystal generating a flash of photons in the visible range, whose distribution on the photodetectors is approximately a Gaussian centered on the interaction point position. The overall distribution of secondary photons is an envelope of the distributions produced by all gamma photons that can pass in the same hole and it is characterized by a full width at half maximum (FWHM) in the order of the diameter of the hole itself. Considering the distance between the source and the collimator, it may be observed that also in this case a trade-off is present: if the source is positioned far away from the collimator, the latter presence becomes unnecessary, as the gamma photons which arrive on its surface have trajectories almost parallel to one another and with a small or null angle to the normal to the surface. However, this decreases the number of detected photons and therefore worsens the signal/noise ratio. Reducing instead this distance increases the dispersion of the trajectories with respect to the normal direction, worsening the reconstruction image quality. In Fig. 2 the geometric relationship between the spatial resolution of the collimator and its distance from the source is shown. All points within the segment indicated by R radiate gamma photons in the hole shown in the figure, giving their contribution to the scintillation events contained in the shaded area of the crystal and thus resulting indistinguishable one from each other [10]. The relationship between the distance R with the angle θ and with the geometrical parameters of the collimator is the following one: $R=(L+z)\cdot tan(\theta)=d+(d/zL)$

SUMMARY AND CONCLUSION

A detail description of the collimators has been presented which are the important part of the imaging system. Specially without collimator nothing will work no picture will be clear It helps to reduce the noise and increase the picture quality better way. .

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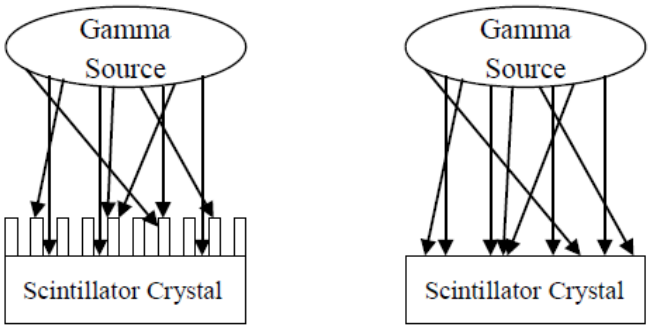

Fig.1: Graphical example of the collimator blocking action

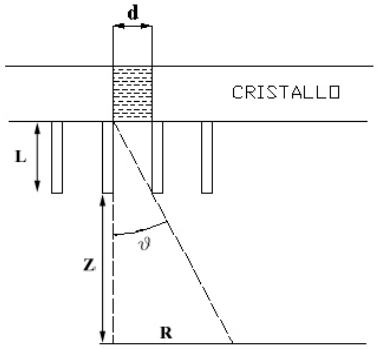

Fig.2: Limitation of the collimator spatial resolution(420 nm) matches well with the sensitivity spectrum of most photomultiplier tubes. It is not hygroscopic and its light yield (32 photons per keV) is about 4

REVIEW ARTICLE

A Review: Natural Polymer as Natural Excipients- Binders & Disintegrants

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ABSTRACT

Polymer is defined as a large molecule or a macromolecule which essentially is a combination of many subunits. The polymers are classified based on structure, source and monomers. Based on structure polymer is divided into three types, they are linear, branched and cross-linked polymers. Based on monomers it is classified into two types- homo-polymers and hetero-polymers. Based on source it is derived into 3 types they are natural, synthetic, Semi-synthetic. Before application of polymers in pharmaceutical industries, physical and chemical properties must be checked. There are several advantages like non-toxic in natural polymers and minor disadvantages like high cost and poor mechanical properties. Polymers are applied as natural excipients. Binders from a natural polymer like mucilage of *Artocarpus heterophyllus, Grewia optiva* as potential natural tablet binder, Evaluation of *Mangifera indica* gum as binder and tamarind gum as binders. Methods of incorporating disintegrants into tablets can be either internal or external .there are various mechanisms of disintegrants like swelling, wicking and enzymatic reaction. Evaluation of the natural polymers can be performed by tests like Osmometry, thermal analysis and viscometry. Natural polymers can be widely applied in formulation of tablets in the form of binders, disintergrants, etc. it can also be used in other formulations like jellies, ointments.

Keywords: Polymer, natural, disintegrant, excipients, binders, applications.

INTRODUCTION

The term "Polymer" comes from Greek roots "Poly" which means several and "Meros" which means elements. Polymers are chemical compound may be a giant molecule or a supermolecule that basically may be a combination of the many subunits[1]. Polymers is found all around us. From the strand of our deoxyribonucleic acid that may be a present biopolymer to poly-propene that is employed throughout the globe as plastic [1, 2].

Poly- Many
Meros- elements

Polymers could also be naturally found in plants and animals (natural polymers) or could also be semisynthetic (synthetic polymers). Completely different polymers have variety of distinctive physical and chemical properties that they realize usage in lifestyle[3]. Polymers may be a substance created from revenant structural units, every of which might be considered derived from a particular compound referred to as compound. The molecular structure and physical properties is proportional to the amount of monomers[1, 4]. The sort of polymerisation mechanism used depends on the sort of useful teams connected to the reactants. In biological contexts, most macromolecules are either completely chemical compound or created from giant chemical compound chains. The trendy thought of polymers was planned by German Staudinger in 1920. This widely discusses regarding covalently bonded organic compound structures[5]. In biological contexts, basically all biological macromolecules are strictly chemical compound, or are composed in giant a part of chemical compound parts. These macromolecules are sometimes proteins (polyamides), nucleic acids (polynucleotides), and polysaccharides e.g, iso- phenyl lipoid changed glycoproteins wherever tiny lipid molecule and saccharide modifications occur on the polymeric amide backbone of the macromolecule[6].

CLASSIFICATION OF POLYMERS[7]

Polymers cannot be classified below one class due to their advanced structures, completely different behaviours and vast applications.

1. Based on Structure
2. Based on Monomers
3. Based on Source

Based On Structure

Most of the polymers around us are created from an organic compound backbone and it's a protracted chain of coupled carbon and hydrogen atoms, due to the powerfulness nature of carbon [2]. Some samples of an organic compound backbone chemical compound are polypropene, poly-butylene, and styrene. Also, there are polymers that rather than carbon produce other parts in its backbone. For instance, Nylon that contains element atoms within the perennial unit backbone[4]. Some polymers may contain a mix of the different basic structures. The four basic chemical compound structures are [1,6].

a) Linear polymer
b) Branched polymer
c) Cross-linked polymer or Networked polymer

Linear Polymers [7, 8]

Linear polymers resemble long chains. The long chains are generally control along by the weaker van der Waals or gas bonding. Since these bonding varieties are comparatively straightforward to interrupt with heat, linear polymers are generally thermoplastic. Heat breaks the bonds between the long chains permitting the chains to flow past one another, permitting the fabric to be remoulded. Upon cooling the bonds between the long chains reform, i.e., the chemical compound hardens.

Example: PVC, styrene, synthetic resin, and polyamides.

Branched Polymers [7, 9]

Branched polymers jibe linear polymers with the addition of shorter chains hanging from the backbone. Since these shorter chains will interfere with economical packing of the polymers, branched polymers tend to be less dense than similar linear polymers. Since the short chains don't bridge from one longer backbone to a different, heat can generally break the bonds between the branched chemical compound chains and permit the chemical compound to be a thermoplastic, though there are some terribly advanced branched polymers that resist this melting and break up (becoming exhausting within the process) before softening, i.e., they are thermosetting .

Example: Glycogen, low density polyethylene, starch, etc.

Crosslinked Polymers [7, 10]

Cross linked polymers resemble ladders. The chains link from one backbone to a different. So, in contrast to linear polymers that are control along by weaker Vander Waals forces, cross coupled polymers are tied along via valency bonding. This abundant stronger bond makes most cross coupled polymers thermosetting, with solely some exceptions to the rule cross coupled polymers that happen to interrupt their cross-links at comparatively low temperatures. It is additionally referred to as networked polymers. These chemical compounds are nearly not possible to melt once heating while not degrading the underlying polymer structure and also thermosetting polymers.

Example: Fluroelastomers, Polybutadiene, Elastomers embody natural rubbers, Styrenebutamide block copolymers, and nitrile rubbers.

Based On Monomers [9]

- Homomers
- Hetero-polymers (or) Co-polymers

Homo-Polymers [11]

Homopolymers additionally referred to as Homomers are created from one form of compound unit and occur in linear, branched or cross-linked chains.

For example: Synthetic resin, Starch, inulin, etc.

Hetro-Polymers [12, 13]

It consists of various form of compound units. Co-polymers is classified supported the units organized on the chain. Linear co-polymer consists of one main chain and branched co-polymers carries with it one main chain with one or additional chemical compound aspect chains.

For example: nylon -6, 6, Muco-polysaccharide, etc.

Based On Source [9]

There are 3 kinds of classification below classes particularly,

- Natural polymers,
- Synthetic polymers
- Semi- Synthetic Polymers

Natural Polymers

They occur naturally and are found in plants and animals. It additionally includes bio degradable polymers that are referred to as biopolymers.The tiny molecules that is utilized in synthesizing a chemical compound referred to as chemical compound .Natural Polymers are those substances that are obtained naturally. These polymers are shaped either by the method of addition polymerisation or condensation polymerisation [14]. Polymers are extensively found in nature. Our body too is created from several natural polymers like nucleic acids, proteins, etc. The polysaccharide may be another natural chemical compound that is a main structural element of the plants. Most of the natural polymers are shaped from the condensation polymers and this formation from the monomers, water is

obtained as a by-product[15]. Some Natural polymers additionally embody DNA and RNA, these polymers are noticeably vital all told the life processes of all the living organisms. This ribonucleic acid is that the one that creates attainable peptides, proteins, and enzymes during a living body. Enzymes within the living organisms facilitate the reactions to happen and therefore the peptides makes up the structural parts of hair, skin, and additionally the horns. The opposite natural polymers are polysaccharides or additionally referred to as sugar polymers and polypeptides like keratin, silk, and therefore the hair. Natural rubber is additionally a natural chemical compound that is principally composed of hydrogen and carbon [16, 17].

Examples of Natural Polymers

There are concerning several samples of natural polymers that occur in nature.

Proteins and Polypeptides [18- 20]

Proteins are the fundamental style of natural polymers that constitutes in the majority the living organisms. Proteins are aforementioned to be most versatile in nature. They will even be used as catalysts. Some proteins are offered within the type of enzymes. These enzymes are liable for numerous chemical reactions occurring in our body and it happens a couple of million times quicker with these enzymes. One style of macromolecule in our blood referred to as haemoglobin carries atomic number 8 from lungs to the cells of human body. A macromolecule is sometimes a present style of polymeric amide. This chemical compound consists of associate organic compound cluster gift within the backbone chain of flesh. For example: proteins, starch, cellulose, and rubber.

Collagen [21]

Collagen is one of the natural polymers and may be a macromolecule. It makes up the connective tissues gift within the skin of personalities. This collagen chemical compound is additionally produce associate elastic layer below the skin and therefore helps keep it fibrous.

Latex[22]

Latex is understood to be a sort of rubber, and rubber may be a natural polymer. This latex happens in each the forms either artificial or natural. The natural type of latex is principally collected from the rubber trees and it's additionally found in style of plants which incorporates the milk weed. It may be ready by artificial means by the method of build-up long chains of molecules of polyvinyl resin.

Cellulose[23]

Polysaccharide is one amongst the foremost organic compounds found on the planet and what is more, the purest type of natural polysaccharide is that the cotton. The paper factory-made from the woods of trees and additionally the supporting materials in leaves and plants principally comprise polysaccharide. Just like the amylose, it's additionally a chemical compound that is created from the monomers of glucose.

Starch [24]

Starch is that the spinoff of condensation polymerisation and consists of aldohexose monomers. These polymers upon chemical reaction split into separate aldohexose molecules. Starch is additionally a member of basic food teams referred to as the carbohydrates and it's found within the grains, cereal and potatoes. Starch may be a homo-polymer of saccharide glucose. The molecules of starch incorporates 2 varieties of amylopectin polymers mainly amylopectin and amylose that are the most element of starch in most of the plants.

Synthetic Polymers [25, 26]

These are artificial polymers. Plastic is that the commonest and wide used artificial chemical compound. It's utilized in industries and numerous farm merchandise. For example: nylon-6, 6, polyether, etc. Artificial polymers are those that are human created polymers. Synthetic resin is taken into account to be concert of the best chemical compound, it is alkane series or ethylene because the chemical compound unit wherever because the linear polymers referred to

as the high density synthetic resin (HDPE). Several of the chemical compound materials have chain like structures that fit synthetic resin.Artificial polymers are typically referred as "plastics" of that the standard ones are nylon and synthetic resin. The polymers that are shaped by linking chemical compound units, while not the any amendment of fabric, are renowned to as addition polymers or additionally referred to as chain growth polymers. Some artificial polymers that are utilized in lifestyle embody nylons utilized in fabrics and textiles, Teflon utilized in non-stick pans, PVC utilized in pipes. The PET bottles we have a tendency to use or ordinarily created from artificial chemical compound referred to as synthetic resin terephthalate. The covers and plastic it contains artificial polymers like synthetic resin, the tyres of vehicles are factory-made from the synthetic rubber. On the other side, there's additionally a rises of environmental problems by the utilization of those artificial polymers like the bio-plastics and people made up of rock oil as they're aforementioned to be non-biodegradable.

Types of artificial Polymers with Examples

There are numerous artificial polymers developed to date. Allow us to study in short concerning few of the artificial polymers utilized in lifestyle.

Nylon [27]

Nylon belongs to the artificial polymers family and is additionally referred to as poly amides. It absolutely was synthesised on February twenty eight within the year 1935 by Wallace Carothers at the DuPont's research facility. Nylon is one amongst the foremost wide used polymers. The backbone of it referred to as organic compound causes it to become hydrophilic than alternative polymers. Nylon gets engaged in gas bonding with water, not just like the pure organic compound polymers that build most of the plastics.

Poly vinyl Chloride [28]

Poly vinyl Chloride or PVC is third most majorly made plastics coming back once polypropylene and poly ethylene. This PVC is employed for construction functions because it is thought to be stronger and cheaper than alternative alternatives like copper or iron. PVC is additionally employed in the vesture, transmission line insulation as well as several alternative applications commutation rubber.

Low Density Polyethylene[29]

The low density polyethylene polymers are the foremost common quite artificial polymers, they are wide employed in households. LDPE could be a quite thermoplastic that is ready from the compound known as ethylene.

Polypropylene [30]

Polypropylene additionally known as poly propene could be a quite thermoplastic artificial chemical compound that is employed in sort of applications like packaging, labelling, stationery, textiles, plastics and in reusable containers, laboratory equipment etc. another examples embrace Thermoplastic polyurethane, Teflon, phenyl-ethylene, High Density polythene, Neoprene, etc.

Semi-Synthetic Polymers [31, 32]

They are derived from present polymers and any chemical modification. Example: nitrocellulose, cellulose ester. Semi synthesis or partial chemical synthesis could be a style of chemical synthesis that uses chemical compounds isolated from natural sources (such as microorganism cell cultures or plant material) because the beginning materials to provide alternative novel compounds with distinct chemical and healthful properties. The novel compounds typically have a high mass or a posh molecular structure, a lot of thus than those made by total synthesis from simplest of materials. Installation of the mandatory aspect chain and ethanol group of paclitaxel by a brief series of steps, ranging from isolated 10 de acetyl group baccatine III. Drug derived from natural supply are typically made by isolation from the natural source or as delineate here, by semi synthesis from such microbial cell culture and plant material isolated agent. From the purpose of chemical synthesis, living organism are exceptional chemical factories that may simply turn out structurally advanced chemical compounds by synthesis. In distinction, built chemical

synthesis is essentially less complicated, with a lower chemical diversity in every reaction, than the implausibly numerous synthesis pathways that are crucial to life. Chemical reaction, such as acylation, during which sure synthesis pathways will generate teams and structures with least economic input that may be prohibitive via total synthesis. Plants, animals, fungi, and microorganism are all used as sources for those difficult precursor molecules, as well as the utilization of bioreactors at the meeting purpose between built and biological chemical synthesis.

Semi synthesis, once it's employed in drug discovery, aims to retain the asked for healthful activity whereas alternative molecule characteristics are altered, like people who have an effect on its adverse events or its oral bioavailability during a few chemical steps. In this regard, semi synthesis stands in distinction with the approach of total synthesis, whose aim is to attain a target molecule. whereas there's no exhausting and quick division between total synthesis and semi synthesis, that rather dissent within the degree of built synthesis that's used, several trade goods precursor molecules with advanced or fragile practical teams are less expensive in observe to extract from organism than to organize from straightforward precursors solely. Hence, strategies of semi synthesis are applied once a required precursor molecule is just too structurally advanced, too costly, or too tough to provide by total synthesis.

Examples of the utilization of semi-synthetic polymers[31, 32]

Samples of semi artificial chemical compound embrace the first business production of the anti-tumour agent paclitaxel from 10-de-acetyl baccatin isolated from the needles of genus Taxus baccatin (European yew), the preparation of LSD former got alkane isolated from fungous cultures of ergot and also the semi-synthesis of the anti-malarial drug artemether from naturally occur ring artemisinin.

IDEAL PROPERTIES OF POLYMERS[33, 34]

- Polymers are lightweight in weight with vital degree of strength.
- They is terribly immune to chemicals.
- Polymers is each electrical and thermal insulators.
- Polymers are materials with an apparently limitless vary of characteristics and colours.
- They is accustomed create things that don't have any alternatives from alternative materials.

ADVANTAGES OF NATURAL POLYMERS[36- 39]

- Natural polymers are readily and abundantly obtainable.
- They are relatively cheap.
- Products of natural polymers are non-toxic.
- They is changed to induce semi-synthetic forms.
- Natural chemical compound are bio-degradable in nature and thus lesser toxicity.
- The therapeutic activity of a drug is increased by mistreatment chemical compound drug conjugates.
- It is on the market in comparatively low value.
- This is wide applied in targeted drug delivery system.

DISADVANTAGES OF NATURAL POLYMERS [36- 39]

- High degree of variability in natural material derived from animal supply.
- This quite polymers is structurally a lot of advanced.
- Extraction method is extremely difficult and high value.
- It typically exhibits poor mechanical properties.
- Process of dose merchandising result takes place, that which is an undesirable result.

POLYMERS AS NATURAL EXCIPIENTS

Natural Excipients [40- 44]

The Herbal or natural excipients have a great benefit over their synthetic analogues as these are non-toxic, economic and widely available. The increasing awareness about these herbal excipients, which are mainly polymers of natural origin, the pharmaceutical industries is getting more reception towards their use in formulation development. The plant derived gums, mucilage from natural sources like carrageen an, thaumatin, lard, storax, agar, gum acacia, tragacanth act in accordance with many requirements of pharmaceutical excipients.

Pharmaceutical Excipients

Pharmaceutical excipients will be outlined as non-active ingredients that are mixed with therapeutically active compounds to create medicines. The ingredients that are developed beside active compound are considered excipients. Excipients have an effect on the behaviour and effectiveness of the drug product a lot of considerably. The variability of active compounds, excipients and method are obvious parts for the merchandise variability.

Classification of Excipients [40-44]

Excipients are unremarkably classified per their application and performance within the drug products:-

- Binder and Diluents
- Lubricants, Glidants, Disintegrants
- Polishing film former, Coating Agents
- Plasticizer, Colouring
- Suspending Agent, Preservatives
- Flavouring agent, Sweeteners, style rising Agent
- Printing Ink, Dispersing Agent Gum

Advantages of Natural Excipients [40- 44]

1. **Biodegradability:** Present compound created by all living organisms. They show no adverse effects on the setting or individual.
2. **Biocompatible and Nontoxic:** With chemicals nearly all of these plant materials are carbohydrates in nature and composed of continuance simple sugar units. Hence they're non-toxic.
3. **Safe and destitute of facet effect:** They're from a natural supply and thence, safe and while not facet effects.
4. **Easy availability:** In several countries they're created thanks to their application in man.
5. **Economical**: they're cheaper and their cost is a smaller amount than artificial material.

Disadvantages of Natural Excipients [40- 44]

1. **Microbial contamination**: throughout production, they're exposed to external setting and thence, there are possibilities of microbial contamination.
2. **Variation**: artificial producing is controlled procedure with mounted quantities of ingredients whereas production of natural polymers is dependent on setting and numerous physical factors.
3. **Uncontrolled rate of hydration**: Due to variations in the assortment of natural materials at totally different times, as well as variations in region, species, and climate conditions the share of chemical constituents gift in a given material could vary.
4. **Slow Process:** As the production rate is depends upon the setting and plenty of alternative factors, it cannot be modified.
5. **Heavy metal contamination:** There are possibilities of significant metal contamination typically related to flavoured excipients.

POLYMERS AS NATURAL BINDERS [42, 43]

Excipients are additives that are employed in active pharmaceutical active ingredients convert into pharmaceutical dose type appropriate for administration in patients. Binders are value-added to the pill formulation to impart

physical property furthermore as will increase lay to rest particulate bonding strength within the pill. Grain conjointly will increase the degree of consolidation or compactions whereas decreasing the brittle fracture tendency throughout pill. The selection of an acceptable binder for a pill formulation needs intensive data of the binder properties for enhancing the strength of the pill and conjointly interaction between numerous materials constituting pill. Gums usually polysaccharides that are compound in nature of natural substance obtained from woody and non-ligneous plant components like bark, seeds, sap, roots, rhizomes, fruit, leaves and plant gums are wide employed in formulation of pharmaceutical dose forms. The foremost application of gum may be a pill, as binding agent. This investigation was aimed toward effectiveness of natural gum & mucilage as binder in pill formulation.

Advantages of Natural Binder [42, 43]

- They can even be wont to modify the discharge of drug and thereby influencing the absorption and bioavailability of the incorporated medication.
- Natural binders are wide employed in the pharmaceutical and food business as excipients and additives thanks to their low toxicity, perishable, handiness and low price.

Disadvantages of Natural Binders [42, 43]

- Polymers as binders will result in process difficulties like speedy over granulation, pill hardness will increase & dissolution performance decrease.
- When compound binders are designated addition of robust disintegrates usually needed however these are substantial high-ticket and have a negative impact on product stability.

Mucilage of *Artocarpus heterophyllus* as Binder[45, 46]

Artocarpus heterophyllus (Moraceae) found wild within the forest region. To isolate mucilage pulp is removed and therefore the macerated with the water then filter solvent technique was wont to isolate mucilage from filter and dried in to hot air kitchen appliance 450 °C until it had been utterly dried. Physiochemical characteristics of mucilage has performed like swelling index 12.2%, loss on drying .This study was applied to match the binding impact of isolated mucilage with starch. Granule properties like angle of repose twenty nine.25 to 28.35^0, Hausner quantitative relation 1:12 to 1:11, carr's index 10.81 to 10.51, therefore it's determined to own smart flow properties. Tablets were ready varied concentration 4.6 and by wet granulation technique model drug mistreatment as paracetamol and compressed into tablets at absolute pressure load unit half-dozen tons. Tablets was evaluated in weight variation & hardness half-dozen.2 to 6.8 (kg/cm2), less crumbliness & tablet showed uniform drug content (98.48 to 98.63%). Mucilage obtained from*Artocarpus heterophyllus* was found to be helpful for the preparation of tablet dose type.

***Grewia optiva* as potential natural tablet binder[47, 48]**

The gum mucilage was isolated from the bark *of G. optiva*. The physical science behaviour gum mucilage was compared with starch. *G.optiva* mucilage was additional subjected to physiological characterization, they showed superior physical science properties. A comparative analysis showed that the granules sure with *G. optiva* mucilage gum were comparatively larger and more durable than those obtained with starch. The hardness, disintegration time & dissolution rate was directly proportional to the concentration of gum mucilage. This concludes that *Grewia optiva* gum mucilage as an inexpensive and simply on the market & appropriate to be used as a pharmaceutical tablet binder.

Evaluation of *Mangifera indica*gum as binder[44, 45]

The *Mangifera indica* gum is appropriate as a binder for pharmaceutical pill formulations. Paracetamol was used as model drug, tablets were ready by wet granulation technique. The ready tablets were evaluated for chemical science characteristics, they showed best friability and disintegration (3-8 min). The binding effectuality of the *Mangifera indica* was such as commonplace binder gum at similar concentration (5% w/w) determined in terms of hardness (6.3 to 6.8 kg/cm^2)which are comparable the quality binder gum (4.8kg/cm2).

Tamarind Gum as Binders [48, 49]

Tamarind Xyloglucan is extracted from reproductive structure of the seed of the tamarindo, tamarind, a member of evergreen family. Tamarind gum, conjointly referred to as Tamarind Kernel Powder (TKP) is obtained from the seeds. The seeds are processed in to gum by seed choice, reproductive structure removal, separation, hammer edge, grinding and sieving. Tamarind gum is sugar composed of glucosyl: xylosyl: galactosyl within the quantitative relation of 3:2:1 xyloglucan could be a major structural sugar within the cell walls of upper plants. Tamarind seed sugar (TSP) that is extracted from the seed kernel of tamarind, tamarind happiness to family leguminacy, Xyloglucans (XGs), conjointly known as amyloids, are widespread in nature in plants. Xyloglucan could be an extremely substituted, food grade, starch-like sugar and is gift within the cell walls of dicotyledons and non-graminaceous monocotyledons. The aldohexose backbone of XG is extravagantly substituted with a (1, 6)-linked xylopyranose branches that successively is also any derivatised by (1, 2)-linked galactopyranosyl residues. A high degree of substitution of the glucan chain produces a stiff, extended conformation for this sugar molecule, with massive volume occupancy in resolution. Concerning 80% of the glucose residues are substituted by a (1, 6)-linked carbohydrate units, that themselves are part substituted by β (1, 2)-galactose residues. Xyloglucans synthesized by all plants examined to this point have a minimum of one in every of the subsequent structural features: facet chains terminated by fucosyl residues; facet chains terminated by arabinosyl residues; a XXGGG-type continuation core consisting of a polysaccharide backbone with 2 facet chains. Xyloglucan could be a compound with a mean mass of quite 50000.

Tamarind gum follows non Newtonian mechanics and yield higher viscosities than most starches at equivalent concentration. This has semiconductor diode to its application as stabilizer, thickener, gelling agent and binder in food and pharmaceutical industries.

Tamarind seeds consists[48, 49]

- Polysaccharide (35 - 55%),
- Fiber (7 - 18%),
- Fat (3 - seven.10%),
- Inorganic salts, Free sugars,
- Moisture (4 – 10%),
- Proteins (18-20%)
- Tamarind bean – raw,
- Lipids (6-10%),
- Ash(1- 3%).

The white kernel obtained of tamarind seeds are utilised for manufacturing Tamarind Kernel Powder. Tamarind kernel is wealthy in macromolecule, Carbohydrates, Fibers and Oils. Tamarind Kernel Powder is that the combination of Galacto Xyloglucan sugar (55-65%). The white kernel obtained of tamarind seeds are utilised for manufacturing tamarind kernel powder. Tamarind kernel is wealthy in macromolecule, carbohydrates, fibers and oils.

POLYMERS AS NATURAL DISINTEGRANTS [52]

Disintegrants expand and dissolve once wet inflicting the pill to interrupt apart within the digestive tube, or in specific segments of the digestion method, cathartic the active ingredients for absorption. They make sure that once the pill is connected with water, it speedily breaks down into smaller fragments, facilitating dissolution.

Examples of Disintegrants include: Cross linked polyvinylpyrrolidone (cross povidone), cross linked sodium carboxymethyl cellulose (cross-carmellose sodium).

Methods of Incorporating Disintegrants into Tablets [53]

Internal Addition (Intragranular)

In Internal addition method, the disintegrant is mixed with alternative powders before wetting the powder mixtures with the granulating fluid. So the disintegrant is incorporated at intervals the granules.

External Addition (Extra granular)

In external addition methodology, the disintegrant is extra to the sized granulation with combination before compression.

Partially Internal And External

During this method, half of disintegrant is extra internally and part outwardly. This ends up in immediate disruption of the tablet into previously compressed granules whereas the disintegrating agent at intervals the granules produces further erosion of the granules to the initial powder particles.

Mechanism of Disintegrants [54- 60]

Disintegrants square measure accustomed improve the effectiveness of solid indefinite quantity forms. This is often achieved by numerous mechanisms. The mechanism by that the tablets square measure broken into little items so produces a consistent suspension is predicated on:

a. Swelling
b. Heat of wetting
c. porousness and capillarity (Wicking)
d. chemical change (Acid-Base reaction)
e. Particle repulsive forces
f. Deformation recovery
g. catalyst reaction

Swelling

Though water penetration may be a necessary beginning for disintegration, swelling is maybe the foremost wide accepted mechanism of action for tablet disintegrants. Particles of disintegrants swell on returning in grips with appropriate medium and a swelling force develops that results in break-up of the matrix. Tablets with high porousness show poor disintegration thanks to lack of adequate swelling force. On the opposite hand, adequate swelling force is exerted within the pill with low porousness. It's worthy to notice that if the packing fraction is incredibly high, fluid is unable to penetrate within the tablet and disintegration is once more slows down.

Heat of wetting

Once disintegrants with exoergic properties get wetted, localized stress is created thanks to capillary air growth, they supports in disintegration of tablet. This clarification is prescribed to atiny low variety of kinds of disintegrants. Thus it cannot describe the action of latest disintegrating agents.

Porosity and capillarity (Wicking)

Wicking is another method by that disintegration happens. Porousness of the pill contributes to extend in area and there by enhances the contact of fluid with tablet. Once we place tablet into appropriate binary compound medium, the medium penetrates into the pill and replaces the air adsorbate on the particles, they weakens the unit bond and breaks the pill into fine particles. Water uptake by pill depends upon hydrophilicity of the drug/excipient and on tableting conditions. For these kinds of disintegrants maintenance of porous structure and low interfacial surface tension towards binary compound fluid is critical that helps in disintegration by making a hydrophilic network round the drug particles.

Chemical reaction (Acid-Base reaction)

The pill is apace broken apart by internal liberation of greenhouse gas in water thanks to chemical change between hydroxy acid and acid (acids) with metallic element carbonates or bicarbonates (bases) in presence of water. The pill disintegrates thanks to pressure generation among the pill. The dissolution of active pharmaceutical ingredients in water also as style masking impact is increased thanks to liberation in greenhouse gas. As these disintegrants square measure extraordinarily sensitive to minute changes in humidness level and temperature, strict management of setting is needed throughout formulation of the tablets. The bubbling mix is either additional straight off before compression or may be additional in 2 separate fraction of formulation.

Deformation Recovery

Deformation recovery theory states that form the form of disintegrant particles is distorted throughout compression and therefore the particles come to their pre-compression shape upon wetting, thereby this larger size of the ill-shapen particles causes the tablet to interrupt apart. Such a development is also a very important facet of the tactic of action of disintegrants like Crosspovidone and starch that hardly exhibit swelling.

Particle Repulsive Forces

This is often an extra mechanism of disintegration that makes an attempt to clarify the swelling of tablet created with non-swellable disintegrants. In step with Guyot-Hermann's particle-particle repulsion theory, water goes through into pill through hydrophilic pores and a continual starch network is created that may convey water from one particle to following, impartation a serious hydrostatic pressure. The water then penetrates between starch grains due to its affinity for starch surfaces, thereby breaking element bonds and alternative forces binding the tablet along. The electro-repulsive force between particles is that the mechanism of disintegration and water is needed for it.

Enzymatic Reaction

Enzymes gift within the body conjointly act as disintegrants. Due to swelling, pressure is applied within the outer direction that causes the tablet to burst or the accelerated absorption of water results in vast increase within the volume of granules to market disintegration. Some samples of disintegrating enzymes square measure,

S.NO	ENZYME	BINDER
1	Amylase	Starch
2	Protease	Gelatin
3	Cellulase	Cellulose and its derivatives
4	Invertase	Sucrose

It's believed that no single mechanism is answerable for the action of most disintegrants. But rather, it's additional doubtless the results of inter-relationships between these major mechanisms.

List of Disintegrants [54- 60]

- Cellulose and derivatives. Sodium carboxy-methylcellulose (NaCMC) and carmellose sodium are two extremely hydrophilic and soluble compounds.
- Microcrystalline celluose. Crystalline celluose (MCC) is one in every of the perfect disintegrants.
- Hydrophilic mixture Substance – Alginates.
- Ion-Exchange Resins.

EVALUATION OF POLYMERS[61-63]

Osmometry

This process is almost similar to dialysis. It involves a semi permeable membrane which has a specific pore size through which solvents can freely pass but retain the polymer molecule. This membrane separates the experimental

apparatus into two chambers- pure solvent and polymer solution. The osmotic pressure and molecular weight of the solute can be determined by using Vant Hoff law.

Light Scattering

This is based on the principle of Lord Rayleigh's electromagnetic theory. Light scattering of liquid can be related to local fluctuations in density due to thermal motion of molecule.

Viscometry

This is not an absolute method like the previous tests. The viscosity is determined by flow time of the solution between two marks in viscometers like Ostwald's viscometer.

Differential Scanning Calorimetry

This method is essential in determination of glass transition temperature, heats of crystallization, crystalline melting points, etc. It includes a reference and sample substance which will be placed in two small metal containers and heated. The temperature is constantly monitored by using thermocouples.

Thermal Analysis

This is usually of high importance in determination of stability of polymer. This can be performed using techniques like thermo gravimetric analysis.

Test For Mechanical Properties

Mechanical properties can be evaluated by establishing the stress-strain relationship. Specimen is in clamped in a tester which is capable of producing extension of specimen at a desired constant rate. This process is continued until the specimen breaks.

APPLICATIONS OF NATURAL POLYMERS

- Microcrystalline polyose is majorly utilized in the pharmaceutical trade as a diluent/binder in tablets for each the granulation and direct compression processes [64].
- Carboxylated methyl group polyose is employed in drug formulations, as binder for medicine, film-coating agent for medicine, ointment base etc. Cellulose ester fibers square measure utilized in Wound dressings [65].
- Agar is employed as Suspending agent, emulsifying agent, gelling agent in suppositories, surgical lubricator, pill disintegrants, medium for microorganism culture, laxative[66].
- It is additionally used for the preparation of jellies, confectionary things, tissue culture studies, and in biological science study[67].
- Thermoplastic starch is used in packaging, containers, mulch films, textile filler agents, adhesives[68].
- Xanthan gum is wide utilized in oral and topical formulations, cosmetics, and in food trade as a suspending and stabilising agent. It has additionally been used to prepare sustained unharness matrix tablets[69].
- Chitosan and their derivatives (N-trimethyl chitosan, mono-N-carboxymethyl chitosan) square measure safe and effective absorption enhancers to improve tissue layer, nasal, peroral drug delivery of deliquescent macromolecules such as amide and macromolecule medicine and heparins. Chitosan nanoparticles and micro particles square measure additionally appropriate for controlled drug unharness [70].
- These wide embrace emulsifiers, foaming agents, mixture stabilizers, perishable film-forming materials, and microencapsulating agents[71].
- Guar gum is significantly helpful for colon delivery as a result of it will be degraded by specific enzymes during this region of the channel tract. The gum protects the drug whereas in the abdomen and intestine atmosphere and delivers the drug to the colon wherever it undergoes assimilation by specific microorganisms or degraded by the enzymes excreted by these microorganisms[72]

CONCLUSION

Polymers represent the most versatile class of materials because of their adaptability to increasingly precise control of structure and properties. Thus, it is anticipated that polymers will be continue to be exploited in many highly specialized biomaterials applications. In times of ecological and economical concerns on the usage of crude oils as raw material for wood adhesives, natural binders found their place back in wood composite production. Guar gum, Agar, Acacia, Tragacanth are some of the widely used polymers in the field of Pharmaceutics. Pure bio-based adhesives might be applied or combinations of bio-based adhesives with conventional synthetic resins or chemical replacements of these or compounds.

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RESEARCH ARTICLE

A Conceptual Study on Opportunities and Challenges of Medical Tourism in Bangalore

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ABSTRACT

The new construct of medical business enterprise, specific to the twenty-first century and add alternative options include: a sizable number of individuals traveling for treatment, low price flights providing low-cost flights, the fast enlargement of the net as a leading supply of data, development in this space each private and public sector and government involvement in promoting medical business enterprise, considering it as a possible, profitable revenue supply. Bangalore has nearly fifteen major hospitals that cater to international medical travel. Some have specialty services like medical science, oncology, or reproductive health. However, most of them are unit multi-specialty hospitals. The study team visited six hospitals; Apollo hospital, Columbia Asia hospital, Fortis hospital, Manipal hospital, Mallya hospital, and Narayana Hrudayalaya. A snowballing technique was used, whereby some personal contacts or organizational contacts were used to induce to bear with somebody at these facilities, moving on till the key persons accountable for medical business enterprise in the organization had been reached—the subsequent sections gift data on these sites and findings from the facilities tours. Due to medical tourism development in a country, Bangalore city became a hub offering advanced health care (less cost for surgery like bypass surgery, kidney transplantation, cancer), which attracts people around global? There are various agents involved in medical tourism which offer after treatment. The study addresses various issues in medical tourism. The study used qualitative analysis. Secondary data was collected through an

in-depth analysis of relevant information from the web, journals of repute, government reports, touristy medical websites, news, and alternative reports.

Keywords: Cost Effectiveness, Medical Service, Medical Tourism, Medical Visa, Multi-Specialty Hospitals

INTRODUCTION

The term of medical business enterprise sounds a touch self-contradictory, is challenging to imagine the associate approach (compatibility) of social life areas: travel and hospitalization. Whereas business enterprise is associated with relaxation and leisure, development and fun, the hospital is evoking pictures of constraints, suffering, and helplessness feelings. The current medical business enterprise section is characterized by associate industrial approach uninsurable or partially insured patients in industrialized countries seeking quality aid reasonable in developing countries. A development referred to as medical outsourcing. The only standard medical services that the area unit needed outside embrace dental treatments, rhytidoplasty, elective surgery, and fertility treatments. The new construct of medical business enterprise, specific to the twenty-first century and add alternative options include: a sizable number of individuals traveling for treatment, low price flights providing low-cost flights, the fast enlargement of the net as a leading supply of data, development in this space each private and public sector and government involvement in promoting medical business enterprise, considering it as a possible, profitable revenue supply.

"Medical tourism," a term unknown till a couple of years past, sounds inexplicable. Indeed, it is onerous to imagine more vital polarity between social life areas than between business enterprise and hospitalization. Tourism, a voluntary leisure activity typically perceived as a Purple Heart reversal of lifestyle and a time for hedonic pleasure, free from obligations and external constraints, stands in sharp distinction to medical treatment and hospitalization domains seem to be incompatible. As a travel author noted: "the medical man chair and the antiseptic smells of a hospital waiting area are substitutable with pain and a sense of helplessness. They solely do not mix with travel and vacations". However, throughout the last decade, the medical travel movement has accelerated sharply. This part of recent medical travel is characterized by an associate business approach whereby uninsurable and underinsured patients from industrialized countries request unique quality at developing country costs, a trend that is unremarkably named medical outsourcing. At an equivalent time, the medical travel business is progressively grounded in business enterprise. Well-developed aid systems and advances in technology have supported medical travel among western countries for several years.

Medical Business Enterprise Sites in Bangalore

Bangalore has nearly fifteen major hospitals that cater to international medical travel. Some have specialty services like medical science, oncology, or reproductive health. However, most of them are unit multi-specialty hospitals. The study team visited six hospitals; Apollo hospital, Columbia Asia hospital, Fortis hospital, Manipal hospital, Mallya hospital, and Narayana Hrudayalaya. The facilities and perceive their processes for medical tourism. Four hospitals– Columbia Asia, Fortis hospital, Manipal hospital, and Narayana Hrudayalaya - provided a facility tour, whereas the opposite provided interviews with the hospitals' international promoting divisions. A snowballing technique was used, whereby some personal contacts or organizational contacts were used to induce to bear with somebody at these facilities, moving on till the key persons accountable for medical business enterprise in the organization had been reached—the subsequent sections gift data on these sites and findings from the facilities tours.

Importance of the Study

Medical and eudemonia touristy is the buzz term across varied countries attempting to convert it into a vehicle to attract a more extensive range of foreign tourists, thereby fueling their economic growth. India, naturally blessed

with an expensive cultural heritage, touristy potential, and a name for antique medicines and therapies like a piece of writing, homeopathy, umami, naturopathy, and yoga, could be a haven for eudemonia touristy. Fortuitously, with relevance to medical touristy, India has been productive to an outsized extent in positioning itself as a viable destination for cost-efficient and qualitative advanced attention.

The medical business is that the construct wherever folks haunt another town or country to induce medical treatment. The most reason behind this traveling is that either the treatment is not accessible in their place or that the treatments can value them a great deal to realize a less expensive place to relinquish them identical facilities at lower rates. Mostly, folks worldwide haunt the most important medical centers in well-developed countries to receive sensible quality treatments. However, within recent years, we can see an increase within the folks from well-developed countries traveling to third-world countries for medical treatments. It is often principally due to the treatments accessible in such countries are low in value.

Statement of Problem

Receiving care at a facility where we do not speak the language fluently might increase the likelihood that misunderstandings will arise concerning care. Medication is additionally counterfeit or of poor quality in some countries. Antibiotic resistance may well be an international downside, and resistant being is additionally loads of joint in several countries than at intervals the U.S. Flying once surgery can increase the prospect for blood clots.

Need and Relevance of the Study

Due to medical tourism development in a country, Bangalore city became a hub offering advanced health care (less cost for surgery like bypass surgery, kidney transplantation, cancer), which attracts people around global? There are various agents involved in medical tourism which offer after treatment. The study addresses various issues in medical tourism. Doctors team measure necessary stakeholders of the medical business enterprise business. They supply the treatment and square measure directly associated with the patient traveling across a long distance. They have to know the issues of the patient despite language or cultural barriers. The doctor's qualification, expertise, and skills have a severe impact on medical business enterprise business. The doctors operating with the sample hospitals were hand-picked for the study.

Objectives of the Study

- To study the issues related to medical tourism and offer suggestions to improve the services.
- To offer policy suggestions to promote medical tourism.

METHODOLOGY OF THE STUDY

The study used qualitative analysis. The descriptive study reviews existing literature reviews that helped validate and extract the vital variables and factors.

Data Collection

Secondary data was collected through an in-depth analysis of relevant information from the web, journals of repute, government reports, touristy medical websites, news, and alternative reports. For this, various libraries and online databases were visited.

The data from entirely different medical tourism stakeholders; medical tourists, hospitals, doctors, and medical tour facilitators were collected, and their opinion was analyzed to understand completely different views of medical, commercial enterprise as elaborated in the study's objectives. This analysis supported the analysis of secondary information.

Strengths, Weaknesses, Opportunities, and Challenges (SWOC) Analysis

Strengths

The strengths are the inner characteristics that may be used to gain external opportunities and overcome potential threats. Indian medical commercial enterprise business's positive attributes act as distinctive commercialism prepositions to draw in patients to India's republic such as low price, prime quality, geographical proximity to supply markets, tourist attractiveness, or comprehensive care is thought-about strengths.

- **Advancement in hospitals:** The advancement of technology is quite a sizable number of hospitals in Asian country area unit equipped with all attainable infrastructure and facilities. There is less defrayal on health care in some countries, and other people from those countries visit Asian countries for their medical treatments. It has become a reason that an oversized variety of tourists visit Bangalore. Also, the most recent medical technologies have become the main target of attraction for medical tourists. Several new kinds of instrumentation area units exist in Bangalore hospitals that create the treatment straightforward and effective.
- **Affordability and cost-effectiveness:** The Bangalore area unit's treatment expenses are low-cost compared to different developed countries like North American and Britain.
- **Immediate and higher treatment services:** In several developed countries, patients have to expect the longer fundamental measure to hunt specialists for their treatment. This immediate treatment facility in Bangalore has created different countries' folks to go to Bangalore for treatment. Also, it would not be wrong to mention that in Asian country foreigners" area units provide higher care and treatment services. There is the provision of doctors to see when they.
- **Easy traveling**: In contrast to the past, once it was not straightforward to travel to another country these days, it is become straightforward to induce visas for medical functions, Rules relating to being ruled in order that it becomes straightforward to induce the medical visa.
- **There are no language issues:** Indian hospitals area unit currently out there with sensible English-speaking doctors and ball-hawking workers that has created it straightforward for the international patients to communicate reality with them.
- **Commercial enterprise**: Asian country conjointly provides the medical holidaymakers the chance to go to several enticing places underneath medical tourist visits. Many folks united nations agency visit for traditional treatment like dental issues and cosmetic care also can relish exploring the destinations here, whereas ill.

Weaknesses

Factors among the organization that accomplishment of goals is thought about as weaknesses. Factors like lack of qualification, not sensible in communication or English language, dangerous airfield infrastructure, inadequate transportation are known as weaknesses for medical, commercial enterprise business for analysis.

- **Promotion and publicity**: The government lacks in promoting Indian hospitals and its tending services to alternative countries. Conferences and exhibitions control by the embassy of Indian in alternative countries would like for the hour.
- **Lack of government involvement:** The government role intending is crucial in Bangalore because it the sole authority that can enhance the infrastructure needed. The state's role within the commercial medical enterprise management is primarily in coming up with finance and coaching.

Opportunities

The external factors that can help and supply risk to expand or improve business are termed as opportunities. Government policy, visa norms, strong economy, and sensible complete image are thought-about opportunities for analysis.

- **High growth potential:** The various steps taken to market medical business enterprise by the aid business, the governments, and policy manufacturers, have received relatively little media area, with media conjointly doing its half to market the activity.
- **Government support:** Medical, a commercial enterprise, maybe a multi-sectorial activity requiring many ministries. The Ministry of health and family welfare is chargeable for creating health-related policies and regulation of hospitals; Ministry of commercial enterprise for commercial enterprise connected policies; Ministry of commerce for trade-related activities; Ministry of Home Affairs for medical visa, Ministry of Overseas Indian Affairs for relation with different countries and Ministry of External Affairs for representing the republic of India abroad. Presently there is no separate policy or law for regulating medical, commercial enterprise within the country.
- **Medical visa:** Medical visa or m visa started in 2005, is issued by the government of Asian nation for patients visiting India for treatment in an exceedingly recognized medical Centre. The patient may be in the course of blood relatives. These relative's area units granted medical visas for an identical amount as m visa.
- **Opportunities for foreign health professionals:** The opportunity is not restricted to merely the nations from that medical tourist's area unit originated. The health care professionals from destination nations will like higher pay and higher operating environments in hospitals that cater to medical tourists. Due to the specialized nature of health care, demand tends to exceed provide. High population density countries like India's republic tend to produce torrential doctors and nurses globally, and plenty of them may welcome the chance to figure in their native countries for higher pay. It can be created possible by the upper-profit margins earned from medical touristy.
- **Stable foreign exchange:** The medical business's economic side is that the most familiar theme espoused by the media is recommended to be the foremost fundamental reason individuals travel to the urban center for medical treatment. The fact that the treatment prices, including travel prices, are a fraction of the patients' prices in their home countries is the most quoted statement.

Challenges

The significant challenges within the field of medical business that countries face across the world square measure as follows:

- **Follow-up problems:** Follow-up care is exceptionally troublesome, just in the case of medical business. If the patient gets any complications when surgery and is back to his own country, the follow-up is not solely troublesome, however, dear additionally. Though' info technology has helped a great deal during this, generally personal meeting with the doctor becomes inevitable. It is a challenge that countries square measure still troubled against in medical business because these reduce the demand.
- **Language barriers:** Language barriers create a significant challenge in the medical business. The country could supply skilled doctors and extremely subtle medical systems; however, if the doctors, nurses, and alternative medical employees do not perceive the patient's language, the entire method becomes very troublesome. The culture and language barriers additionally influence demand.
- **Brain drains:** Within countries with a pool of gifted doctors and nurses like India, it is a severe challenge to retain these professionals. There is a shortage of such masterful professionals in most countries globally, and therefore they are offered the simplest salaries abroad. Drain takes place thanks to the lack of opportunities within the home country.
- **Lack of infrastructure:** Several developing countries and India face issues thanks to poor infrastructural support in medical services. There square measure issues associated with correct water and power offer, poor hygiene in hospitals, unsanitary surroundings, untidy employees and caliber food and lodging, in conjunction with insufficient air property to support patients‟ flow within the country.

- **Difficulties in promotion**: The countries like India additionally suffer from issues of promotion in the medical business. There is a scarcity of quality certification and regulation within the hospitals and alternative medical service suppliers. Except this, there is no uniform evaluation and standardization of services acting as a barrier in building patients' trust in the services offered.
- **Legal problems:** One of the intense medical business considerations relates to variations in in-laws in several countries. There are no uniform laws and more; in most countries, their square measure weak laws for malpractice in medical services that leave patients with fewer choices to fight for their rights just in case they are cheated or if one thing goes wrong throughout the entire medical method.

Experience, Learning, and Conclusion

Experience

Bangalore, with its cosmopolitan style and speedy technological advancements, has become a haven for globe trotters. The town features pleasant and pleasant weather throughout the year. Medical tourists United Nations agency area unit on a visit to the town will get exemplary services from health care professionals, United Nations agency area unit trained within the planet's top-rated medical colleges. City medical, commercial enterprise additionally boasts numerous hospitals that have international certification. The hospitals even have several putative doctors from abroad United Nations agency supplies practice services. A remote tour can never sound out of place here, owing to the numerous made-to-order services and facilities that area units offered for them. The town with its fast-paced life and friendly individuals is sure to form your keep here an unforgettable and pleasant one.

Learning

The medical business enterprise may be a significant call downside for the patient; it is far more concerned than deciding to go to an area aid supplier. The patients' expertise of medical business enterprise is that the main issue that influences his/her satisfaction that successively would influence back intention. Thus, it ought to be a severe strategic priority for medical business enterprise hospitals and their directors to develop a system that will offer patients positive expertise.

CONCLUSION

The touristy medical business has drawn attention from international patients, travel agencies, governments, and the international certification sector. The patients may organize medical tourism by researching and booking on the web and medical travel agencies. Therefore, medical tourists have info on the simplest and most well-known aid suppliers and travel arrangements before embarking on medical tourism (pre-experience). Hence, the touristy medical expertise (recent experience) affects whether the holidaymaker can advocate the medical supplier to alternative potential patients (post experience). Thus, this paper advances the concept that each stage of a patient's expertise affects the touristy medical business. In this empirical study, we tend to be collected information to look at pre-experiences (e.g., reputation, searching info, and communication), recent experiences (e.g., cost, care quality, and supporting system and data), and post-encounters (e.g., relationship building, recommendation, and feedback) within the touristy medical business. The study sheds light on medical tourists' perception of care quality and prices, similarly to their future intention to get aid within the same hospital or country. Patient expertise supported their interaction with medical employees and coordinators ought to run the maximum amount of importance as the accuracy of identification, treatment, and procedures. The most vital service attributes that are incredibly enticing to international patients can help medical travel agencies improve the data provided and develop in-innovative ideas among key players in medical touristy. As unfold of knowledge retrieval functions grows and digital devices spread, medical tourists can gain a competitive edge by providing touristy medical info. Shoppers also will have additional opportunities to access comparative victimization searches through entirely different media. Academically and much, this paper provides many implications. First, developing and increasing a well-developed medical travel procedure

supported patient experiences a requirement for winning medical touristy. Desegregation kinds of client expertise may measure such decision-making methods to reinforce client satisfaction. As a result of several hospitals and travel agencies developing new protocols victimization advanced technologies, the planned model ought to be simple to access, and the reservation method ought to be easy.

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RESEARCH ARTICLE

Synthesis and Characterization of Polyaniline doped with TiO_2 Nanoparticle

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ABSTRACT

The Polyaniline (PANI) and Titanium dioxide (TiO_2)/PANI composite nano particle in terms of chemiabsarbor mercury sensing application are obtained in this paper. Pure PANI and TiO_2/PANI composites with various weight percentage of TiO_2 were synthesized by chemical oxidative polymerization of aniline using ammonium per sulfate in acidic medium at room temperature for the conductivity property. The structural, optical properties and conductivity of these composite have been characterized by X-ray diffraction (XRD) and UV–Visible (UV–Vis) spectroscopy and conductivity meter respectively. Morphological and structural properties of these composites have also been characterized by scanning electron microscopy (SEM).

Keywords: Polyaniline, TiO_2, Conductivity, nanoparticles

INTRODUCTION

Nowadays the environment getting more pollution owing to release of so many heavy metals like mercury, chromium, lead, arsenic extra which has suitable attention. According to the heavy metals have been possess more toxic potential which are accumulated by animals, plants, human and other living micro organisms and environmental samples. In the Most stable compound Hg (II), is Inorganic compound [1]. A widespread heavy metals contaminated such as air, water and soil, atmosphere with a high cellular toxicity and several disease formed by human health such as the brain, kidney, stomach, heart, and intestines[2]. Methyl mercury is the most common organic source of mercuricion which is generated by microbial biomethylation of Hg (II) ions [3]. Methyl mercury is a serious neurotoxin which can accumulate in the human body through the food chain [4]. The US Environmental Protection Agency (EPA) limit of Hg(II) for drinkable water is 10 nm which is much lower than the detection limit of

most available assays [5]. Although inductively coupled plasma mass spectrometry (ICPMS) is a powerful technique for the detection of heavy metal ions, it is complex, expensive and is thus not practical for routine monitoring of Hg(II) and As(III) [6]. Much effort has been devoted to design optical sensing systems for the detection of Hg(II) and As(III) based on organic chromophores or fluorophores, biomolecules such as proteins, antibodies, oligonucleotides, DNA, enzymes and also semiconductor quantum dots, conjugated polymers and inorganic materials. However, poor selectivity, inefficient sensitivity and stability are some limitations with most of these methods. Most of these methods involve a color change from red to blue or an extremely sharp change in melting transitions through aggregation in the presence of Hg(II) [7-9]. As a portable instrument, electrochemistry instrumentation, which can perform anodic stripping voltammetry (ASV) and cathodic stripping voltammetry (CSV) has some advantages over the various "naked-eye" arsenic test kits. These electrochemical techniques can determine mercury at trace levels within few minutes. In addition, these techniques can also distinguish between different oxidation states, are easy to operate and, compared with other instrumental techniques, are comparatively cheap. Electrochemical measurements can also be used to detect heavy metal ions, which have shown numerous advantages including rapid analysis speed, good selectivity and sensitivity. For metal ion analysis three conditions should be met during electrochemical measurements:[10-11] selective adsorption of metal ions [12] enhancing electron exchange between the working electrode and the metal ions[13] the strong electrochemical response. The nano particle-modified electrode can meet the three conditions. Tenano particle modified electrodes can be divided to metal oxide nanoparticles, carbon material nanoparticles, polymer material nanoparticles and self-assembled nanoparticles [14-16].

MATERIAL AND METHODS

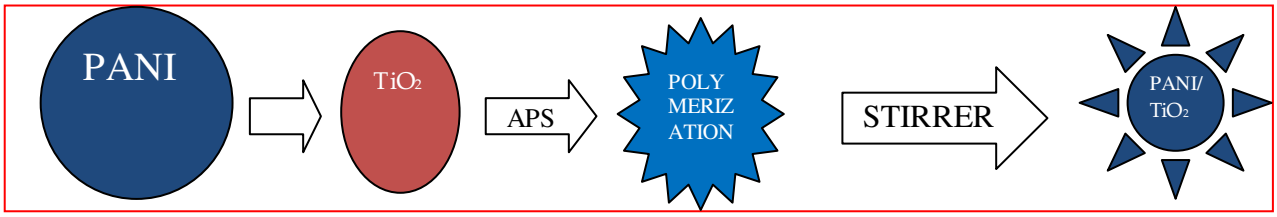
Aniline(Sigma-Aldrich), HCL Merck, 37%, ethanol (99.8% Merck), 30% H_2O_2(Sigma-Aldrich), 95%,H_2SO_4 (Merck), 98% (Sigma) Ammonium ferrous sulphate, trace metals basis, 70%HCl (Aldrich), 99.99% trace metals basis and for metal ion binding / assay using distillation water and 97% of TiO_2.Fourier Transform Infrared. FTIR spectra of PANI and its nanocomposites were recorded on a Shimadzu FTIR-8400 spec- trometer (Tokyo, Japan) in the wave number range of 400– 4000 cm^{-1} UV–visible absorption spectra of PANI and its nanocomposites were recorded in NMP on a Hitachi U-2900 spectrophotometer (Tokyo, Japan) in the range of 250–800 nm. The X-ray diffraction (XRD) measurements of the materials were performed using X'Pert–PRO X-ray diffract meter. All samples were analyzed in the range between 10 and 80^o as 2θ and Cu as anode (K-Alpha -1.54060 Å).

Synthesis of Polyaniline

Synthesis of polyaniline composite was carried out by In-situ chemical oxidation polymerization technique. Aniline (1M) 9mL was mixed in (1M) 3 mL hydrochloric acid and stirred for 15 min to form Aniline hydrochloride. To this solution, 0.1M of ammonium persulphate (APS), acts as an oxidizer was slowly added drop-wise with continuous stirring at 0-5^0C for 4 hrs to be completely polymerized. The precipitate was filtered, washed with deionized water, acetone and finally dried in an oven for 24hrs to achieve a constant mass.

Synthesis of Polyaniline Titanium dioxide (PANI/TiO_2)nano Composites

Synthesis of PANI/TiO_2 composites was carried out by In-situ chemical oxidation polymerization technique. Aniline (1M) 9ml was mixed in (1M) 3 ml hydrochloric acid and stirred for 15 min to form Aniline hydrochloride. TiO_2 powder is added in the mass fraction to the above solution with vigorous stirring in order to keep the TiO_2 homogeneously suspended in the solution. To this solution, 0.1M of ammonium persulphate (APS), acts as an oxidizer was slowly added drop-wise with continuous stirring at 0-5^0C for 4 hrs to be completely polymerized. The precipitate was filtered, washed with deionized water, acetone and finally dried in an oven for 24hrs to achieve a constant mass. In this way, polyaniline/TiO_2 composites with various weight percentages of TiO_2 (5%, 10%, 15%, 20% and 25%) were synthesized. Later, the synthesized samples were made a fine powder with the help of agate mortar.



RESULTS AND DISCUSSION

Fourier- Transforms Infrared Spectra

FT-IR spectra of TiO_2 and PANI/TiO_2 are shown in figures. In addition to observed peaks due to TiO_2 in Figure 1.The main characteristic bands of polyaniline were seen in. The bands at 1581 and 1496 cm^{-1} corresponded to quinoid and benzenoid structure of PANI, respectively. Also the band at 1246 cm^{-1} assigned to C-N stretching of a secondary aromatic amine. The peaks at 1149 and 834 cm^{-1} belong to asymmetric and symmetric C =O stretching and this confirms the presence of PANI/TiO_2 in the complex. Because titanium is a transition metal, it has intense tendency to form coordination compound with nitrogen atom in PANI macromolecule. This interaction may weaken the bond strengths of C=N, C=C and C-N in PANI macromolecule. These results confirm to the presence of PANI and PANI/TiO_2 of various nanocomposite.

UV- Visible Spectrum of Polyaniline with TiO2

The UV-Vis spectrum of the PANI and PANI/TiO_2nanocomposite are shown in Figure 2(a) and (b). In the two characteristic bands of doped PANI with TiO_2 appear at about 585 and over 380 nm, which are attributed to the transitions metal respectively. From Figure 2(b), it can be seen that the prepared nanocomposite can strongly absorb the UV and visible light. The hybrid samples present characteristic bands of PANI at about 580.nm. Moreover, the peak at over 580 nm in PANI doped with TiO_2 is obviously shifted to 380 nm in the nanocomposite. It indicates that encapsulation of TiO_2 NPs has the effect on doping of conducting polyaniline. This shift shows shortening in the conjugation length that reported the coordinating complex formation between TiO_2 NPs and PANI chains.

X-RAY Di Fraction of PANI/TiO2

X-ray diffraction pattern of Polyaniline and PANI/TiO_2 composites respectively. The analysis of x-ray diffraction of Polyaniline suggests that it has amorphous structure with a broad peak cantered on $2\theta \approx 250$. Figure 3 Shows that the X-ray diffraction pattern of PANI/TiO_2 composite shows well defined broad peaks, which indicates good crystalline of the materials. The observed 2θ values are consistent with the standard JCPDS no-1I/TiO_2-250.The resulting diffract gram shows a perfect crystalline structure which may be due to the presence of TiO_2. The comparison of XRD pattern of PANI/TiO_2 composite suggests that there is no change in the structure of TiO_2 due to its dispersion in polyaniline during polymerization reaction. The average nano particle size of PANI-TIO_2 is 1.641 nm

Scanning Electron Microscope (SEM)

The SEM micrograph for PANI nanoparticles electrodeposited in solution 1mM aniline (pH=5) are shown in Figure 4. The PANI nanoparticles has medium globular (rice grain) morphology similar to that previously reported. However, the bulk powder rice grain features are fused together rather than being discrete particles. Te results show the PANI nanospheres were successfully prepared (Figure 3). Te average width of PANI nanospheres formed on screen printed carbon electrode is 20 µm and the average thickness between 40 to 100 nm

Studies of Conductance

The figures (5 A-F) shows that the conductance increases with various concentration of Titanium dioxide doped with Polianline. The titanium dioxide enhances the conductivity of polianilne nanoparicles

CONCLUSION

The Conductivity and dielectric properties such as dielectric constant and dielectric loss have been measured and the conduction mechanism has also been investigated. It is good 25wt% Composite.The PANI/TIO_2 nanocomposite exhibit remarkable improvement of electrical conductivity and dielectric properties when compared with pure PANI. In this another application of mercury detection over range of cyclic voltametric study above the data.

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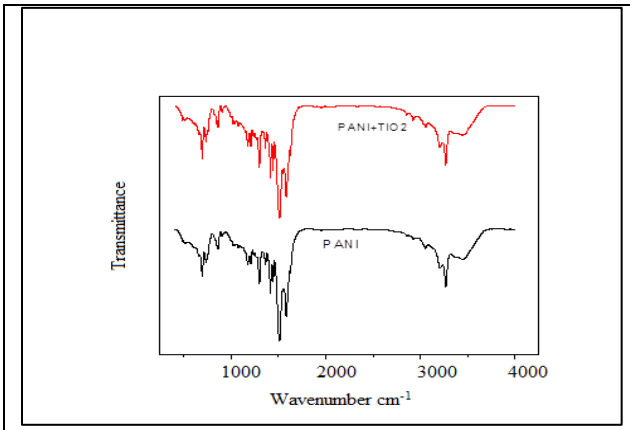

Fig 1: FT-IR Spectrum of polyaniline with Titanium dioxide

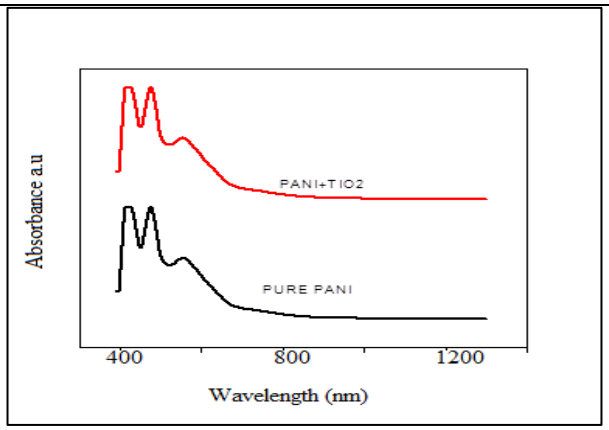

Fig 2: UV-Vis of spectrum of (2a.) PANI (2b). PANI+ TiO_2

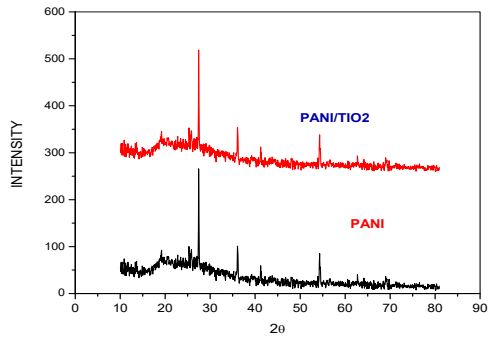

Fig 3: XRD IMAGE OF PANI-TiO_2

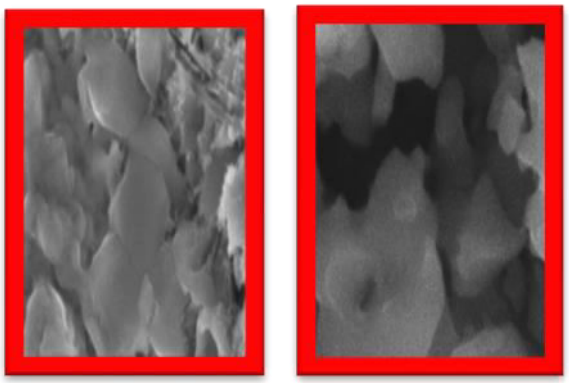

Fig 4: SEM Image of(a) PANI and(b) PANI dopped with TiO_2

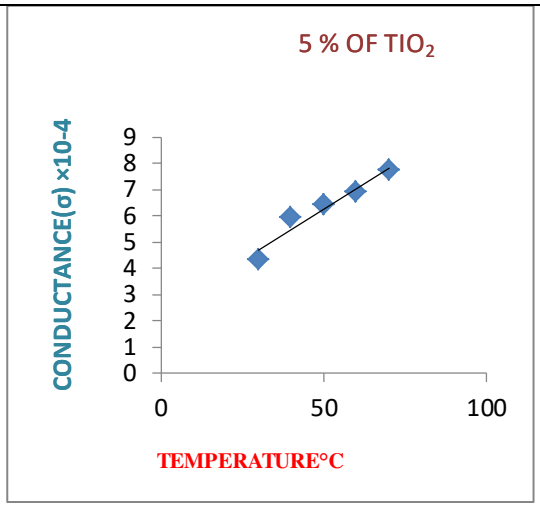

FIG .5 (A) PANI

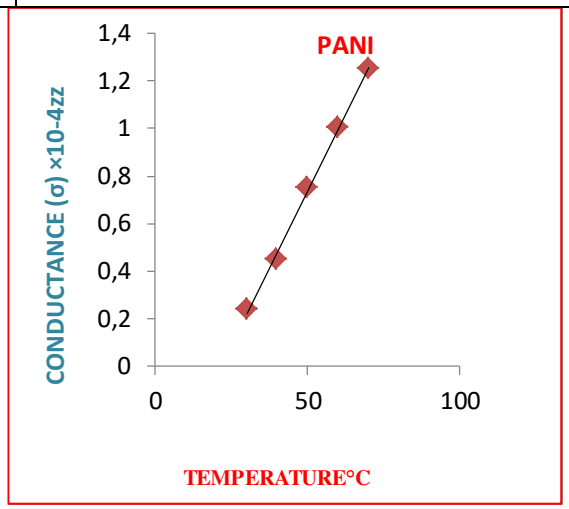

FIG 5. (B) PANI/TiO_2 5%

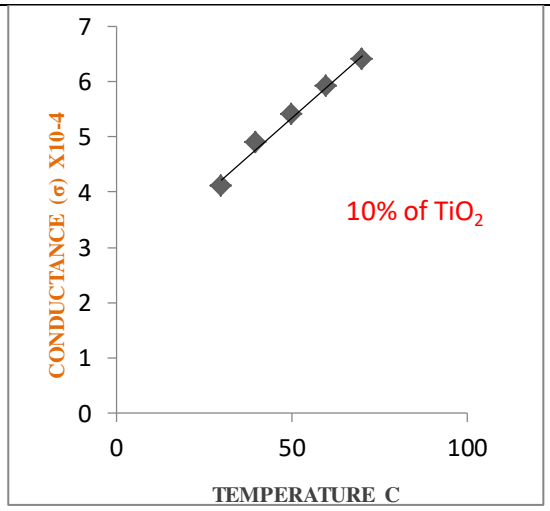

FIG .5 (C) PANI/TiO_2 10%

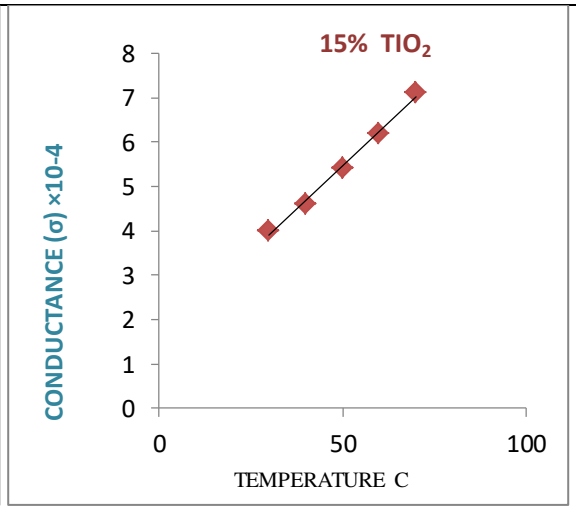

FIG.5 (D) PANI/TiO_2 15%

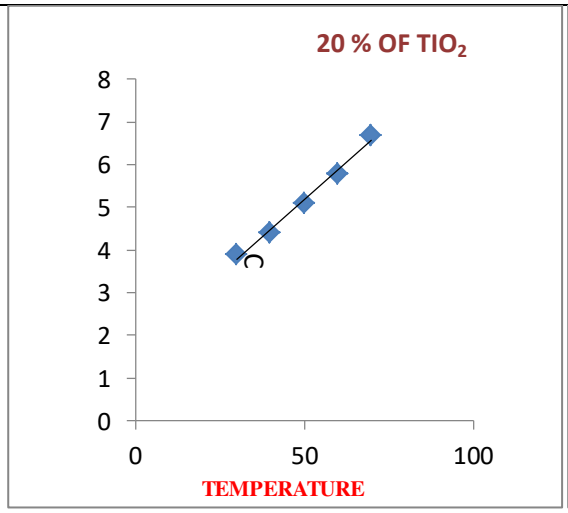

FIG .5 (e) PANI/TIO2 20%

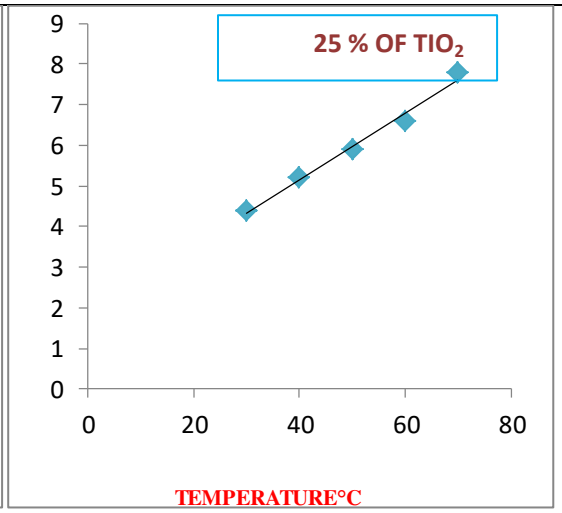

FIG .5 (f) PANI/TIO2 20%

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RESEARCH ARTICLE

Characterization and Identification of Volatile Compounds and Functional Groups in Kodaikanal Hill Garlic Cultivar

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ABSTRACT

Garlic is used as a spice in different cuisines around the world due to its unique aroma. The aroma of garlic is attributed to the presence of sulfur-containing compounds such as thiosulfinates and polysulfides. The extremely volatile nature of the sulfur compounds hinders with the detection of these compounds using simple techniques. Highly sensitive and reliable techniques are required to evaluate the volatile compounds in garlic. In the present study, the Kodaikanal hill garlic (KHG), was analysed using sensitive spectroscopic and chromatographic techniques. Diallyldisulfide was identified as the major volatile compound present in the investigated garlic cultivar by HR-GCMS technique and the abundance of sulfur groups representing the sulfur containing compounds in KHG was revealed in the FT-IR analysis.

Keywords: *Allium sativum*; Kodaikanal Hill garlic; Organosulfur compounds; Volatile compounds; FTIR; HS-GCMS

INTRODUCTION

Allium sativum(Garlic) is one of the popular herbs cultivated in all parts of the world [1]. Garlic plays an inevitable role in ancient medicinal practices that prevail in different traditions owning to its prophylactic and therapeutic properties. Moreover, the reputation of garlic as a medicinal herb still triumphs in modern culinary [2]. Garlic belongs to the *Allium* genus and is rich in aromatic organosulfur compounds (OSCs) such as Allicin, Allyldisulfide, Ajoene, Methyl-2-propenyl trisulfide and S-methylcysteines [3]. Garlic was used by the Chinese and Indians to treat digestive and respiratory disorders, Greeks and Romans describe the healing properties of garlic in their ancient scripts and Egyptians have used Garlic to cure several ailments [4-6]. Numerous studies have reported the antioxidant [7], antimicrobial [8], antidiabetic [9] and anticancer [10] activity of Garlic. Fresh garlic juice and garlic concentrate may be considered as a preventive measure against severe acute respiratory syndrome corona virus 2

(SARS-Cov-2/COVID-19) infection due to its immune boosting mechanism and secretion of pro-inflammatory cytokines [11]. OSCs of garlic are largely responsible for the aromatic flavour and medicinal properties [12]. Allicin is the key bioactive compound and widely studied among the different sulfur containing compounds of garlic. When an intact Garlic clove is crushed or macerated, the enzyme Allinase is activated and in turn is responsible for the conversion of Alliin to Allicin [13]. However, the use of fresh garlic has been reduced in modern culinary and several garlic based products have become popular as kitchen products. Garlic oil, garlic paste, garlic salt, garlic powder and garlic flakes are some of the products that are available commercially [14]. The preparation of commercially available products include suitable cooking pre-treatments and treatment methods such as soaking, roasting, macerating, steaming, stir-frying, deep-frying, roll-boiling or drying [15]. The aroma and the pungent flavour of fresh garlic cloves are altered during these processing techniques [16]. This is due to the reason that the principal bioactive compounds of Garlic are mostly volatile in nature which is responsible for the characteristic pungent smell of the cloves [17]. In recent years, the interest among scientists on these organic compounds to treat chronic diseases such as cancer and cardiovascular diseases has increased [18]. Since many of these compounds are volatile in nature, the suitable method to analyse these compounds is Headspace Gas Chromatography/Mass Spectrometry (HS-GC/MS) technique. The advantage of this method is the exclusion of steam distillation, extraction or solid phase micro-extraction techniques and can be performed in a short duration [19]. Hence the present research aimed at identifying the functional groups and volatile compound profile of KHG (Malaipoondu) using FTIR and HS-GC/MS technique.

MATERIALS AND METHODS

Sample collection and processing

Fresh KHG (Singapore red cultivar) was procured from the native farmers of Kodaikanal hills, Tamilnadu. The bulbs were carefully transported to the laboratory in polythene bags and kept free of moisture. Prior to the analysis, the bulbs were pealed, crushed and transferred into the Head Space vials and sealed. The analysis was performed immediately after crushing the cloves in order to avoid enzymatic degradation of the bioactive compounds present in the bulbs. For FTIR analysis the cloves were chopped and shade dried for 15-20 days. Later, they were grinded into fine powder using a laboratory mixer grinder and the powder was stored at room temperature until analysis.

HS-GCMS analysis of KHG

HS vials sealed with caps were used for the analysis. An Aligent 7890 gas chromatographer coupled to a Jeol Accu TOF GCV with a mass range of 10-2000 amu and mass resolution of 6000 was used for the separation and detection of the bioactive volatile compounds from garlic cloves. KHG was freshly chopped, crushed and 2 g was transferred into the HS vial. The ion chamber temperature was set to 210°C for 15 minutes. The needle temperature and transfer line temperature was set to 90°C and 110°C respectively. Head space pressure of 30 psi and vial pressurise time of 1.00 min was used. Injection time and withdrawal time was set as 0.02 and 0.20 minutes respectively.

FTIR analysis of KHG

FTIR analysis was performed to identify the functional groups present in the KHG cultivar. The dried powder was compressed with 100 mg of Potassium bromide (KBr) to form a pellet. A transparent pellet ensures better characterization of the sample [20]. The pellet is then loaded into the FTIR spectroscope (Perkin Elmer spectrum 100) with a resolution of 4 cm^{-1} and 400 to 4000 cm^{-1} scanning range.

RESULTS AND DISCUSSION

FT-IR analysis provides high possibilities for the identification of organic and inorganic phytocompounds with precise sensitivity [21]. Functional groups present in KHG cultivar was investigated using this technique. Major compounds identified in the FT-IR spectrum are represented in Figure 1. The OH stretching vibration obtained at 3418.00 cm^{-1}corresponds to the alcohol groups mainly present in the primary metabolites of garlic bulbs. The

frequency 2922.21 $cm^{-1}$is related to the alkane compounds which suggested the presence of lipids in the bulbs. The characteristic absorption peak corresponding to carboxylic acids and primary amines depicted the occurrence of proteins and amino acids in the sample. Absorption frequencies at 1315.61 cm^{-1}, 1067.38 cm^{-1} and 678.2 cm^{-1}corresponded to sulfur and ionic sulphones strongly present in the KHG cultivar. Other functional groups as mentioned in Table 1 suggested the presence of primary and secondary metabolites that have different biological properties such as antioxidant and antimicrobial activity. The FT-IR characteristic absorption peaks observed in the present study was parallel with the results of Nagarajan et al., 2017 [2] who reported the presence of alcohol, alkane, primary amine, amino acids and sulfur groups in garlic bulbs. Characterization of whole garlic plant by Rajam et al., 2013 [22] reported the presence of similar functional groups observed in KHG and was correlated with the presence of secondary metabolites such as flavonoids, phenols, saponins and terpenoids. The mechanism of accurate functional group determination by FTIR technique is due to the transitions that occur between quantized vibrational energy states [23]. When a molecule is subjected to IR radiation, photons are transferred to the molecule and excited to higher energy states [24].

The methods and techniques used for the analysis of garlic have a significant impact on the composition of the determined compounds. In the present study HS-GCMS analysis was performed to detect the compounds present in fresh KHG cultivar. The results revealed the presence of Diallyldisulfide as the major organosulfur compound present in the garlic bulbs (Figure 2). Lee et al., 2013 [19] compared the volatile compounds present in garlic processed by various techniques including steam distillation, distillation combined with solvent extraction, headspace solid-phase microextraction and solid-phase trapping solvent extraction. Polysulfiides such as diallyldisulfide and diallyltrisulfide were detected as the major compounds in garlic by distillation combined with extraction, whereas, diallyldisulfide was the predominant compound identified through headspace solid-phase microextraction technique. Table 2 shows that diallyldisulfide was highly volatile in nature and thiosulfinates such as Allicin was not detected in the sample. Alliin and Allicin are the precursor molecules in the synthesis of sulfur containing compounds are highly reactive and degraded in the presence of high temperature [25]. This could be postulated as the possible reason for the absence of thiosulfinates in the chromatogram (Figure 3). Organosulfur compounds and flavonoids present in KHG cultivar have showed impressive anti-proliferative effects against A549 lung cancer cells and also possessed antioxidant activity [26]. Based on the above results, polysulfides were identified to be strongly associated with the strong aroma and flavour of KHG.

CONCLUSION

KHG is popular in India due to its unique flavour, strong aroma and medicinal properties. Highly sensitive and reliable spectroscopic and chromatographic techniques were employed to identify the major phytoconstituents. Diallyldisulfide was identified as the major volatile compound present in the investigated garlic cultivar by HS-GCMS technique and the abundance of sulfur compounds in the garlic bulbs was revealed in the FT-IR analysis. Further, this study supports the inevitable role of organosulfur compounds in the medicinal properties of KHG.

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Table 1: Vibrational frequencies and functional groups present in KHG cultivar

S.No	Characteristic absorptions(cm^{-1})	Functional Group	Type of vibration	Intensity
1.	3418.00	O-H	Stretch	Strong, broad
2.	2922.21	C-H	Stretch	Strong
3.	1732.30	C=O	Stretch	Strong
4.	1615.07	N-H	Stretch	Medium
5.	1444.72	CH_2	Stretch	Medium
6.	1315.61	C=S	Bend	Strong
7.	1263.01	C-N	Stretch	Medium, weak
8.	1106.69	C-H	Symmetrical stretch	Strong
9.	1067.38	SO_3	Stretch	Strong
10.	678.2	S-S	Stretch	Medium, variable

Table 2: List of volatile compounds identified in KHG cultivar by HS-GCMS

S.No	Compound	Molecular Formula	Retention index (iu)	Non-polar retention index (iu)	Peak width (FWHM)	Area	Volatile nature
1	Carbonic anhydride	C=O	152	-	0.1739	5161451	Super volatile
2	Diallyldisulfide	$C_6H_{10}S_2$	1056	1099	0.0985	1101701.61	Highly volatile
3	N-trifluoroacetyl O-O′,O″-tris(trimethylsilyl) norepinephrine	$C_{19}H_{34}F_3NO_4Si_3$	1933	1933	0.0899	78140.36	Medium volatile

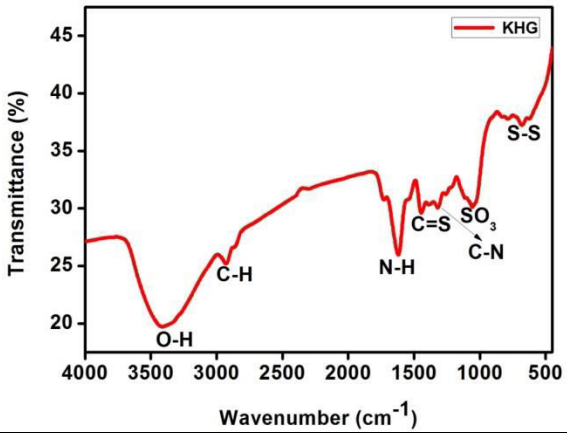

Fig. 1. FTIR spectrum of KHG cultivar

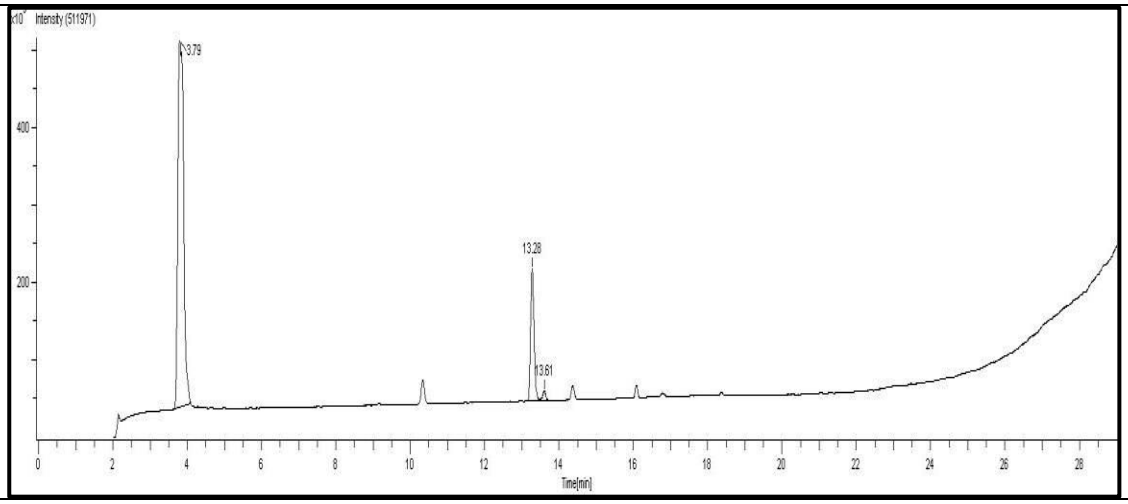

Fig. 2. HS/GC chromatogram of fresh Kodaikanal hill garlic cultivar

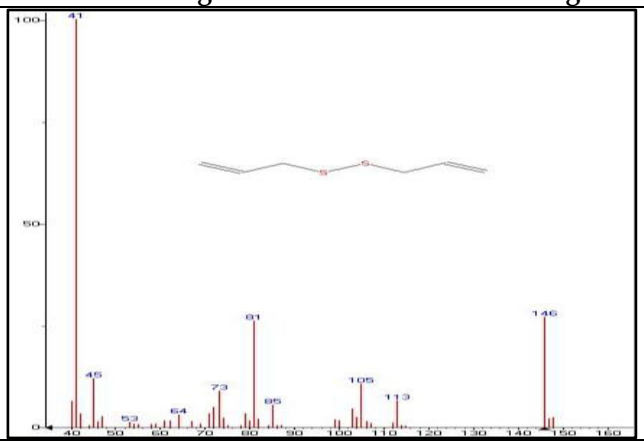

Fig. 3. Mass spectrum of Diallyldisulfide present in KHG cultivar

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REVIEW ARTICLE

Bio-Adhesive Polymers as Promising Drug Delivery

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ABSTRACT

Bio-adhesion is adhesions to facilitate occur in fixing of two surfaces and also involve binding of polymers. A bio-adhesive delivery arrangement reside on a biological exterior allows the localized therapeutic liberation by releasing bio-active molecule in the vicinity of the site of action. It undergoes two mechanism such as, contact stage and consolidation stage. Oral administration is the major direction for drug delivery. Oral controlled release systems are used for controlled action of active ingredients to the targeted site. But oral controlled release systems have many problems such as first pass hepatic metabolism, enzyme degradation, swallowing problem etc. The mechanism of bio-adhesion has been explained by various theories like electrostatic theory, wett ability theory etc. Polymers that are employed for production of the bio-adhesive drug delivery platforms are broadly classified into, Non-specific bio-adhesive polymer (old generation) and Specific bio-adhesive polymers. For development of an effective bio-adhesive drug delivery system, evaluation of its bio-adhesive property is imperative. Adhesion strength of a bio-adhesive system can be evaluated by various tests like in-vitro and in-vivo tests. Its advantages, disadvantages and applications are discussed as below.

Keywords: Bio- adhesive, polymers, muco-adhesion, fixing, theory, action.

INTRODUCTION [1-4]

Bio-adhesion is distinct as adhesion that occurs in biological settings where as adhesion is known as development of fixing of two surfaces with one another. It also involves binding of polymers (natural or synthetic) to a biological substrate. The adhesion takes place at mucosal membrane termed as 'muco-adhesion'. Polymers mostly used as bio-adhesives show binding with mucin and also a lack of deep penetration into underlying epithelial tissues.

A bio-adhesive delivery system residing on a biological surface allows the localized therapeutic delivery by releasing bio-active molecule in the vicinity of the site of action. Furthermore, research shows that bio-adhesion could also refer to the usage of bio-adhesives in order to link the two surfaces together, especially in drug delivery, dental and surgical applications.

ORAL MUCOSA [5-7]

A mucous membrane or mucosa is a membrane that lines various cavities in the body and covers the surface of internal organs. It consists of one or more layers of epithelial cells overlying a layer of loose connective tissue. It comprises stratified squamous epithelium, termed "oral epithelium" and an underlying connective tissue termed lamina propria.

ANATOMY AND PHYSIOLOGY OF ORAL MUCOSA

Light microscopy reveals several distinct patterns of maturation in the epithelium of human oral mucosa based on various regions of the oral cavity. Three distinctive layers of the oral mucosa are,

- Theepithelium.
- Basementmembrane.
- Connectivetissues.

ANATOMY OF THE ORAL MUCOSA

The basement membrane forms a distinctive layer between the connective tissues and the epithelium. It provides the required adherence between the epithelium and the underlying connective tissues and functions as a mechanical support for the epithelium. The permeability barrier property of the oral mucosa is predominantly due to intercellular materials derived from the membrane coating granules (MCGs). MCGs are found near the upper, distal, or superfacial border of the cells and few occurs near the opposite borders. MCGs are spherical or oval organelles that are 100300 nm in diameter. These organelles have also been referred as small spherically shaped granules-corpusula, small dense granules, small lamellated bodies keratinosomes. The oral cavity is lined with the epithelium, below which lies the supporting basement membrane. The basement membrane is supported by connective tissues.

PHYSIOLOGY OF ORAL MUCOSA [8,9]

The buccal epithelium is classified as a non-keratinized tissue. It is penetrated by tall and conical-shaped connective tissues. These tissues, which are also referred to as the lamina propria, consist of collagen fibers, a supporting layer of connective tissues, blood vessels, and smooth muscles. The rich arterial blood supply to the oral mucosa is derived from the external carotid artery. The buccal artery, some terminal branches of the facial artery, the posterior alveolar artery and the infra- orbital artery are the major sources of blood supply to the lining of the in the buccal cavity. Bio-adhesive polymers offer a means by which a delivery system is attached to the buccal mucosa and hence provide substantially longer retention times at the absorption site. They also provide a means to confine and maintain high local concentrations of the drug or excipients to a defined, relatively small region of the mucosa in order to minimize loss to other regions and limit potential side effects.

FACTORS AFFECTING MUCO-ADHESION IN THE ORAL CAVITY

Muco-adhesive characteristics are a factor of both the bio-adhesive polymer and the medium in which the polymer will residue. Some varies factors that affect the mucoadhesive properties of polymers suchas,

- Flexibility
- Hydrogen bondingcapacity
- Molecularweight
- Concentration
- Hydration(swelling) of apolymer

- Charge
- Cross-linked density

FLEXIBILITY [10,11]

Bio-adhesion involves with the diffusion of the polymer chains in the interfacial region. It is important that the polymer chains contain a substantial degree of flexibility in order to achieve the desired entanglement with the mucus. Arecent publication demonstrated the use of tethered poly(ethylene glycol)-poly(acrylic acid) hydrogels and their copolymers with improved muco-adhesive properties. In general, mobility and flexibility of polymers can be related to their viscosities and diffusion coefficients, where higher flexibility of a polymer causes greater diffusion into the mucus network.

HYDROGEN BONDING CAPACITY[12,13]

Hydrogen bonding is another important factor in muco-adhesion of a polymer. Park and Robinson found that in order for muco-adhesion to occur, desired polymers must have functional groups that are able to form hydrogen bonds. Polymers such as poly(vinyl alcohol), hydroxylated methacrylate and poly(methacrylic acid),as well as all their copolymers, are polymers with good hydrogen bonding capacity.

MOLECULAR WEIGHT [14,15]

In general, the bio-adhesive strength of a polymer increases with molecular weights above 100,000 Da. As one example, the direct correlation between the bio- adhesive strength of poly-oxyethylene polymers and their molecular weights is established around in the range of 200,000 Da to 7,000,000 Da.

CONCENTRATION[16]

The importance of this factor lies in the development of a strong adhesive bond with the mucus, and can be explained by the polymer chain length available for penetration into the mucus layer. When the concentration of the polymer is too low, the number of penetrating polymer chains per unit volume of the mucus is small and the interaction between polymer and mucus is unstable. High concentrations of flexible polymeric films based on polyvinylpyrrolidone or poly(vinyl alcohol) as film- forming polymers did not further enhance the muco-adhesive properties of the polymer.

HYDRATION(SWELLING) OF A POLYMER[17]

Hydration is required for a muco-adhesive polymer to expand and create proper 'macromolecular mesh' of sufficient size and also to induce mobility in the polymer chains in order to enhance the interpenetration process between polymer and mucin. Polymer swelling permits a mechanical entanglement by exposing the bio-adhesive sites for hydrogen bonding and electrostatic interaction between the polymer and the mucous network.

CHARGE [18,19]

Some generalizations about the charge of bio-adhesive polymers have been made where non-ionic polymers seem to undergo a small degree of adhesion compared to anionic polymers. Some cationic polymers are likely to demonstrate superior mucoadhesive properties, especially in a neutral or slightly alkaline medium. Some cationic high-molecular weight polymers, such as chitosan, have shown to possess good adhesive properties.

CROSS LINKED DENSITY[20]

The average pore size, the number average molecular weight of the cross- linked polymers, and the density of cross-linking are important and interrelated structural parameters of a polymer network. This general of polymers, in which the degree of swelling at equilibrium has an inverse relationship with the degree of cross- linking of a polymer.

MECHANISM OF BIO-ADHESION [21-24]

The mechanism of muco-adhesion is generally divided in two steps,

- Contact stage
- Consolidation stage

Contact stage

The first stage is characterized by the contact between the muco-adhesive polymer and the mucous membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer. In some cases, such as for ocular or vaginal formulations, the delivery system is mechanically attached over in other cases, the deposition is promoted by the aero dynamics of the organ to the membrane, the system is administered, such as for the nasal route.

Consolidation stage

In the consolidation step, the muco-adhesive materials are activated by the presence of moisture. Moisture plasticizes the system, allowing the muco-adhesive molecules to break free and to link up by weak Vander Waals Force and hydrogen bonds.

NEED OF BIO-ADHESIVE POLYMERS [25-29]

Oral administration is the major route for drug delivery. Oral controlled release systems are used for controlled action of active ingredients to the targeted site. But oral controlled release systems have many problems such as first pass hepatic metabolism, enzyme degradation, swallowing problem etc. So, as compared to oral controlled release systems, muco-adhesive delivery system have several advantages like prolongation of residence time, drug targeting, intimate contact between dosage form and the absorptive mucosa.

In addition, muco-adhesive dosage forms have been used to target local disorders at the mucosal surface to reduce dose and to minimize the side effects. Muco adhesive formulations use polymers as the adhesive component. These polymers are water soluble. When polymers are used in a dry form, they attract water from the mucosal surface and leads to a strong interaction which increases the retention time over the mucosal surfaces. Prolonged contact time of a drug with a body tissue through the use of a bio-adhesive polymer can significantly improve the performance of many drugs.

THEORIES OF BIO-ADHESION [30-35]

Over the years, the mechanism of bio-adhesion has been explained by various theories like,

- Electrostatic theory
- Wettability theory
- Diffusion interpenetration theory
- Adsorption theory
- Fracture theory

Each theory represents a supplementary process involved in different phases of substrate mucus interaction.

ELECTROSTATIC THEORY

The electrostatic theory of bio-adhesion states that the transfer of electrons between muco-adhesive dosage form and mucus, occurring due to differences in their electronic structures, is responsible for the process of muco-adhesion. Formation of the double layer of electric charges occurs at the interface between mucus and bio-adhesive dosage form due to transfer of electrons between the two. Strong attractive forces are generated within this double-layered region due to this process.

WETTABILITY THEORY

According to this theory, "spread ability" of a bio-adhesive drug delivery system across a biological substrate affects bio-adhesion. This theory is applicable only to low viscosity or low muco-adhesion systems. The wettability theory states that bio adhesive system penetrates to the irregular substrate surface followed by hardening and anchoring itself towards the surface. Spread ability and wett ability are the critical parameters governing adhesive performance of such delivery systems. Low interfacial tension between bio-adhesive system and substrate surface increases the wettability and spread ability. Bio-adhesive polymers having the same functional group as that of the mucus layer show a very high degree of polymer spread ability over mucosal surface due to increased miscibility.

DIFFUSION INTERPENETRATION

According to this theory, bio-adhesion is due to time dependent diffusion of bioadhesive polymeric chains into the mucus layer consisting of a complex glycoprotein network. Diffusion-based penetration of the polymeric chains into substrate depends upon the diffusion coefficient of both the interacting polymer and the substrate. Furthermore, cross-linking density, molecular weight, chain mobility/flexibility, temperature, expansion capacity of both networks governs effective penetration of polymer into the mucus network. Interpenetration and polymer mobility is reduced due to excessive chain cross-linking. Maximum interpenetration and bio-adhesive strength are achieved when solubility parameter is similar for interacting polymer and mucus glycoprotein.

ADSORPTION THEORY

This theory states that bio-adhesion is a result of surface interactions between the polymer and mucus substrate. Surface interaction may occur due to primary or secondary bonding. Primary bonds include covalent, metallic, and ionic bonds, which may provide permanent interaction between polymer and substrate. Bonds arising due to hydrophobic interactions, Vander Waals forces, and hydrogen bond are secondary in nature; surface interaction generated due to them is semipermanent. In most cases, muco-adhesion involves secondary bonds.

FRACTURE THEORY

This theory demonstrates the relationship between adhesive bonds and forces necessary to separate both surfaces from one another, i.e., fracture theory relates the strength of mucus adhesive bonds with the force required for polymer detachment. It is observed that longer polymeric network strands and reduced degree of cross linking with in polymer leads to greater work fracture.

CLASSIFICATION OF BIO-ADHESIVE POLYMERS [36]

Polymers that are employed for production of the bio-adhesive drug delivery platforms are broadly classified into,

- Non-specific bio-adhesive polymer (old generation)
- Specific bio-adhesive polymers (new generation)

NON- SPECIFIC BIO-ADHESIVE POLYMER[37]

Conventional muco-adhesive polymers may be,

- Anionic
- Cationic
- Non- ionic polymers

On the basis of the charge carried by them, Furthermore, cationic and anionic polymers are employed for muco-adhesive platforms because of their high muco adhesive capability.

ANIONIC POLYMERS [38-42]

Anionic bio-adhesive polymers are extensively used because of their low toxicity profile and rich muco-adhesive functionality. Such polymers have sulfate and carboxyl functional groups in their molecular structure, providing them a negative charge. Examples of such polymers are poly, sodium-carboxy methyl cellulose (Na CMC), Polycarbophil, and carbomer. Anionic polymers interact through strong hydrogen bonding with mucus covering.

PAA derivatives, carbomers, and polycarbophil are especially used to develop muco-adhesive systems for effective delivery of drugs to the GI tract.

They have categorized PAA polymers as a GRAS class for delivery of dosage forms via the oral route. PAA polymers have properties like transparency, wide molecular weight range, non-toxicity, non-irritancy. Polycarbophil polymer shows high swelling index under neutral pH condition and very low solubility in water. The high swelling index promotes efficient entanglement of polymer within the mucus. Carbomer has an equivalent use compared to polycarbophil but its swelling index is slightly low compared to polycarbophil. The cross-linking capacity of carbomer is slightly low compared to polycarbophil and it is cross-linked with allylpentaerythritol or allyl sucrose, while cross-linking of polycarbophil is carried out with divinyl glycol. Polycarbophil and carbomer intermingle with mucus through a hydrogen bond between carboxylic group and mucosal surface.

CATIONIC POLYMERS[43-46]

Chitosan is an example of cationic polymers widely used for muco-adhesive investigations. It is produced from de-acetylation of chitin, which is the second-most abundant polysaccharide in the world. Chitosan has a film-forming capacity and it is widely used as a strengthening agent in paper manufacturing, and is the dye binder in the textile industry. Due to its hypo-lipidemic effect, it is an important constituent of dietary materials. Chitosan has good bio-degradable, toxicological, and biocompatible characteristics, thus promoting its use as a bio-adhesive polymer. The ionic interaction between an amino functional group of chitosan and sulfonic acid orsialic acid component of mucus is responsible for muco adhesion. Sufficient chain flexibility provided by linearity of chitosan molecules promotes its interpenetration in the mucus layer. Chitosan based bio-adhesive systems also promote absorption of various bio-active molecules through a para-cellular route, due to the anionic charge neutralization existing between mucosal cells in the tight junction area. Chitosan is a very beneficial polymer as it can be modified easily by the addition of various chemical groups into its structure, especially at the C-2 position. Various pharmaceutical challenges can be overcome by using chemically modified chitosan as the muco-adhesive polymer of choice.

SPECIFIC BIO-ADHESIVE POLYMERS[47]

Non-specific polymers may be less effective as they may sometimes attach to a site that is not the desired target (off-target binding). At the same time, non-specific polymers are highly susceptible to mucus turnover rates. At a higher mucus turn overrate, efficiency of bio-adhesion of non-specific polymers decreases. So, new generation specific bio-adhesive polymers have been used recently by pharmaceutical scientists due to their independency from mucus turn overrates and effective targeting of mucus surface based upon the presence of carbohydrates and protein composition on it.

Newer polymers are capable of forming covalent bonds with the mucus and the underlying cell layers and hence exhibit improved chemical interactions. The new generation of muco-adhesives (with the exception of thiolated polymers) can adhere directly to the cell surface, rather than to mucus. They interact with the cell surface by means of specific receptors or covalent bonding instead of non-specific mechanisms. Example of recently discovered bio-adhesive polymers are the incorporation of L- cysteine into,

- Thiolated muco-adhesive polymers
- Lectin based polymers.

THIOLATED MUCO-ADHESIVE POLYMERS[48,49]:

Thiolated polymers include derivatives of various hydrophilic polymers like chitosan or poly-acrylates. The main examples of thiolated polymers are poly (acrylic acid)– cysteine, poly (methacrylic acid)–cysteine, chitosan–thioglycolic acid (TGA), chitosan–thioethylamidine, and alginate–cysteine. Thiolated polymers show improvement in residence time and bioavailability due to the formation of covalent bonds between cysteine-rich parts of the mucus layer. Thiol group is responsible for this covalent bonding. Thiomers also have the capability to become covalently anchored in the mucus layer due to formation of disulfide bonds. Disulfide bonding also influences the drug release

mechanism of a muco-adhesive system because of the increase in cross-linking and rigidity. Thiolated new generation polymers usually show diffusion-controlled drug release mechanism.

LECTIN BASED POLYMERS[50,51]

Lectins are chemically proteins which are involved in various phenomena like biological adhesion and adherence. More specifically, they are structurally diverse glycoproteins having the capability to bind with carbohydrate residues. Lectins can reside on a cell surface during initial mucosal cell adherence. However, in the case of receptor-mediated adherence, they show the internalization effect by following endocytosis. Examples of various lectin-based polymers used in bio-adhesive platforms are peanut agglutinin, *ulex europaeus* agglutinin, and lentil lectin.

Lectin based bio-adhesive polymers show targeted specific bio-adhesion phenomenon along with controlled delivery of bioactive molecules active cell mediated uptake process. Lectins do not show premature inactivation by the shed off mucus as observed in the case of first-generation polymers, thus promoting high distribution of lectin-based delivery systems through reversible adherence. Despite all these advantages, lectins may also show various toxicological and immunological problems. It is also reported that lectin-induced antibiotics have the capability to block the interaction between bio-adhesive surface and lectin-based drug delivery systems.

IDEAL PROPERTIES OF BIO-ADHESIVE POLYMERS [52,53]

A muco-adhesion promoting agent or the polymer is added to the formulation which helps to promote the adhering of the active pharmaceutical ingredient to theoral mucosa. The agent can have such additional properties like swelling so as to promote the disintegration when in contact with the saliva.

- Polymer must have a high molecular weight up to 100.00 or more. This is necessary to promote the adhesiveness between the polymer and mucus.
- Long chain polymers-chain length must be long enough to promote the interpenetration and it should not be too long that diffusion becomes a problem.
- High viscosity and polymer should not beimmuno genic.
- Degree of cross linking- it influences chain mobility and resistance to dissolution. Highly cross-linked polymers swell in presence of water and retain their structure. Swelling favors controlled release of the drug and increases the polymer/mucus interpenetration
- Spatial conformation amd polymer should possess cohesiveness to provide strength inside the inner layer.
- Flexibility of polymer chain- this promotes the interpenetration of the polymer within the mucus network.
- Concentration of the polymer- an optimum concentration is required to promote the muco-adhesive strength. It depends however, on the dosage form.

Charge and degree of ionization- the effect of polymer charge on muco adhesion was clearly shown by Bernkop-Schnurch and Freudl. Cationic chitosan HCl showed marked adhesiveness when compared to the control. The attachment of EDTA an anionic group increased the muco-adhesive strength significantly. DTPA/chitosan system exhibited lower muco-adhesive strength than cationic chitosan and anionic EDTA chitosan complexes because of low charge. Hence the muco adhesive strength can be attributed as:

Anion>Cation>Non-ionic

Excessive hydration leads to decreased muco-adhesive strength due to formation of a slippery mucilage.

Muco-adhesion is optimum at low pH `conditions but at higher pH values a change in the conformation occurs into a rod like structure making.

EVALUATION PARAMETERS OF BIO-ADHESIVE POLYMERS [54]

For development of an effective bio-adhesive drug delivery system, evaluation of its bio-adhesive property is imperative. Adhesion strength of a bio-adhesive system can be evaluated by various tests as follows:

- *In-vitro* tests
- *In-vivo* tests

***IN-VITRO* EVALUATION PARAMETERS**

Various in-vitro evaluation parameters for bio-adhesive polymers reported in the literature are discussed below.

- Measurement of detachment force.
- Tensile strength measurement.
- Measurement of adhesion strength.
- Falling liquid film technique.
- Colloidal gold staining technique.

MEASUREMENT OF DETACHMENT FORCE[55,56]

This test involves measurement of the force required to separate two parallel glass slides covered with polymer and mucus layer respectively. This method includes attachment of the glass plate covered with polymer through micro-force balance and its immersion in the mucus sample under the controlled environmental condition. Detachment force is measured as force required dragging the plate out of the mucus sample.

TENSILE STRENGTH MEASUREMENT [57]

Tensile strength measurement is carried out by using different equipment like M30K, in which aqueous dispersion of a bio-adhesive polymer is placed between two discs made up of polyoxymethylene. The upper disc shows movement while the lower disc is stationary, as it is fixed on a stationary frame of the machine. After application of the tensile force, maximum force required for detaching next to the fracture is calculated by using a force displacement curve. A force that is required to detach bioadhesive cup in a perpendicular fashion from bovine buccal mucosa is termed as tensile strength.

MEASUREMENT OF ADHESION STRENGTH [58-60]

Adhesion strength measurement can be carried out by using the fluorescent probe method. Probes are used to analyze the polymer and mucin interaction. This process involves labeling of pyrene as a probe over mucosal surface. Polymer adhesion to the mucosal surface causes a change in degree of fluorescence, which is proportional to the polymer binding.

FALLING LIQUID FILM TECHNIQUE[61]

This method involves *in-situ* quantification of adherence of particles on a mucosal surface. Briefly, a particulate system like microspheres in suspension form are allowed to flow down through an inclined plastic slide covered with mucosal membrane. The difference between applied microsphere amount and flowed microsphere amount gives a value of adhering microspheres.

COLLOIDAL GOLD STAINING TECHNIQUE[62]

This technique is used for quantitative comparison of bio-adhesive properties of various hydrogels. This method involves interaction of mucin-gold conjugates with hydrogel surface leading to red coloration. Mucin-gold conjugates are composed of red colloidal gold particles having adsorbed mucin molecules in the surface. Measurement of intensity of red color produced due to interaction between conjugate and muco-adhesive hydrogel gives quantitative evaluation of bio-adhesive property of hydrogel.

***IN-VIVO* EVALUATION PARAMETERS**

Various *in-vivo* evaluation parameters for bio-adhesive polymers reported in the literature are discussed below.

- Gamma Scintigraphy Technique
- Isolated Loop Technique
- X-Ray Studies

GAMMA SCINTIGRAPHY TECHNIQUE[63,64]

In this technique, the bio-adhesive property of micro spheres was calculated in terms of mean residence time, followed by injection into the in-site perfused gut segment. An in-vivo distribution pattern of any dosage form is confirmed by using gamma scintigraphy technique.

ISOLATED LOOP TECHNIQUE[65]

In this technique, the bio-adhesive property of microspheres was calculated in terms of mean residence time, followed by injection into the in situ perfused gut segment. The intestinal transit of bio-adhesive microspheres is investigated by using the isolated ileal loop model.

X-RAY STUDIES[66]

GI transit time of bio-adhesive formulations can be confirmed through X-Ray inspection by coating the formulations with radio-opaque markers like barium sulfate.

Ray photographs are taken from an animal body at different time intervals to give an idea about GI transit time.

ADVANTAGES OF BIO-ADHESIVE POLYMERS [67-69]

Prolongs the residence time of the dosage form at the site of absorption, hence increases the bio-availability.

- Excellent accessibility, rapid onset of action.
- Rapid absorption because of enormous blood supply and good blood flow rates.
- Drug is sheltered from degradation in the acidic environment in the GIT.
- Improved patient compliance.
- Enhanced patient compliance due to the easy application of dosage forms in comparison to the injections and don't provide any painful sensation.
- Due to the high extent of perfusion the rate of drug absorption is faster.
- The drugs, which show poor bio-availability via the oral route, can their bioavailability can be enhanced by formulating their muco-adhesive delivery systems.
- The sustained drug delivery can be achieved by using the muco-adhesive polymers of 'SR' grades.
- The mucosal membranes are highly vascularized so that the administration as well as removal of a dosage form is easy.

DISADVANTAGES OF BIO-ADHESIVE POLYMERS[70-72]

- Occurrence of local ulcerations due to prolonged contact of the drug possessing ulcerogenic property.
- One of the major limitations in the development of oral mucosal delivery is the lack of a good model for in-vitro screening to identify drugs suitable for such administration.
- Patient acceptability in terms to taste and irritancy.
- Eating and Drinking is prohibited.
- The continuous secretion of saliva (0.5-2 l/day) leads to successive dilution of thedrug.
- Medications administered orally do not enter the blood stream immediately after passage through the buccal mucosa. Instead they have to be swallowed and then have to through a portion of the GIT before being absorbed.
- Oral ingestions result in more exposure of a drug to the GI tract. One of the side effects of many antibiotics is the destruction of normal GI flora resulting in diarrhea and over growth with dangerous organisms such as *C.difficile.*
- The absorption of muco-adhesive drugs is adversely affected by the presence of food. Tetracyclines, in particular, obscure the administration of this class of antibiotics via the oral route.
- Enzymatic and immunogenic degradation of both drug and bio-adhesive must be addressed in any route of administration but seems to be very important in the GI tract.
- Another drawback of GI route is that drugs that enter the general circulation are subjected to first-pass metabolism as they pass through the hepatic–portal system leading to lower systemic availability.

APPLICATIONS OF BIO-ADHESIVE POLYMERS [73,74]

- Bio-adhesives are generally used in wound healing and haemostasis, and their use is incipient in other bio-medical applications such as tissue engineering and regeneration.
- The practical applications of bio-adhesive biomaterial research in medical aspects, it is necessary to mention that over the past decade, a growing amount of attention has been paid to one tissue engineering for research and development in bio-adhesive bio-materials' biomedical applications, and resource management, around the world to meet the societal challenges.
- The progressive innovation in bio-adhesive biomaterials has trended sharply upward, and is expected to double by 2020, especially with a focus on the application of bone tissue engineering.
- The applications of MP and MP-based bio-composites in the health and nanobiotechnology sectors (cell to-cell interactions, bio-film formation, and cell protection against environmental extremes), such polysaccharides are also used as thickeners, bio-adhesives, stabilizers, pro-biotics, and gelling agents in the food and cosmetic industries, and as emulsifier, bio-sorbents and bio- flocculants in the environmental sector.
- The relevance of bio-compatibility studies has also emphasized the development of BC-based bio-materials' medical applications in one, skin and cardiovascular tissue engineering.
- Bio-adhesive polymers can also be used in following applications such as,

VAGINAL DRUG DELIVERY[75,76]

The vagina is a fibro muscular and tubular organ having a length of about 9 centimeters extending from the cervix of uterus to the vaginal vestibules. The vagina is generally considered as mucosal tissue without gland and vaginal secretions are a mixture of various fluids from a number of sources. Vaginal mucus coating plays an important role in various physiological functions along with drug absorption. The pH of vaginal fluid ranges from 4.5 to 5.5 and menstrual cycle has a distinct impact on its rheology, composition, and volume. Vaginal drug delivery offers various advantages like avoidance of enzymatic degradation, drug interactions, and first pass effect. The most common polyacrylic acid (PAA)derivatives used as muco adhesive polymers in vaginal preparations are Carbopols and polycarbophil. Polycarbophil is a lightly cross linked PAA while carbopols are very high molecular weight polymers of acrylic acid.

BUCCAL DRUG DELIVERY SYSTEM[77,78]

The oral route is the most patient-compliant route for delivery of various therapeutic active molecules as it avoids discomfort, pain, and chances of infections caused by injections. However, the utility of the oral route has been hampered by some associated disadvantages like acidic degradation of bio-active molecules in the stomach, least macromolecular permeability through intestinal epithelium, and degradation through proteolytic enzymes. Muco-adhesive polymers such as agarose, chitosan, gelatin, hyaluronic acid, various gums from the source of semi-natural category are used in Buccal Drug Delivery Systems.

RECTAL DRUG DELIVERY[79,80]

The rectal route serves as an alternative to oral or invasive administration. The rectal route of drug delivery is utilized when oral medication is not possible and the patient has difficulty swallowing due to nausea and vomiting produced in patients after oral administration. The rectal route offers various advantages like avoidance of first pass effect, absorption of medicament into the lymphatic system, and absorption enhancement. The last portion of intestine is known as the rectum, which have a length of 12–18 cm along with two or three curves within its lumen generated through submucosal folds. Bio-adhesive polymers such as Poloxamer 407 used in rectal drug delivery system in the form of bio-adhesive gel from the drug 5Fluorouracil. It also includes polymer like Xanthangum.

NASAL DRUG DELIVERY[81-83]

Nasal mucosa may be a prominent choice for systemic drug delivery as this route is open to self-medication and is painless. The nose is usually considered a local drug delivery route. This route of delivery is preferred in management of conditions like severe nausea and vomiting. In comparison to the oral route, drugs like protein and

peptide administered through nasal delivery systems show increased absorption, which may be due to high epithelial permeability/porosity along with a limited enzymatic activity. By utilizing various nasal muco-adhesive polymers, controlled release formulation can be developed and there are a large number of polymers that come under the category of GRAS (Generally Regarded as Safe). Several studies have also categorized nasal mucosa as the preferred site for immunization purpose prepared bio-adhesive starch microspheres loaded with insulin and investigated their effect on the nasal absorption enhancement capacity of various enhancers with insulin sheep as the animal model. Bio-adhesive polymers such as Hydroxypropyl methyl cellulose used in Nasal Drug Delivery System from the drug Insulin. It also includes bio-adhesive polymers like starch, pectin and cross linked poly (acrylic acid).

CONCLUSION

Finally, it can be said that this review article delivers an understanding of the consequences of the bio-adhesion of bio-materials and its implications for redefining healthcare management as a novel approach, even though some research has been performed in order to describe the polysaccharides based adhesive application at a micro level or at a nano level, which has been done for the preparation of molecularly smooth films for healthcare resolution. The analyses revealed some important research assumptions that were predictive of the healthcare management and innovative bio-materials applications, which state that the bio-adhesion of bio-materials for redefining healthcare management is not a new concept. Its implementation has been used for several years for medical applications, such as dentistry and orthopedics, and is now entering new fields, for example, tissue sealing and directed drug delivery systems. From the practical implication point of view, the results provide an important insight into the notion of involving healthcare delivery organizations.

Bio-adhesive polymer-based systems may play an important role in delivering various bio-active molecules with the arrival of new large and small molecules in the field of drug research. Although bio-adhesive polymers are becoming trendy in the field of drug delivery, they are still ranked according to multiple available techniques due to lack of a universal technique for testing of their muco-adhesive strength. Hence, development of a universal bio-adhesion evaluation technique is necessary for selection of polymers.

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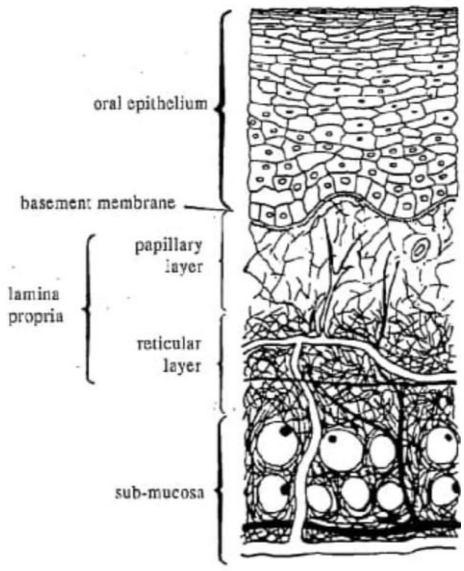

Fig.1. Anatomy of Oral Mucosa