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RESEARCH ARTICLE

Generational Transmission of ZnO, Phosphorus and Anatase -Tio$_2$ Nanoparticles to Promote Growth, Yield and Qualitative Trait in Tomato (*Lycopersicon esculentum* L.)

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ABSTRACT

In the present scenario, the application of nanoparticles in the agriculture area shows the potential effect on improving plant growth in yield and safety at very emerging phases. Nanoparticles have the potential to improve the growth and yield of tomatoes. The main objective of this study was to perform the effect and generational transmission of ZnO, Phosphorus and Anatase-TiO_2 nanoparticles on yield attributing and biochemical traits of Tomato. The response to nanoparticles to induce optimum economic yield was variable. Higher concentrations of ZnO (10 ppm) and Phosphorus (40 ppm) were found comparatively significant for most of the characters except the number of cluster plant^{-1} and 50% flowering; however, lower concentration of Anatase-TiO_2 (20 ppm) treatment had an optimum effect on characters primary branches, plant height, number of fruits plant^{-1}, number of cluster plant^{-1}, the weight of the fresh plant, lycopene contents, B-carotene and fruit yield plant^{-1}**.** Given all the treatments, an increase of 50.08% (14 ppm ZnO), 55.31% (50 ppm Phosphorus) and 52.57% (20 ppm TiO_2) of fruit yield were recorded maximum by application of NPs. In the second generation, higher concentrations of ZnO and Phosphorus have shown optimum response to enhance the economic yield of Tomato, while lower concentrations of TiO_2 induced similar results. Generational differences in response to different concentrations may be due to differential accumulation of nanoparticles from seed to root and its translocation to plant parts.

Keywords: Generational transmission, Nanoparticles, ZnO, Phosphorus, TiO_2, Tomato, Growth promoter

INTRODUCTION

Nanotechnology occupied a prominent position in transforming agriculture among the latest technological innovations, which boost food production by incorporating nanoparticles into plant systems (Cossins, 2014, Rohira H., Kumar V., Chugh A., 2015). The beneficial effect of nanoparticles in plant growth and development depends on the type of nanoparticles, definite concentration, and plant species (Hong et al., 2005; Gao et al., 2006; Ma et al., 2010). Some properties of nanoparticles are small size, high surface to volume ratio, quantum effect and increase biochemical activity to plants (Dubchak et al., 2010).

Significant improvement of plant growth visualizes by nanoparticles treatment. However, at the molecular level, the interaction mechanisms of nanoparticles remained lagging (Barrena et al., 2009). Preliminary investigations also documented the beneficial effect of several nanomaterials on the growth and development of crop plants. A comprehensive review described a variety of nanoparticles (NPs), mostly metal-based and carbon-based, for their uptake and accumulation, with concomitant effects on growth characteristics in an array of crop plants (Rico et al., 2011, Rohira H., Kumar V., Chugh A., 2015). These reports include improved germination rate, germination percentage, seedling vigour index, root growth, root shoot ratio, root length, fresh biomass and moisture content in seed in several vegetable crops, including radish, cucumber, lettuce, tomato and onion (Rico et al. 2011).

Among metal-based nanoparticles (MBNPs), ZnO, TiO_2 and Phosphorous nanoparticles are widely used in agricultural sciences, exploiting significant results of our earlier report on Tomato seed germination and seedling growth (Das et al., 2015). It was postulated that the beneficial effect of ZnO nanoparticles in cucumber and peanut was significantly enhanced growth, yield and starch content (Zhao et al., 2013; Prasad et al., 2012). Applying biosynthesis phosphorous nanoparticles in urd, mung and cowpea resulted in a significant increase in seed germination (38.1%, 20.83% and 20.83%) and seedlings growth (Priya et al., 2015). On the other hand, TiO_2NPs in optimum concentration accelerates seed germination of spinach (Zheng et al., 2005), enhance mRNA, protein level, activities of rubisco activase, rubisco carboxylase and rate of photosynthetic carbon reaction, chlorophyll content that led to increased plant dry weight and promoted photosynthesis of spinach (Gao et al., 2006). However, none of this investigation documented any improvement in crop yield and quality and generational transmission of nanoparticles, although such improvements have been reported in soybean, bitter melon and rice (Sheykhbaglou et al., 2010; Kole et al., 2013; Lin et al., 2009). On these outskirts, the present study was taken to investigate the impact of various concentrations of ZnO, Phosphorus and TiO_2 nanoparticles and their accumulation, translocation and generational transmission on morpho-physiological, yield and biochemical traits in tomatoes.

MATERIALS AND METHODS

The materials used: Biosynthesized ZnO and Phosphorus nanoparticles (NPs) with a particle size of (<100 nm) were collected from CAZRI, Jodhpur, Rajasthan. The TiO_2 (Anatase) nanoparticles with a purity of 99.5% and particle size of (<100 nm) were purchased from Sigma-Aldrich, USA.

Characterization of nanoparticles: The particle size analysis to determine the particle size of ZnO, Phosphorus and TiO2 nanoparticles was studied using dynamic light scattering (DLS). Transmission electron microscope (TEM) measurements were carried out using the drop coating method to confirm the size and shape of nanoparticles. To measure single nanoparticles of ZnO and Phosphorus, high-resolution transmission electron microscope (HR-TEM) image of the sample was used in the JEM-2100F TEM instrument. For measurement of crystal structure of ZnO nanoparticles XRD analysis were done by thin film mode of X-ray Diffraction using X'PERT PRO MRD model.

Scanning electron microscopy (SEM) is used to determine the topology of the nanoparticles using the Hitchi-S-3400 N SEM instrument. The uptake of nanoparticles in root and shoot was examined by field-emission scanning electron microscope (SEM) and electron diffraction spectrum (EDS) analysis studied for estimation of the quantitative elemental proportion of nanoparticles.

Seed treatment and Field study: To test the effect of ZnO, Phosphorus and TiO_2 nanoparticles, our experiment was set under laboratory and field conditions using tomato local variety Patharkuchi (Department of Genetics and Plant Breeding, BCKV). Healthy seeds were isolated and surface sterilized with 0.1% Mercuric Chloride solution for 1 min, then repeatedly rinsed with sterilized distilled water (DW). Then uniform and healthy tomato seeds were treated with six different concentrations, including control for 48 hrs of ZnO, Phosphorus and TiO_2 nanoparticles. Six different concentrations including control of ZnO NPs (0, 2, 4, 8, 10, 14 ppm), Phosphorus NPs (0, 10, 20, 30, 40, 50 ppm) and TiO_2 NPs (0, 10, 20, 30, 40, 50 ppm) were treated for 48 hrs. of tomato seeds (var. Patharkuchi) and sown in the field based on randomized block design (RBD) with 3 replications.

During the entire period of two successive *Rabi* seasons of tomato plants, growth and yield parameters such as 50% flowering, plant height, fruit number plant^{-1}, number of primary branches, number of cluster plant^{-1}, total biomass and yield plant^{-1} and biochemical parameters such as chlorophyll content, lycopene and beta carotene content in the tomato fruit were recorded. Each plant was weighed after harvesting fruit except for roots to obtain fresh plant weight (kg). The spectrophotometric method estimated the total chlorophyll content from young leaf, lycopene, and β-carotene content of the freshly harvested ripe tomato pulp (Davies 1976). In the second season, the first season harvested seeds from each crop having nanoparticles treatments were sown in the field and again, all the morpho-physiological, yield and biochemical parameters were recorded.

Statistical Analysis: Each treatment NPs was studied with three replication and the results were presented as mean ± SE (standard error of the mean) and CD value. The experimental data were analyzed according to the Duncan's multiple range test (DMRT) and the mean value was compared to its control. Statistical significance among the treatment was accepted when the probability of the result was less than 0.05 (level of probability). All the experimental data were analyzed in OPSTAT software.

RESULTS AND DISCUSSION

ZnO, Phosphorus and TiO_2 nanoparticles characterization: The size of ZnO, Phosphorus and TiO_2 nanoparticles was analyzed by DLS using a particle size analyser. Their histogram resulted in particle size ranges from 1.2 to 6.8 nm, 4.6 to 51.8 nm and 10.3 to 105.8 nm of ZnO, Phosphorus and TiO2 nanoparticles, respectively (Fig. 1A, 2A and 3A). The size, shape and morphological of the nanoparticles were measured TEM. ZnO and P nanoparticles were measured in TEM (Fig. 1B and 2B) and showed spherical characteristics.SEM analysis was confirmed the size of TiO_2 nanoparticles (Fig. 3 B). The structural morphology of the individual nanoparticles could be revealed by observing a highly magnified TEM micrograph (Fig. 1C, 2C and 3C)**.** Again ZnO nanoparticles was studied by X-ray Diffraction (XRD) analysis (Fig. 1D) and found crystal structure. The EDS spectrum of phosphorous nanoparticles was shown in Fig. 2D, that confirmed the purity of phosphorous nanoparticles. The EDS spectrum found peak intensity of phosphorous (62 atom %) and besides this, calcium (11 atom %) peak was present due to the chemical composition of salt.

Effect of ZnO, Phosphorus and TiO_2 nanoparticles for yield and biochemical traits of Tomato: The obtained results demonstrated a significant difference within the treatment (with different concentrations) of ZnO, Phosphorus and TiO_2 nanoparticles, suggesting standardization of treatments with different nanoparticles to obtain the optimum result. Our finding depicted early flowering in Patharkuchi by nanoparticles treatment. Application of ZnO nanoparticles early flowering was observed in 10 ppm treatment followed by 14 ppm. But in the case of Phosphorus and TiO_2 treated tomato plants, early flowering was seen in Patharkuchi at 10 ppm and 20 ppm (Table 1). The most

favourable effect on plant height when treated with ZnO, Phosphorus and TiO_2 was found to be 9.84% (10 ppm), 18.96% (50 ppm) and 18.39% (30 ppm) increase over the control (Table 1). Significantly at the maturity stage, more number of fruit plant^{-1} was produced with 10 ppm ZnO (69.27%), 30 ppm Phosphorus (70.23%) and 20 ppm TiO_2 (75.38%) in comparison to control. Different treatments produce maximum numbers of fruits as compared to control (Raliya et al., 2015b). A significant increase in the number of primary branches was observed in all of the treatments. However, more number of primary branch plant^{-1} was noticed with 10 ppm ZnO (13.75%), 30 ppm Phosphorus (9.04%) and 10 ppm TiO_2 (9.08%) in comparison to control in Patharkuchi. The number of clusters showing an increase of 144.81% (10 ppm ZnO), 68.59% (30 ppm P) and 68.29% (20 ppm TiO_2) over the control (Table 1). Significantly enhancement of fresh weight of plant biomass exhibited with 14 ppm ZnO (35.38%), 50 ppm Phosphorus (24.61%) and 20 ppm TiO_2 (26.15%) in comparison to control. In particular, after seed treatment with the colloidal solution of nanoparticles, chlorophyll content increased with treatment by 43.34% (2 ppm ZnO), 51.00% (50 ppm Phosphorus) and 9.33% (40 ppm TiO_2), respectively, as compared to the control. The chlorophyll content increased in tomatoes by application of TiO_2 and ZnO nanoparticles (Tarafdar et al., 2014); (Raliya et al., 2015a). In ripened fruits, lycopene content increased by 16.70%, 11.67% and 17.30% with 10 ppm ZnO, 50 ppm P and 10 ppm TiO_2 nanoparticles. Beta carotene content (mg/gm.) in tomato fruits was also observed in tomato fruits increased significantly by ZnO, Phosphorus and TiO_2 nanoparticles delivered by seed treatment. Overall, a significant increase of B-carotenoid content for ripen fruit was investigated 26.31% (4 ppm ZnO), 26.31% (20 ppm Phosphorus) and 26.31% (30 ppm TiO_2) over the control. A significant increase of fruit was estimated among the nanoparticles treatments. Considering all the treatment, Patharkuchi was found best for yield and showing an increased fruit yield for 50.08% (14 ppm ZnO), 55.31% (50 ppm Phosphorus) and 52.57% (20 ppm TiO_2) treated nanoparticles among the three varieties. Consistent results of the application of TiO2 and ZnO nanoparticles in tomato plants are found with the earlier reports (Raliya et al., 2015b). An earlier report also suggested that CeO, iron oxide and fullerol nanoparticles increased wheat, soybean and bitter gourd yield by 36.6%, 48% and 128%, respectively (Yang et al., 2006; Sheykhbaglou et al., 2010; Kole et al., 2013).

Comparative analysis on effect exhibited of ZnO, Phosphorus and TiO_2 nanoparticles in the second generation of Tomato: In the second season, the first season harvested seeds from each crop having nanoparticles treatments were sown in the field to test the transmission and genetic inheritance of yield attributing and biochemical traits against control. The comparative study of nanoparticles transmission following the second generation has been summarized in Fig 4. The progeny obtained from different treatments of nanoparticles showed variable responses for different characters for observed best treatment concerned with different nanoparticles. The best performance of some characters in the second generation highlighted from the same concentration of nanoparticles similar to the first generation from where the second generation raised or it was from higher or lower concentration compared to the first generation. In the second generation, higher concentrations of ZnO and Phosphorus depicted optimum response to enhance economic yield while lower concentrations of TiO_2 induced similar results in tomatoes. In the second generation, many characters in tomatoes responded to high to higher concentrations except plant height, number of fruit plant^{-1}, biomass and B-carotene content. Conspicuously economic yield showed an unchanged dose effect in both generations. In the second season, fruit yield showing an increase of 32.85% (10 ppm ZnO), 39.28% (P at 50 ppm) and 57.14% (TiO_2 at 20 ppm) improvement over the control found in Patharkuchi. Other than economic yield, chlorophyll content in tomato the similar best results as compared to first-generation obtained in second-generation which might be due to persistence of genetic information to produce necessary ingredients culminating to enhanced development of specific character though transmission of nanoparticles in the second generation is comparatively less and confirmed in the present investigation (Lin et al., 2009). The impact of persistence of genetic information may be the resultant effect of point mutation or cryptic mutation (Kumari et al., 2009; Singh et al., 2009). But in the second situation, the same concentration failed to provide the best result as decreased transmission of nanoparticles failed to complement the necessary genetic information obtained from a higher concentration of first-generation treated population. The third category where the concentration of nanoparticles in the first generation was high and then in a second generation low could be due to interaction with a small number of nanoparticles with genetic system conditioning a particular character, so large number of particles transmitted in the second generation may

remain aggregated and inactive. However, few of them interact with the genetic system and others failed to improve the concerned characters.

Accumulation and translocation of nanoparticles in first-generation and their transmission in the following second generation: The accumulation and translocation of ZnO and TiO_2 by the seed to the plant parts were confirmed by SEM-EDAX measurements (Figure 5). Thin sections of root and shoots of the tomato were examined for SAM analysis. Generally, the transmission of nanoparticles in plant cells and tissues is rarely documented in most crop plants (Navarro et al., 2008). The present investigation illustrated the potential impact of exposure of crops in nanoparticles on plant development and its genetic consequences. SEM analysis was performed for confirmation of nanoparticles inside the root and shoots of tomato from the variety of Patharkuchi with the best concentration of ZnO and TiO2 nanoparticles. Figure 5 showed the SEM images of the root and shoots of tomato with ZnO and TiO_2 nanoparticles, and it was clear that the nanoparticles in high frequency were present near vascular tissues. The present study represents direct evidence of nanoparticles transportation through the vascular system. The control plants also prepared samples for SEM analysis. ZnO and TiO_2 nanoparticles uptake, translocation, and tomato response were also examined in earlier studies (Raliya et al., 2015b). The accumulation of nanoparticles in second-generation raised from seeds of treated first-generation plant revealed sequence of nanoparticles transmission from seed and translocation through roots and subsequently shoots and other organs. Generational differences in response to different concentrations may be due to differential uptake of nanoparticles from seed to root and its translocation to plant parts to accelerate metabolic activities concerned with those tissues. Transmission of nanoparticles from first to succeeding generation was always found lower in amount. The situation when concentration remained the same may be due to the persistence of genetic information from the first generation. The most frequent was the first mechanism, followed by the second, and the least frequent was the third. SEM analysis indicated the accumulation and translocation of ZnO and TiO_2 nanoparticles in the plant organs (roots and shoot) and the generational transmission effect.

CONCLUSION

The differential response emphasized standardization of treatments with different nanoparticles considering the tomato plant so that a specific dose can be identified to achieve the maximum beneficial effect on most of the important characters. Response to the nano-particle to induce optimum economic yield was variable. Higher concentration of Phosphorus (40 ppm) NPs conspicuously enhanced the economic yield, whereas the medium concentration of ZnO (10 ppm) and Nano TiO_2 (20 ppm) NPs induced similar improvement in tomato. A higher concentration of three nanoparticles was found effective in enhancement of production of important bio-chemicals in the fruit of tomato which lycopene, B-carotene have important phyto-medicinal value. In second generation, higher concentrations of ZnO and Nano-Phosphorus NPs in tomatoes depicted optimum response to enhance economic yield while lower concentrations of TiO_2 induced similar results. Generational differences in response to different concentrations may be due to differential uptake of nanoparticles from seed to root and its translocation to plant parts to accelerate metabolic activities concerned with those tissues. This work shows strong evidence for the high efficiency of nanoparticles on plant morpho-physiological characteristics and quality enhancement.

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Table 1. Effect of ZnO, Phosphorus and TiO2 NPs for yield and biochemical traits of Tomato (first generation)

Treatments	Days to 50% flowering	Plant height (cm)	Fruit no. plant^{-1}	No. of primary branch	No. of cluster plant^{-1}	Fresh plant weight (kg)	Total Chlorophyll (mg/100g)	Lycopene (mg/100g)	Beta carotene (mg/100g)	Yield plant^{-1} (kg)
Control	53.10^{a}	105.41^{j}	38.67^{l}	10.83^{c}	19.68^{i}	0.65^{j}	192.75^{i}	4.97^{j}	0.38^{g}	1.166^{h}
ZnO-2 ppm	51.20^{bcd}	107.09^{ij}	39.87^{kl}	8.57^{e}	30.57^{d}	0.66^{ij}	276.29^{b}	5.04^{hij}	0.42^{f}	1.013^{i}
ZnO-4 ppm	51.32^{bcd}	106.74^{ij}	40.93^{jk}	8.52^{e}	28.47^{e}	0.71^{f}	208.44^{de}	5.10^{fghi}	0.48^{ab}	1.625^{de}
ZnO-8 ppm	51.10^{bcd}	111.92^{fg}	49.31^{g}	9.29^{d}	32.07^{c}	0.78^{d}	195.56^{hi}	5.50^{bc}	0.42^{f}	1.742^{bc}
ZnO-10 ppm	50.47^{de}	115.79 ^{de}	65.46^{b}	12.32^{a}	48.18^{a}	0.85^{b}	213.03^{c}	5.80^{a}	0.48^{ab}	1.730^{c}
ZnO-14 ppm	50.76^{cde}	109.01^{hi}	47.98^{gh}	11.55^{b}	30.11^{d}	0.88^{a}	203.95^{f}	5.71^{a}	0.45^{cd}	1.750^{c}
P-10 ppm	48.03^{g}	121.34^{b}	42.37^{j}	8.47^{e}	26.66^{f}	0.69^{fg}	204.08^{f}	5.00^{ij}	0.43^{ef}	1.483^{f}
P-20 ppm	50.14^{ef}	116.59^{cd}	56.00^{e}	8.73^{e}	25.38^{g}	0.67^{hi}	199.23^{gh}	5.14^{fgh}	0.48^{a}	1.802^{ab}
P-30 ppm	51.51^{bc}	111.80^{fg}	65.83^{b}	11.81^{b}	33.18^{b}	0.76^{e}	195.99^{hi}	5.32^{de}	0.42^{f}	1.753^{c}
P-40 ppm	48.46^{g}	124.99^{a}	60.96^{d}	11.75^{b}	25.28^{g}	0.75^{e}	204.44^{ef}	5.19^{fg}	0.47^{ab}	1.733^{c}
P-50 ppm	51.86^{b}	125.40^{a}	63.59^{c}	10.84^{c}	26.55^{f}	0.81^{c}	291.07^{a}	5.55^{b}	0.45^{bc}	1.811^{a}
TiO_2-10 ppm	49.92^{ef}	118.60^{c}	45.48^{i}	11.81^{b}	24.32^{h}	0.78^{d}	197.37^{h}	5.83^{a}	0.47^{ab}	1.676^{d}
TiO_2-20 ppm	47.06^{h}	113.95^{ef}	67.82^{a}	11.50^{b}	32.53^{bc}	0.82^{c}	202.99^{fg}	5.76^{a}	0.48^{a}	1.779^{c}
TiO_2-30 ppm	49.37^{f}	124.80^{a}	48.81^{g}	10.82^{c}	23.56^{h}	0.70^{f}	199.29^{gh}	5.22^{ef}	0.48^{a}	1.306^{g}
TiO_2-40 ppm	50.80^{cde}	118.16^{cd}	46.73^{hi}	10.75^{c}	23.78^{h}	0.68^{gh}	206.44^{ef}	5.42^{cd}	0.44^{cde}	1.430^{f}
TiO_2-50 ppm	49.45^{f}	111.30^{gh}	54.04^{f}	11.72^{b}	25.41^{g}	0.71^{f}	210.75^{cd}	5.08^{ghij}	0.44^{de}	1.623^{e}

Different letter of mean value are significantly different at P<0.05 according to the Duncan's multiple range test (DMRT)

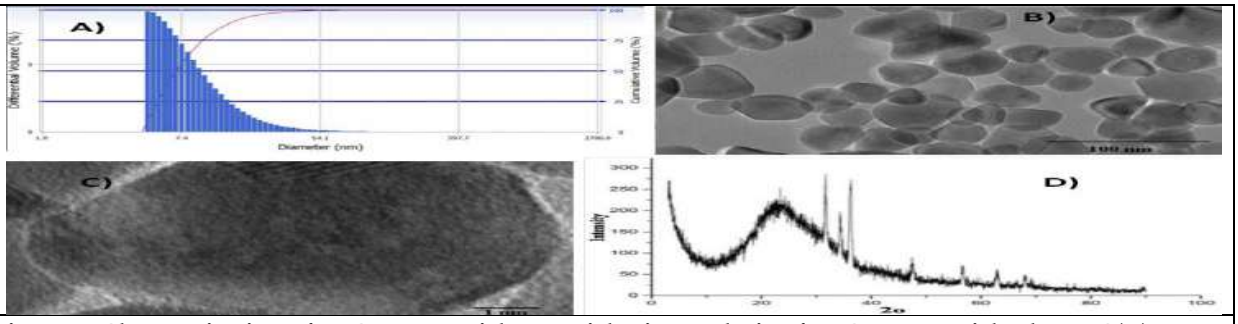


Figure 1. Characterization of ZnO nanoparticles. Particle size analysis of ZnO nanoparticles by DLS(A), TEM micrograph (B) HR-TEM micrograph (C), XRD spectra (D).

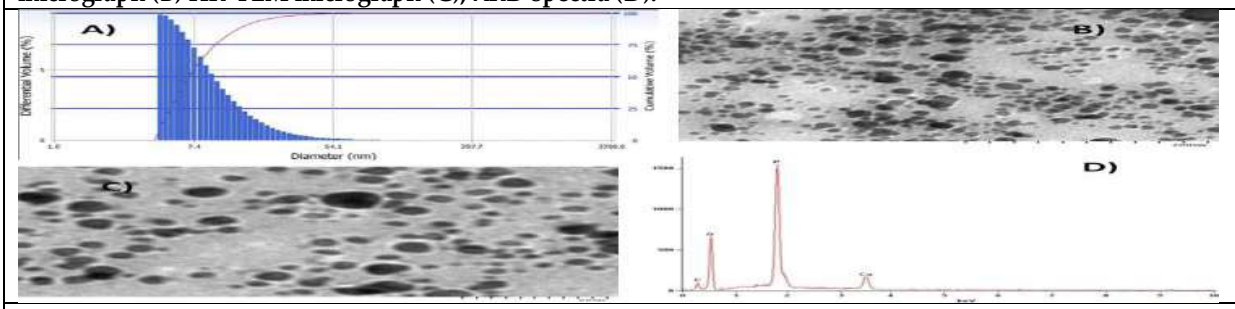


Figure 2. Characterization of P nanoparticles. Particle size analysis of Phosphorous (P) nanoparticles by DLS (A), Low magnification TEM image showing mono-disperse phosphorous nanoparticles (B), High magnifications TEM image phosphorous nanoparticles showing size of individual particles (C), EDS spectrum showing the presence of pure elemental phosphorous nanoparticles (D).

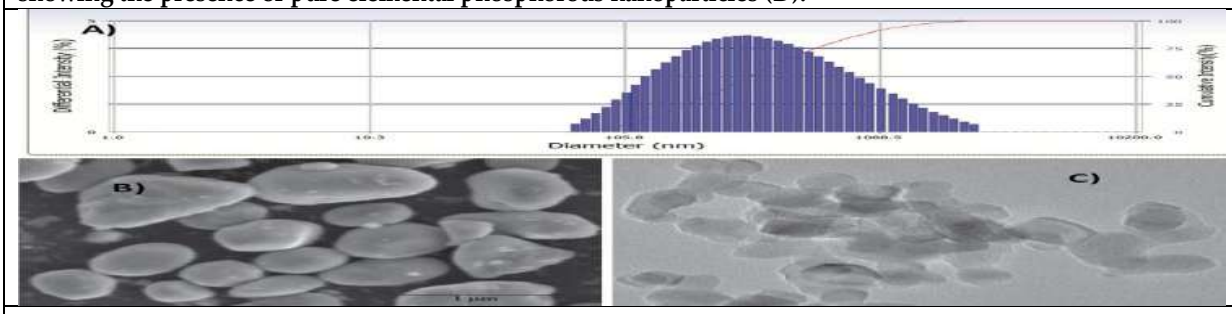
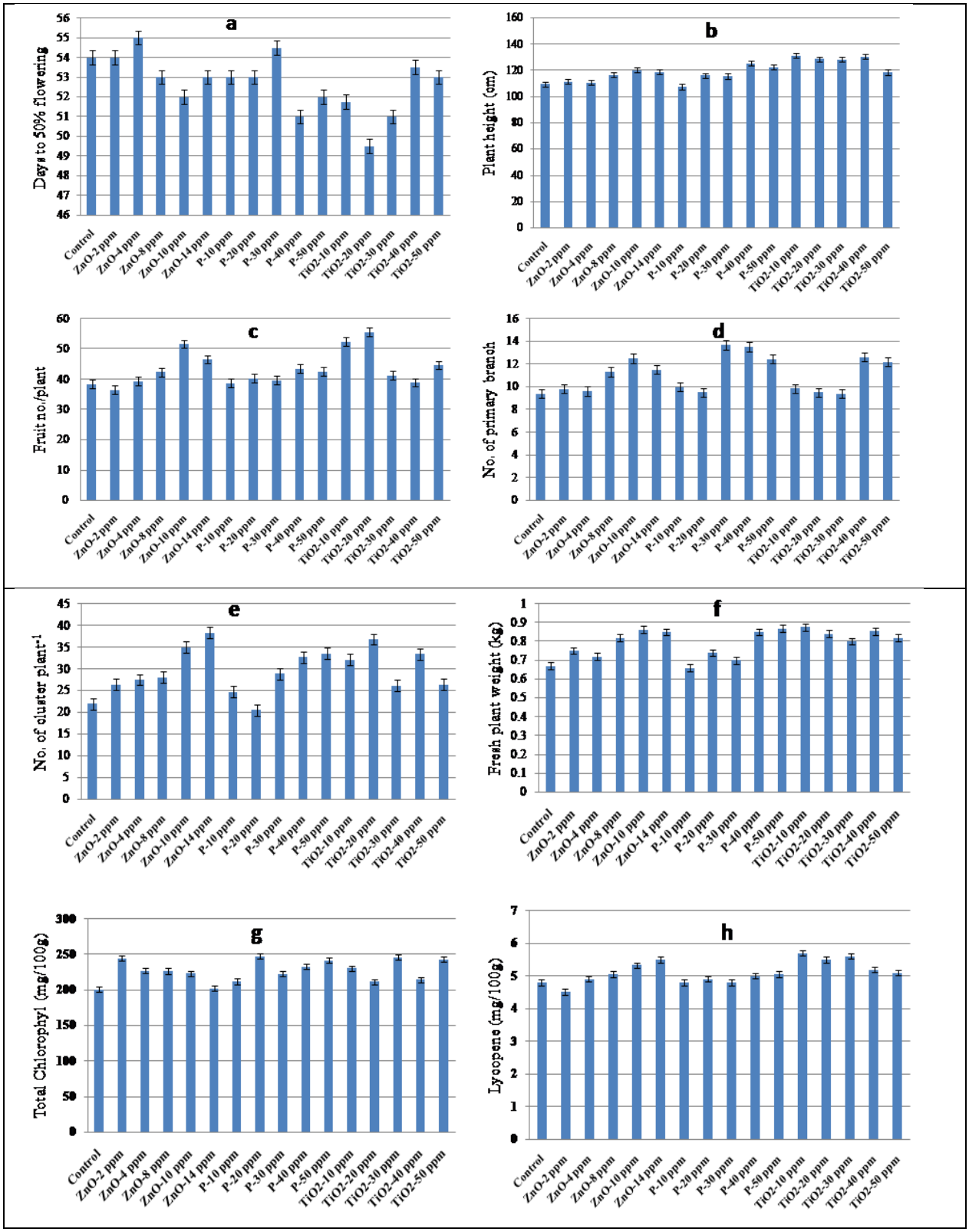


Figure 3. Characterization of TiO_2nanoparticles.Particle size analysis of TiO_2 nanoparticles DLS histogram (A), SEM image of TiO_2 (B), TEM micrograph of TiO_2 nanoparticles (C).


a
Days to 50% flowering
b
Plant height (cm)
c
Fruit no./plant
d
No. of primary branch
e
No. of cluster plant-1
f
Fresh plant weight (kg)
g
Total Chlorophyl (mg/100g)
h
Lycopene (mg/100g)
Control
ZnO-2 ppm
ZnO-4 ppm
ZnO-8 ppm
ZnO-10 ppm
ZnO-14 ppm
P-10 ppm
P-20 ppm
P-30 ppm
P-40 ppm
P-50 ppm
TiO2-10 ppm
TiO2-20 ppm
TiO2-30 ppm
TiO2-40 ppm
TiO2-50 ppm

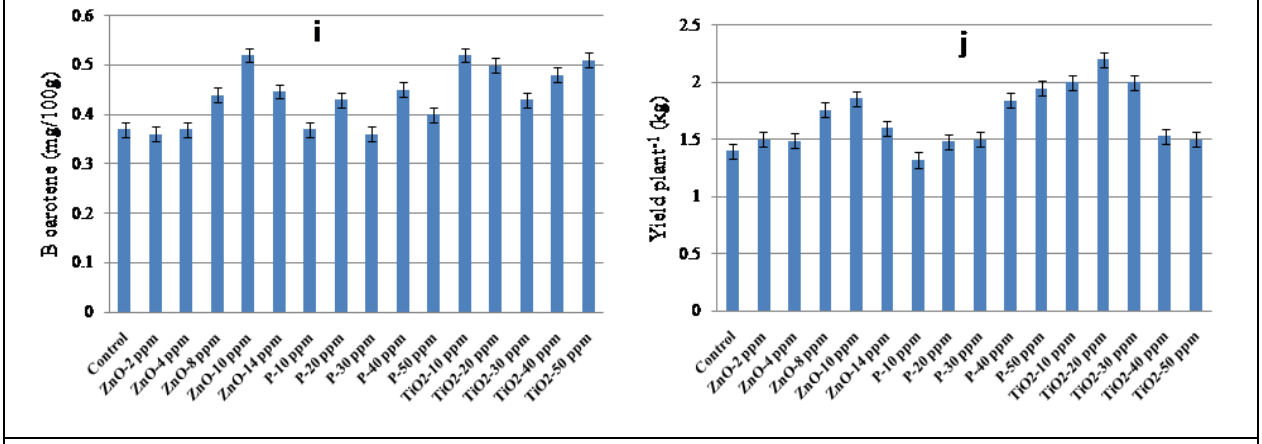


Figure 4. Effect of ZnO, P and TiO_2 nanoparticles at second generation nanoparticles transmitted from first generation among three different variety viz. Patharkuchi, Pusa Ruby and Navadhyaya in tomato; a) 50 % flowering b) Plant height (cm) c) Fruit number plant^{-1} d) Number of primary branch e) Number of cluster plant^{-1} f) Fresh plant weight (kg) g) Total chlorophyll (mg/100g) h) Lycopene (mg/100g) i) Beta carotene (mg/100g) j) Yield plant^{-1}

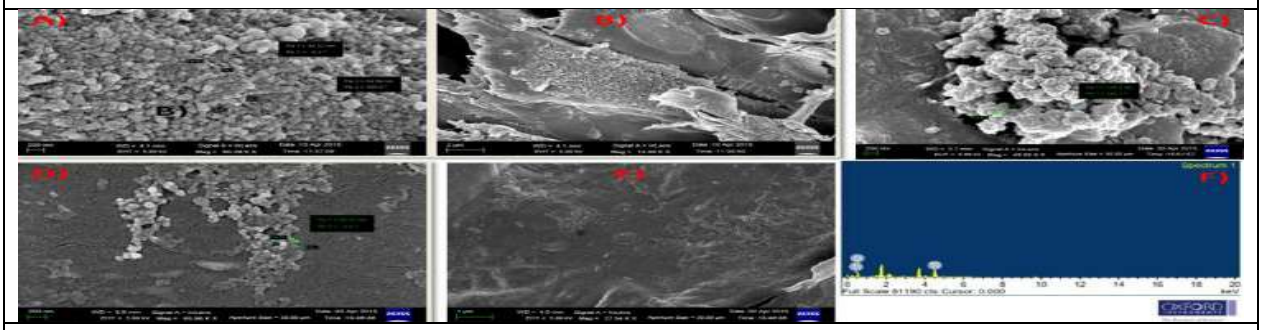


Figure 5. Translocation and Accumulation of ZnO and TiO_2 nanoparticles by SEM and EDS. ZnO accumulation in root (A) ZnO accumulation in shoot (B), TiO_2accumulation in root (C), TiO_2accumulation in shoot (D), Control situation (E) and EDS confirmation TiO_2naoparticle (F).

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REVIEW ARTICLE

Empirical Review on Applications of Summability Theory

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ABSTRACT

Techniques for summability are widely used as a useful tool for filtering alerts with inside the shape of a series(Infinite Series, Fourier series, Wavelets etc.) using various summability methods such as Matrix Summability, Nörlund summability, Cesàro Summability, Tauberian conditions and theorems. In this paper an empirical review has been done on applications of summability theory. Several classical and modern methods and applications of summability theory and their evolution with pioneering time are discussed.

Keywords: Tauberian conditions; Matrix methods and their applications; Fourier effectiveness of matrix methods; History- The Devil's invention; Cauchy's limit theorem; Borel method.

INTRODUCTION

The concept of summability is used in a variety of ways in evaluation and applied mathematics. The ideas of summability were prolonged to the sequences of fuzzy numbers and additionally to the theorems of ergodic idea. A summability approach, on the other hand, is a property of a collection of partial sums in a chain that leads to a value. Thus, in its broadest meaning, summability is the idea of the assigning of limits that is essential in evaluation, feature idea, topology, and purposeful evaluation. To study the summability theory we usually get past several subcategories viz., Convergence tests, Divergent series, Sequence spaces, Summability methods, Tauberian theorems. Under the convergence tests we have Able's test, Cauchy's convergence test etc., Grandi's series and Harmonics series are the evolved applications of the divergent series. All these methods and series are derived applications of Summability Theory.

Literature Review

Mathematically, the concepts of summability have been extended to the sequences of chaotic numbers and also to the theorems of historically specified and complimented theories. Summability is an alternative formulation of convergence of a series that is divergent in the traditional sense.

The 5 subcategories that we study under the summability theory are

1. Convergence tests
2. Divergent series
3. Sequence spaces
4. Summability methods
5. Tauberian theorems

Reflecting well on the history and development methods of the summability concept, this paper mainly covers

- ❖ Matrix method and sub-concepts
- ❖ Tauberian conditions
- ❖ Cauchy's limit theorem
- ❖ Borel method
- ❖ Summability methods defined by power series

Background and History

As we reflect towards the end of the 19th century, there are many historians who were true pioneers in mathematics that worked towards the development of ideas in order to form a firm foundation of the applicative operations of theory of summability. Godfrey Harold Hardy was an English mathematician known for his achievements in mathematical analysis and the numerical series. Hardy quoted about the definitions of 'sum' and the infinite series which seem to be more applicable than the classical definition of Cauchy. In1890 Cesaro published a paper about the multiplication of series. According to him, the limit of a sequence (x_n) can be defined to be lim y_n where (y_n) is the sequence of Cesaro means the sequence (x_n) given by

$$y_n = \frac{1}{1+n}\sum_{i=0}^{n} x_i$$

The classical summability concept offers with a generalization of the concept of the convergence of sequences and collection of actual or superior numbers. One in all of the initial concept become to assign, in a few way, a restrict to divergent sequences or collection. Classical techniques of summability had been additionally delivered for packages to issues in evaluation along with the analytic continuation of strength collection and development of the price of convergence of numerical collection. These dreams had been carried out through thinking about a remodel instead of the authentic collection or collection. This may be executed in numerous specific ways. In the process of dealing with the summability, Toeplitz theorem is a basic and affirmative way to characterise different conservative summability methods. It establishes necessary and sufficient conditions for the entries of a matrix to dene a conservative method of summability.

Summability Methods

With an objective to cover the true meaning of the summability concept a set of definitions are stated with an evidential explanation of several examples.

Sequence space

To outline simply, a chain area is a vector area whose factors are endless sequences of actual or complicated numbers. Similarly it could be described as, it's far a feature area whose factors are features from the herbal numbers to the sector K of actual or complicated numbers.

A series of factors in ℓ1 converges within side the area of complicated sequences ℓ1 if and best if it converges weakly on this area. If K is a subset of this area, then the subsequent are equivalent

1. *K* is compact;
2. *K* is weakly compact;
3. *K* is bounded, closed, and equismall at infinity.

K being equismall at infinity means that for every $\epsilon > 0$ there exists a natural number $n_\epsilon \geq 0$ such that $\sum_{n=n_\epsilon}^{\infty} |s_n| <$ ϵ for all
$s = (s_n)_{n=1}^{\infty} \in K$

Classical and Modern Methods in Summability (Early Methods):
Matrix Methods
A matrix summation method is one of the methods for summing series and sequences using an infinite matrix.
The matrix of a summation technique all entries of that are non-poor is known as a fine matrix. Among the matrix summation strategies one finds, for example, the Voronoi summation technique, the Cesàro summation strategies, the Euler summation technique, the Riesz summation technique (R, p_n), the Hausdorff summation technique.

Able's Partition Summation Formula

Let (a_v), (b_v) $\in \omega$ $x_n := \sum_{v=0}^{n} a_v$ $(n \in N^0)$ and $x_{-1} := 0$ then the equality

$$\sum_{v=n}^{n+k} a_v b_v = \sum_{v=n}^{n+k} x_v(b_v - b_{v+1}) - x_{n-1}b_n + x_{n+k}b_{n+k+1}$$

Holds for all n,k $\in N^0$. If $x_v b_{v+1} \in c$ the series $\sum_v a_v b_v$ converges if and only if the series $\sum_v x_v(b_v - b_{v+1})$ does, that is

$$a_v b_v \in cs \leftrightarrow \sum_v x_v(b_v - b_{v+1}) \in cs$$

Here

$$\sum_{v=n}^{n+k} a_v b_v = \sum_{v=n}^{n+k} x_v(b_v - b_{v+1}) - x_{n-1}b_n + x_{n+k}b_{n+k+1}$$

Is called Able's partial summation formula and

$$a_v b_v \in cs \leftrightarrow \sum_v x_v(b_v - b_{v+1}) \in cs$$

Is called Able's convergence test

Dedekind's Test:
- If $(b_v) \in bv$ and $(a_v) \in cs$ then $(a_v b_v) \in cs$
- If $(b_v) \in bv_o$ and $(a_v) \in bs$ then $(a_v b_v) \in cs$

One of the aims of this test is to prove Cauchy's theorem for ouble series.

Rearrangement: If $\sigma : N^0 \to N^0$ is a bijective map, then for a given series $\sum_v a_v$ the series $\sum_v a_{\sigma(v)}$ is called rearrangement of it.

Mean Value Property

The characteristic should be non-stop in the closed c programming language and differentiable in the open c programming language to exercise the Mean Value Theorem. This property is a polynomial property that is non-stop and differentiable along the entire actual range line and hence fits those requirements. The imply cost theorem guarantees that the derivatives are positive, whereas the intermediate cost theorem guarantees that the characteristic is positive among specified values. The imply cost theorem guarantees that the derivatives are positive, whereas the intermediate cost theorem guarantees that the characteristic is positive among specified values. The mean value theorem states that for a curve f(x) passing through two given points (a, f(a)), (b, f(b)), there is at least one point (c, f(c)) on the curve where the tangent is parallel to the secant passing through the two given points. The mean value theorem is defined herein calculus for a function f(x): [a, b] → R, such that it is continuous and differentiable across an interval.

- The function f(x) is continuous across the interval [a, b].
- The function f(x) is differentiable across the interval (a, b). There exists a point c in (a, b).
- f'(c) = $\frac{f(b)-f(a)}{b-a}$

The tangent at c is parallel to the secant travelling through the points (a, f(a)), (b, f(b) as we have seen. This mean value theorem is used to prove a statement across a narrow range. Further, Rolle's theorem is derived from this mean value theorem. The value of c in the mean value theorem is defined such that the slope of the tangent at the point (c, f(c)) is equal to the slope of the secant joining the two points. The value of c in Rolle's Theorem is defined such that the slope of the tangent at the point (c, f(c)) is equal to the slope of the x-axis.

Following Peyerimhoff's work on mathematical studies of additives the mathematical condition for mean value property o satisfy on a regular triangle to be of type M is given below A matrix $A = (a_{nk})$ is said to satisfy the mean value property with a constant K > 0 or

(**$M_K(A)$** for short) if

$$\left|\sum_{k=0}^{r} a_{nk}\, x_k\right| \leq K \; suppose \; 0 \leq v \leq r \; then \; \left|\sum_{k=0}^{\infty} a_{vk} x_k\right|$$

For $(0 \leq r \leq n \in N^0 \; and \; (x_k) \in \omega_A)$

Modified Methods

i) Kronecker identity

$(u_n - \sigma_n(u) = V_n(\Delta u)$

and since $u_n = V_n(\Delta u) + \sum_{k=1}^{n} \frac{V_k(\Delta u)}{k} + u_0$

A sequence (u_n) is Cesaro summable to s if $\lim_n \sigma_n(u) = s$

Similarly a sequence is backward convergent if $\Delta u_n = 0$

And a sequence is backward Cesaro summable if $\Delta\sigma_n(u) = 0$

The classical control modulo of the oscillatory behaviour of $(u_n)$is denoted by $\omega_n(u) = n\Delta u_n$

ii) Tauberian Conditions:

Tauberian condition is naively the weakest possible condition in dealing with a summability case. Tauberian theorems are defined for several summability methods.

Tauberian theorem for Cesaro Methods

❖ Slowly decreasing:

A real sequence $x = (x_k)$ is said to be **slowly decreasing** if

$$\liminf_{1 \leq \frac{r}{n} \to 1, n \to \infty} (x_r - x_n) \geq 0$$

❖ Slowly oscillating:

A complex sequence (x_k) is said to be slowly oscillating if it satisfies

$$\liminf_{1\leq\frac{r}{n}\to 1, n\to\infty} (x_r - x_n) = 0$$

- ❖ Each convergent sequence is slowly oscillating, on the basis of following the Cauchy criterion
- ❖ If a sequence is both slowly increasing and slowly decreasing then it is evidently termed slowly oscillating
- ❖ If $x \in c_{C_1}$ and if x is slowly decreasing, then $x \in c$; that is, each slowly decreasing C_1- summable sequence is convergent.

iii) Cauchy's Limit Theorem:

A collection is known as a Cauchy collection if the phrases of the collection finally all turn out to be arbitrarily near one another. That is, given ε > zero there exists N such that if m, n > N then

$|a_m - a_n| < \varepsilon$. Every real Cauchy sequence is always convergent. A metric space (X, d) is known as entire if each Cauchy sequence (xn) in X converges to a few factor of X. A subset A of X is known as entire if A as a metric subspace of (X, d) is entire, that is, if each Cauchy sequence (xn) in A converges to a degree in A. In order to state the guarantee of the limits o the sequences being conserved We say that a sequence of real numbers {an} is a Cauchy sequence provided that for every $\epsilon > 0$, there is a natural number N so that when n, m ≥ N, we have that $|a_n - a_m| \leq \epsilon$. The theorem states that, "*Every Cauchy sequence of real numbers converges to a limit.*"

iv) Borel Method of Summability:

- Particularly useful for *summing the asymptotic series* and proposed by the French mathematician, Emiel Borel; the Borel summation method is used for the summation of divergent series and in summary gives the best possible answer for the summing of a series.
- There are three basic methods in processing the Borel summation and they are particularly consistent i.e., while summing a series any two of the three Borel methods are sure of giving the same answer.
- Mittag-Leffler summation is a modified method for the actual Borel summation.
- Any series $A(z)$ that is weak Borel summable at $z \in C$ is also Borel summable at z. However, one can construct examples of series which are divergent under weak Borel summation, but which are Borel summable.
- Relating other methods to Borel summation, (**B**) is the special case of Mittag-Leffler summation with $\alpha = 1$.

v). Borel's Integral Summation Method:

Suppose that the Borel transform converges for all positive real numbers to a function growing sufficiently slowly that the following integral is well defined (as an improper integral), the Borel sum of A is given by

$$\int_0^\infty e^{-t} BA(tz)dt$$

If the integral converges at $z \in C$ to some $a(z)$, we say that the Borel sum of A converges at z, and write .

$$\sum a_k z^k = a(z)(B)$$

For a number series $\sum_{k=0}^{\infty} a_k$

S being a real number and S_n is the partial sums of the series,

The series is said to be Borel summable to number S if

$$\lim_{n\to\infty} e^{-x} \sum_{k=0}^{\infty} \frac{x_k}{k!} S_k = S$$

There also exists an integral summation $\int_0^\infty e^{-u} \sum_{k=0}^{\infty} \frac{a_k u^k}{k!} du = S$

vi). Summability Methods defined by Power Series

A energy collection is a kind of collection with phrases concerning a variable. More specifically, if the variable is x, then all of the phrases of the collection contain powers of x. As a result, a energy collection may be idea of as an endless polynomial. It have become viable to have a look at analytic features thru energy collection, a software tried with the aid of using the Italian French mathematician Joseph-Louis Lagrange for actual features with inside the 18th century however first achieved effectively with the aid of using the German mathematician Karl Weierstrass with inside the nineteenth century. Graphically, you may graph partial sums of the collection due to the fact every partial sum is a polynomial with a finite variety of phrases. A energy collection "focused at x=a" is an endless collection in powers of x-a, like a polynomial that is going on forever. For example, $1+x+x^2+x^3+\ldots = 1/(1-x)$ is a energy collection focused at x=0.

Power series methods in summability fall under the class of continuous summability methods as the parameter of this limiting process is continuous.

Let p= (p_k)

$$C \coloneqq C_p \coloneqq \left\{ f :]-R, R[\to \mathrm{R} \mid \lim_{0<t\to R-} \frac{1}{p(t)} f(t) \ \ exists \right\}$$

And $C_{P_p} \coloneqq \{x = (x_k) \in \omega \mid p_x(t) \coloneqq \sum_k p_k x_k t^k\}$ has a converging radius greater than or equal to R and $p_x \in C$

$$P_p : C_{P_p} \to C_P, x \to p_x \ with \ p_x :]-R, R[\to \mathrm{R}, t \to p_x(t) := \sum_k p_k x_k t^k$$

And $P_p - lim : C_{P_p} \to$ K, x= $(x_k) \to \lim_{0<t\to R-} \frac{1}{p(t)} \sum_k p_k x_k t^k$

Then (P_p, C_{P_p}, P_P-lim), or P_P for short, is a summability method which is called a *power series method*.

CONCLUSION

The summability theory has numerous applications in analysis and applied mathematics. Summability theory will be useful to engineers and physicists working with Fourier series or analytic continuation in their research. The idea of summability has been extended to fuzzy number sequences as well as ergodic theory theorems. This paper explains and illustrates the various aspects of summability in a logical manner. The authors' goal in writing this paper is to give graduate students, researchers, physicists, and engineers a practical introduction to summability theory.

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RESEARCH ARTICLE

Design of a Circular Ring Monopole Antenna for Wideband Applications

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ABSTRACT

Ahumble and compacted circular ring serrated wideband monopole antenna has been proposed in this article. The proposed antenna consists of a circular monopole antenna, which was connected through a 50-Ω microstrip fed line and a round-cornered finite ground plane. It exhibits a very wide frequency band from 5–20 GHz with a voltage standing wave ratio less than 2. By employing a U-shaped parasitic element near the round corned finite ground plane and a T-shaped stub inside the radiating patch, a single band-notched characteristic in the frequency band of 5.2–5.825GHz, industrial scientific and medical (ISM) band is generated. In order to realize the second band-notched function for X-band satellite communication systems (7.2–8.4 GHz), a U-shaped slot has been inserted in the round-cornered finite ground plane. The required dimension of the proposed antenna is 24 mm × 30 mm× 0.787 mm.It is a miniaturized antenna as compared to the existing wideband monopole antenna.

Keywords: Monopole, Circular Ring, Wideband, Return Loss, Radiation Pattern.

INTRODUCTION

Nowadays there is an increasing demand for wideband antennas in the modern wireless communication system showing to their extremely large bandwidth and very high data transmission rate. In the modern era, antenna plays a vital role in the field of the radio communication system. With no doubt, it is known to be the electronic eye and ear of radio communication technique [1]. The monopole antenna (MA) is an ideal candidate for super wideband applications due to its numerous attractive features such as small size, low cost, planar structure, operation over extremely large impedance BW and ease to accommodate with small space provided by handheld gadgets [2]. As we deal with electromagnetic waves, the antenna acts as a transducer between guided and unguided electromagnetic wave. The antenna is part of a circuit which behaves as a radiator [3].The proposed antenna composed of a circular ring MA, which is connected through a 50-Ω triangular tapered microstrip fed line and a round-cornered finite ground plane.

ANTENNA DESIGN METHODOLOGY

The design of the proposed circular ring notched monopole antenna is shown in figure 1. The RT/Druid 5870 substrate of thickness t = 0.787 mm with a dielectric constant is 2.23, which is excited through a 50-Ω microstrip fed line. For the signal transmission, a two-hole Sub Miniature version A (SMA)-connector has been utilized &we have chosen the RT/Druid 5870 substrate as FR4 substrate becomes highly lossy at higher frequencies. The proposed antenna the overall dimensions of about 24 mm × 30 mm × 0.787 mm consists of a circular ring radiating patch with a T-shaped stub inside circular ring radiating patch. The rear side of the RT / Duroid substrate is composed of a round-cornered finite ground plane with embedded U-shaped slot and U-shaped parasite element, which is placed under the circular ring patch. The side view of the proposed antenna is shown in figure 2.

SIMULATED RESULTS ANALYSIS

The proposed antenna simulated return loss S_{11} Vs frequency is shown in figure 3.This result shows that it can work for frequency range from 5.2 GHz to 20 GHz for wideband applications. The E-Plane and H-plane radiation pattern analysis have been simulated using HFSS software. The simulated radiation pattern with different values of phi-angle is shown in figure 4. The simulated 3D polar plot is shown in figure 5. It shows that the gain of the proposed design antenna is 4.96 dB.So this antenna is more efficient than existing wideband antennas with miniaturized dimensions.

CONCLUSION

A compact wideband monopole antenna has been proposed and investigated in this paper. A 50 Ω triangular tapered microstrip fed line as well as round corned finite ground plane have been used for broadband matching. The proposed circular ring notched monopole antenna can operate from 5.2 GHz–20 GHz. By employing USS and USPE, DBN characteristics have been obtained. The peak gain of the proposed antenna is 4.96 dB. This proposed antenna can be used for satellite communication, super wideband applications, and ultra-wideband (UWB) applications.It is small in dimensions, low cost, planar structure. It has a high data transmission rate and also it can operate over high impedance. It is very easy to put up with small space available in communication devices.**The goal of this proposed work is to bring innovations into antenna design.**

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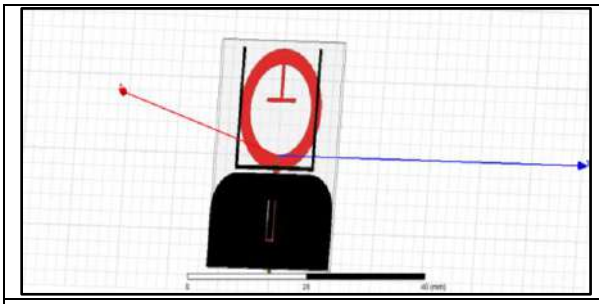

Figure 1. Design of Circular ring notched monopole antenna using HFSS

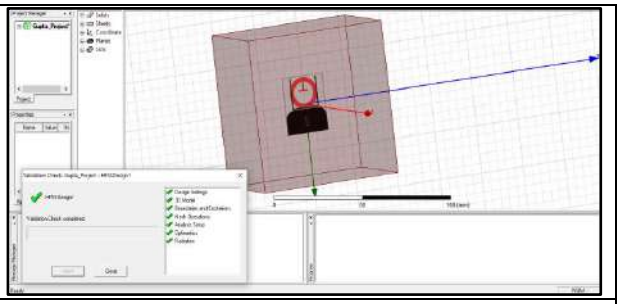

Figure 2 (a) Side view of proposed antenna

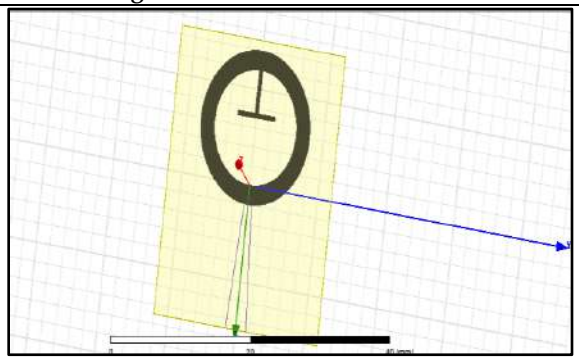

Figure 2 (b) Side view of proposed antenna

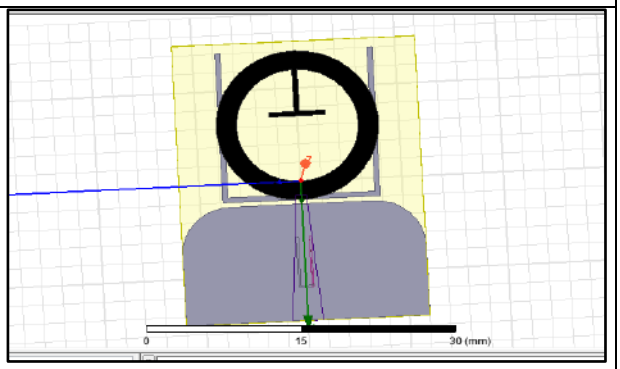

Figure 2 (c) Side view of proposed antenna

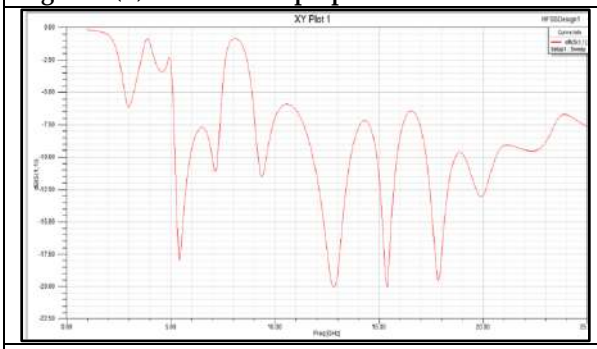

Figure 3. Simulated S_{11} Vs frequency plot

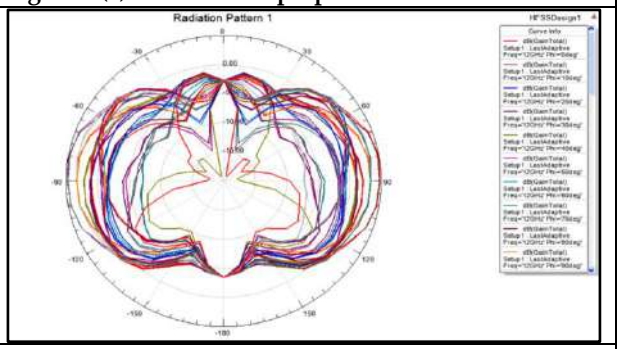

Figure 4. Simulated radiation pattern

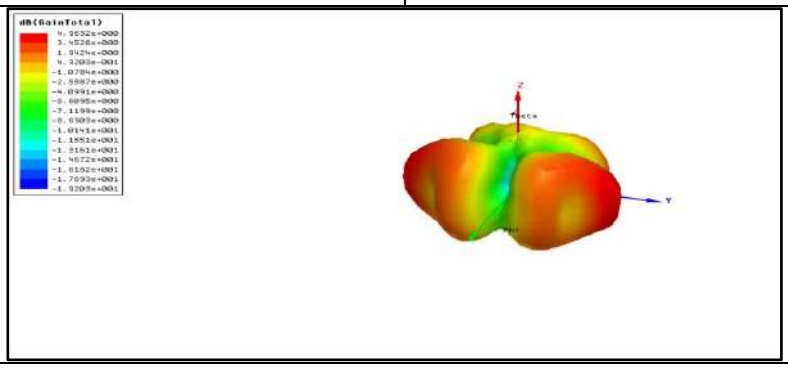

Figure 5. Simulated 3D Polar Plot

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RESEARCH ARTICLE

Fibonacci Difference Geometric Sequence Spaces

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ABSTRACT

The goal of this study is to introduce the space of Fibonacci difference sequences. Inclusion relations and topological features between the generated geometric sequence spaces are also studied here. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure).

Keywords: Orlicz function, Fibonacci sequence space, Summability, Geometric sequence space.

INTRODUCTION

Then Shiue [11, 12] studied the Cesàro sequence spaces and Cesàro function spaces in 1970. Since then Cesàro sequence spaces attracted the attention of researchers in various directions.

The strongly $(V,\lambda)-$ summable sequence spaces were introduced by Leindler [8] with

$$[V,\lambda]=\left\{\xi=(\xi_k)\ \in\ \omega\colon \lim_{n\to\infty}\frac{1}{\lambda_n}\sum_{k\ \in\ I_n}|\xi_k-\ell|=0,\ for\quad some\quad \ell\right\},$$

$$(V,\lambda)=\left\{\xi=(\xi_k)\ \in\ \omega\colon \lim_{n\to\infty}\frac{1}{\lambda_n}\sum_{k\ \in\ I_n}(\xi_k-\ell)=0,\ for\quad some\quad \ell\right\}.$$

It is observed that when $\lambda_n=n$ the $(V,\lambda)-$ summable sequence spaces reduces to Cesàro sequences space.

The concept of difference sequence spaces was presented by Kızmaz [6] $X(\Delta)$such that

$$X(\Delta)=\{\xi\ \in\ \omega\colon\Delta\xi\ \in\ X\}$$

with $\Delta\xi\ =(\Delta\xi_k)=(\xi_k-\xi_{k+1})$, for $X=\ell_\infty,c\ and\ c_0$.

The difference sequence spaces attracted many such as Atlay and Başar [1],Et and Çolak [4], Et and Bektas [3] for further extensions.

Orlicz sequence space was introduced by Lindenstrauss and Tzafriri [8] as

$$\ell_M=\left\{\xi=(\xi_k)\colon\sum_{k=1}^{\infty}M(\frac{|\xi_k|}{\rho})<\infty\quad for\ some\quad \rho>0\right\}$$

The following is the norm of a Banach space:

$$\| \xi \| = \inf\left\{\rho > 0: \sum_{k=1}^{\infty} M\left(\frac{|\xi_k|}{\rho}\right) \leq 1\right\}$$

ℓ_M coincides with ℓ_p for $1 \leq p \leq \infty$ and $M(\xi) = \xi^p$

Fibonacci Difference Sequence Spaces

The sequence of Fibonacci numbers have wide range of applications in arts,science and architecture. Fibonacci numbers satisfy the Golden ratio [7].

The Fibonacci infinite matrix $\hat{R} = (\widehat{l_{nk}})$ is defined as

$$(\widehat{l_{nk}}) = \begin{cases} -\frac{f_{n+1}}{f_n} & (k = n-1), \\ \frac{f_n}{f_{n+1}} & (k = n), (n.k \in \mathbb{N}). \\ 0 & (0 \leq k < n-1 \ or \ k > n), \end{cases}$$

Geometric sequence spaces were introduced by Türkmen and Başar [17] with geometric zero one, geometric identity e, geometric addition $(\oplus)$, geometric subtraction $(\ominus)$ and geometric multiplication $(\odot)$ defined in [2, 13, 14, 15, 16].

Now we introduce the new Fibonacci difference geometric sequence spaces as follows:

$$[V, \lambda, M, \hat{R}, p]_0^G = \left\{\xi = (\xi_k) \in \omega(G): G\lim_{n\to\infty} \frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|_G}{\rho})]^{p_k^G} = 1, \quad \rho > 1\right\}$$

$$[V, \lambda, M, \hat{R}, p]^G = \left\{\xi = (\xi_k) \in \omega(G): G\lim_{n\to\infty} \frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|(\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}) \ominus \ell|}{\rho})]^{p_k^G} = 1, \quad \rho > 1\right\}$$

$$[V, \lambda, M, \hat{R}, p]_\infty^G = \left\{\xi = (\xi_k) \in \omega(G): G\lim_{n\to\infty^G} \frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho})]^{p_k^G} < \infty, \quad \rho > 1\right\}$$

MAIN RESULTS

Theorem 3.1 $[V, \lambda, M, \hat{R}, p]_0^G$, $[V, \lambda, M, \hat{R}, p]^G$ *and* $[V, \lambda, M, \hat{R}, p]_\infty^G$ *are linear spaces over* $\mathbb{C}(G)$ *for any sequence* $p^G = (p_k)^G$ *of strictly positive real numbers. Proof,* It is a routine verification and hence omitted.

Theorem 3.2 *For space* $[V, \lambda, M, \hat{F}, p]_0^G$ *which is a paranormed space by,*

$$g(\xi) = inf\left\{\rho^{\frac{p_n}{H}} G: (\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho})]^{p_k^G})^{\frac{1}{H}} \leq e, n = e, 2e, 3e \ldots\right\}$$

where $H = max(e, sup\ p_k^G)$.

Proof. Now $g(\xi) = g(\ominus\ \xi)$.From linearity we have if $\alpha = \beta = e$ then $g(\xi \oplus y) \leq g(\xi) \oplus g(y)$.

Since $\frac{1}{\lambda_n} M(1) = 1$, we get $inf\left\{\rho^{\frac{p_n}{H}}\right\} = 1 \quad for\ \xi = 1$.

Conversely, suppose $g(\xi) = 1$, then

$$g(\xi) = inf\left\{\rho^{\frac{p_n}{H}} G: (\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho})]^{p_k^G})^{\frac{1}{H}} \leq e\right\} = 1.$$

Now for a given $\varepsilon > 1$, there is some $\rho_\varepsilon (1 < \rho_\varepsilon < \varepsilon)$ such that

$$(\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho_\varepsilon})]^{p_k^G})^{\frac{1}{H}} \leq 1.$$

Then

$$(\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\varepsilon})]^{p_k^G})^{\frac{1}{H}}$$

$$\leq (\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho_\varepsilon})]^{p_k^G})^{\frac{1}{H}}$$

$$\leq e \quad for\ each\ n.$$

Suppose $y_k \neq 1$ for some $k \in I_n$ where $y_k = \frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}$.

Let $\varepsilon \to 1$, then

$$(\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|y_k|}{\varepsilon})]^{p_k^G})^{\frac{1}{H}} \neq 1,$$

which is a contradiction.

This implies $y_k = 1$ for each k.

For continuity of scalar multiplication consider for any complex number μ ,

$$g(\mu \odot \xi) = inf\left\{\rho^{\frac{p_n}{H}}: (\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\mu(\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1})|}{\rho})]^{p_k^G})^{\frac{1}{H}} \leq e, \quad n = e, 2e, \ldots\right\}$$

$$= inf\left\{(|\mu| \odot s)^{\frac{p_n}{H}}: (\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{s})]^{p_k^G})^{\frac{1}{H}} \leq e,\ n = e, 2e \ldots\right\}$$

where $s = \frac{\rho}{|\mu|}$.

Now $g(\mu \odot \xi) \leq (max(e, |\mu|^{sup\ p_n^G}))^{\frac{1}{H}}$

$$\times \quad inf\left\{s^{\frac{p_n}{H}}: (\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{s})]^{p_k^G})^{\frac{1}{H}} \quad \leq e,\ n = e, 2e \ldots\right\}$$

as $|\mu|^{p_n^G} \leq max(e, |\mu|^{sup\ p_n^G})$.

Here $g(\mu \odot \xi) \to 1$ as $g(\xi) \to 1$ in $[V, \lambda, M, \hat{F}, p]_0^G$.

Suppose $\mu_m \to 1$ as $m \to \infty$ and y_k be a sequence fixed in $[V, \lambda, M, \hat{F}, p]_0^G$.

$\frac{1}{\lambda_n} G \sum_{k\ \in\ I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho})]^{p_k^G} < (\frac{\varepsilon}{2})^H$ for some $\rho > 1$ and all $n > N$.

$\frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho})]^{p_k^G} < \frac{\varepsilon}{2}$ for some $\rho > 1$ and all $n > N$.

Let $1 < |\mu| < e, n > N$, we get

$$\frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|\mu(\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1})|}{\rho})]^{p_k^G}$$

$$< \frac{1}{\lambda_n} G \sum_{k \in I_n} [|\mu| M(\frac{|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}|}{\rho})]^{p_k^G} < (\frac{\varepsilon}{2})^H$$

as M is convex.

As M appears to be continuous everywhere in $[1, \infty)$, for $n \leq \mathbb{N}$ and any scalar t we have

$$f(t \odot \xi) = \frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|t(\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1})|}{\rho})]^{p_k^G}$$

is continuous at 1. So $e > \delta > 1$ such that $|f(t)| < (\frac{\varepsilon}{2})^H$ for $1 < t < \delta$.

Now

$$g\{(\mu_m \odot \xi^m) = (\frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|\mu_m(\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1})|}{\rho})]^{p_k^G})^{\frac{1}{H}} < \frac{\varepsilon}{2}.$$

Which implies

$$(\frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|\mu_m(\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1})|}{\rho})]^{p_k^G})^{\frac{1}{H}} < \varepsilon,$$

as $\varepsilon \to 1$ so $g(\mu \odot \xi) \to 1$.

Hence $g\{(\mu_m \odot \xi^m) \ominus (\mu \odot \xi)\} \leq \{(\mu_m \ominus \mu) \odot g(\xi^m)\} \oplus \{|\mu| \odot g(\xi^m \ominus \xi)\}$.

λ −Statistical Convergence

We say a sequence $\xi = (\xi_k)$ is $S_\lambda^G(\hat{R}) -$ convergent to [ ] if

$$G \lim_{n \to \infty} \frac{1}{\lambda_n} |\left\{k \leq n: (|\frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1} \ominus \ell|) \geq \varepsilon\right\}|^G = 1.$$

for every $\varepsilon > 1$, the cardinality of the set is indicated by the bars.

Write for simplicity $y_k = \frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}$.

Theorem 4.1 $[V, \lambda, M, \hat{F}]^G \subset S_\lambda^G(\hat{F})$

Proof. Let $\xi \in [V, \lambda, M, \hat{F}]^G$ and $\varepsilon > 1$ be given.Then for $y_k = \frac{f_k}{f_{k+1}}\xi_k \ominus \frac{f_{k+1}}{f_k}\xi_{k-1}$ consider

$$\frac{1}{\lambda_n} G \sum_{k \in I_n} [M(\frac{|y_k \ominus \ell|}{\rho})] \geq \frac{1}{\lambda_n} G \sum_{k \in I_n, |y_k \ominus \ell| \geq \varepsilon} [M(\frac{|y_k \ominus \ell|}{\rho})]$$

$$> \frac{1}{\lambda_n} \odot M \odot (\frac{\varepsilon}{\rho}) |\{k \in I_n: |y_k \ominus \ell| \geq \varepsilon\}|.$$

Hence $\xi \in S_\lambda^G(\hat{F})$.

Definition 4.2 $M(2u) \leq KM(u), \quad u \geq 0,$ *for any positive constant* $K > 2$ *then we say* M *satisfy* Δ_2 *−condition.*

Theorem 4.3 $[V, \lambda, \hat{F}, p]^G \subseteq [V, \lambda, M, \hat{F}, p]^G.$, *if* M *satisfies* Δ_2 *−condition.*

Proof. Suppose $\xi \in [V, \lambda, \hat{F}, p]^G$. Then

$$A_n \equiv \frac{1}{\lambda_n} G \sum_{k \in I_n} |(\frac{f_k}{f_{k+1}} \xi_k \ominus \frac{f_{k+1}}{f_k} \xi_{k-1}) \ominus \ell| \to 1$$

as $n \to \infty$ for some ℓ.

Let $\varepsilon > 1$ and choose δ with $1 < \delta < e$ such that $M(t) < \varepsilon$ for $1 \le t \le \delta$.

Let $y_k = |(\frac{f_k}{f_{k+1}} \xi_k \ominus \frac{f_{k+1}}{f_k} \xi_{k-1}) \ominus \ell|_G$ and consider

$$\frac{1}{\lambda_n} G \sum_{k \in I_n} M(|y_k|) = \frac{1}{\lambda_n} G \sum_{k \in I_n, |y_k| \le \delta} M(|y_k|) \oplus \frac{1}{\lambda_n} G \sum_{k \in I_n, |y_k| > \delta} M(|y_k|).$$

Since M is continuous, $\frac{1}{\lambda_n} G \sum_{k \in I_n, |y_k| \le \delta} M(|y_k|) < \lambda_n \odot \varepsilon$ and for $y_k > \delta$ we use

$$y_k < \frac{y_k}{\delta} < 1 \oplus \frac{y_k}{\delta}.$$

Now

$$M(y_k) < M(1 \oplus \delta^{-1} y_k) < \frac{1}{2} M(2) \oplus \frac{1}{2} M(2\delta^{-1} t y_k)_G.$$

as M is non-decreasing and convex. By definition 4.2 for $K > 2$, $M(2\delta^{-1} y_k)_G \le (\frac{1}{2} K \delta^{-1} y_k M(2))_G$,

so

$$M(y_k) < (\frac{1}{2} K \delta^{-1} y_k M(2))_G \oplus (\frac{1}{2} K \delta^{-1} y_k M(2))_G = (\frac{1}{4} K \delta^{-1} y_k M(2))_G.$$

Hence $\frac{1}{\lambda_n} G \sum_{k \in I_n, |y_k| > \delta} M(y_k) \le \frac{1}{4} K \delta^{-1} y_k M(2) \lambda_n A_n$

which together with $\frac{1}{\lambda_n} G \sum_{k \in I_n, |y_k| > \delta} M(|y_k|) \le \varepsilon \lambda_n$

yields $[V, \lambda, \hat{F}, p]^G \subseteq [V, M, \hat{F}, p]^G$.

Similarly the result holds for

$[V, \lambda, \hat{F}, p]_0^G \subset [V, \lambda, M, \hat{F}, p]_0^G$ and $[V, \lambda, \hat{F}, p]_\infty^G \subset [V, \lambda, M, \hat{F}, p]_\infty^G$.

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REVIEW ARTICLE

Modification of Cellulose Surface by Chemical Means in Homogeneous Media: A Review

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ABSTRACT

Modification of cellulose have drawn the attention of researchers in present days .In the present review we have discussed the different solvent systems for cellulose and subsequently several methods of grafting by monomers onto cellulose surface by chemical means in homogeneous media. Various properties of cellulose e.g. thermosensitivity, pseudo plastic behavior, appearance , softness , ironing, hydrophilicity, hydrophobicity, graft yield and grafting efficiency after grafting and their sustainable applications are also discussed.

Keywords: thermosensitivity, pseudo plastic behavior, ironing, hydrophilicity, hydrophobicity, sustainable.

INTRODUCTION

Cellulose

Cellulose is the most abundant naturally occurring biopolymer and it's derivatives have many important applications in fiber, paint, and paper industries. The polymeric material with desired properties is a current need of the society. To control the properties such as hydrophobicity, adhesivity , drug delivery, wett ability and thermo sensitivity graft copolymerization of suitable monomers is the versatile technique for cellulose modification. Although cellulose has good properties it has some undesirable ones such as low tensile strength , high moisture regain , and low strength against microbial attack. The process in which the above mentioned drawbacks are eliminated by modifying cellulose surface with suitable monomers without loss of it's original properties is called "grafting".

Solvent system for homogeneous grafting of cellulose

Warwicker , Jayme , Philipp , Pohjola and Brand up have done a lot of work to find out suitable solvents or solvent systems for cellulose. So far four methods of dissolving cellulose are known , where cellulose it self act as a base or forms complexes or derivatives while going into solution. Cellulose can be dissolved in protonic acids like 78% phosphoric acid , 68% nitric acid , 42% hydrochloric acid or 70% sulphuric acid at room temperature. Lewis acids , quaternary pyridinium salts , also dissolve cellulose .In all these cases cellulose it self act as a base while going into solution . Dissolving cellulose by first swelling in inorganic bases like NaOH or liquid ammonia and then treatment with other reagents is also known. Hess and Trogus litt also tried to dissolve cellulose in hydrazine.Addition of various salts to liquid ammonia however results in cellulose dissolution. Thus Scheraer reported that NaI, $NaNO_3$, NaNCS, NH_4I and NH_4NCS when added to liquid ammonia dissolve cellulose. Some organic bases are also known to swell cellulose to give solutions. Kowra et al. reported that 16.5% methylamine in dimethylsulfoxide (DMSO) gave better cellulose solution than any other amine. Cellulose is believed to dissolve by reaction with an equimolar complex of CH_3NH_2 / DMSO. Cellulose acts as an acid while going into solutionin organic and inorganic bases.

Cellulose forms complexes with inorganic salts to dissolve itself. The use of various copper complexes to dissolve cellulose is well known. The fourth or most the important class of cellulose solvent is the aqueous solvents where cellulose goes into solution forming derivatives. The non aqueous solvents for cellulose consists of a variety of binary and ternary solvents , the reaction mechanism for most of them though proposed , have not been fully systematized. How ever a few of the systems have attained commercial use. Kimura et al. who used a modified organic type system for xanthation report one attempt along this line. DMSO/CS_2/amine was used to dissolve cellulose and produced fibers. Several investigators have also studied the use of SO_2/amine solvent systems. Philip and coworkers report extensive work in this area. Fowler et al. have reported that various solvents when used in conjugation with N_2O_4, give different responses to the action of this reagent on cellulose .The amount of oxidation appears to be related to the polarity of the solvent employed ; the non polar solvents such as CCl_4 , N_2O_4 produced mostly oxidation products where as more polar solvents have produced cellulose solutions with greatly diminished oxidation.

Following these class of disclosures by Fowler other researchers began to examine even more polar solvents for use with N_2O_4. Thus William studied the use of DMSO/N_2O_4 as a solvent system for cellulose .It was later demonstrated by Hergant and Topolis that the DMSO/N_2O_4 system would dissolve cellulose more effectively if a small amount of water was present to keep the cellulose structure open for reaction. Later on it was reported that excellent solution of cellulose in N_2O_2/DMF or N_2O_4/DMSO could be readily prepared. With an important to the solvent system Johnson et al. have reported dissolving cellulose in a mixture of DMSO and paraformaldehyde. Recently Turbak et al. have reported that cellulose can be dissolved in a high concentration upto 16% in a solvent system of lithium chloride/N,N – dimethyl acetamide (LiCl/DMAc) and LiCl/N-methyl-2-pyrrolidione(LiCl/NMP) with out degradation of the polymer chain. For the present work the system used is lithium chloride / N,N – dimethyl acetamide (LiCl/DMAc) and dimethyl sulfoxide /paraformaldehyde(DMSO/PF).

Polymer reaction and properties

Ring opening polymerization(ROP) of ε-caprolactone(ε-CL) and L-lactide (L-LA) was carried out using Tin(II) 2-ethyl hexanoate as catalyst in order to introduce more available hydroxyl groups on the surface and subsequently higher grafting efficiency was achieved after modifying the cellulose surface with xyloglucan-bis(methylol)-2-methyl propanamide (XG-bis-MPA) and 2,2- bis(methylol) propionic acid (bis-MPA) respectively. The grafted product was characterized by FT-IR spectroscopy , contact angle measurement , atomic force microscopy and enzymatic degradation and the result showed successful grafting of poly(ε-CL) and poly(L-LA) onto cellulose and improved grafting efficiency after activation of cellulose surface with bis-MPA[1]. Graft copolymerization of methyl methacrylate onto wood fiber in presence of sodium bisulfite/potassium persulfate (SB/KPS) pair as the initiator .The grafted copolymer was characterized by SEM showing presence of small agglomerates of PMMA regularly distributed on the surface of modified fiber and remained on after 24 hrs of $CHCl_3$ extraction. IR analysis of the acid hydrolysis product of modified fiber shows a peak at 1734 cm^{-1} for carbonyl group of PMMA [2].

The sensitivity of photo induced grafting, polymerization, and the filtration performance of six different grafted monomers [2 neutral(N-2-vinyl pyrrolidinone(NVP), 2-hydroxy ethyl methacrylate (HEMA), 2 weak carboxylic acids(acrylic acid (AA), 2 acrylamido glycolic acid (AAG), and two strong sulfonic acids (3-sulfopropyl methacrylate (SPMA), 2-acrylamido-2-methyl-1-propane sulfonic acid(AMPS)] on poly(ether sulfone) PEE membrane were measured [3]. When ethyl acrylate used as monomer at 35 ± 0.1^0C , the rate of grafting has a order of 1.5 w.r.t. CAN concentration which decreased on addition of sodium lauryl sulfate (NaLS) and increased on addition of cetyl trimethyl ammonium bromide(CTAB) and activation energy was calculated as 28.9 kJ mol^{-1} with in the temperature range of 20 to 50^0 C .The product was characterized by TG,DTG, and IR spectra [4].

A temperature responsive cellulose was obtained when N-isopropylacrylamide (NIPAAM) grafted onto cellulose using CAN as initiator at 25 ± 0.1^0 C in acidic medium. The grafted product was characterized by IR showing presence of carbonyl amide and isopropyl groups , thermal studies(TG,DTG) showing energy of decomposition of grafted cellulose(253 KJ/mol) is higher than that of pure cellulose (202 KJ/mol) , thermosensitivity character shows the degree of swelling above LCST(32^0 C) decreased for PNIPAAM grafted side chains due to it's hydrophobic nature and improving trend in hydrophobic nature of grafted copolymer than original cellulose from contact angle measurement [5]. Starting from fibrous dissolving pulp from softwoods, photo grafting (λ>300nm) of N-isopropayl acrylamide (NIPAAM) onto cellulose was investigated at 500C in water using rikorotary photo chemical reactor RH400-10W as a high pressure lamp(400W) and with Ce^{+4} /HNO_3 system under N_2 atmosphere[6].Oxidation and swelling of cellulose sample with aqueous sample of periodic acid and sodium hydroxide initiate the photo grafting to introduce 80% of NIPAAM monomer into the cellulose as grafted chains. Maximum graft yield was obtained from photo grafting than Ce^{+4}/HNO_3 system. Cellulose –g –PNIPAAM sample exhibits a temperature responsive character around 30 ^{0}C which is affected by swelling treatment of cellulose before grafting [6].

Homogeneous graft copolymerization of AN onto high α – cellulose was investigated in LiCl/DMAc solvent system using benzoyl peroxide (BPO) and azobisisobutyronitrile (AIBN) as initiator.The graft yield was higher for AN-BPO system than AN-AIBN system . At higher concentrations of BPO viscosity of the system and GY decreased due to degradation of cellulose backbone and gradual termination of grafting on primary hydroxyls of cellulose macroradicals respectively where as at higher concentrations of AIBN, TC increased and GY, GE decreased .The product was characterized by IR spectra [7]. Grafted copolymer of acrylonitrile and ethyl methacrylate binary mixtures with cellulose was synthesized in presence of Ce(IV) ion in acidic media at 30± 0.1^0 C. on increasing feed molarity of comonomers upto 0.8 and reaction time graft yield increases due to synergic effect of ethyl methacrylate on acrylonitrile which shows poor affinity for grafting when used alone.The grafted product was characterized by IR spectra and elemental analysis to determine the composition and reactivity ratios of acrylonitrile and ethyl methacrylate found to be 0.68 and 1.15 respectively.Rate of grafting depends squarely on concentration of comonomer with in feed molarityrange of 0.05 to 2.5 mol dm^{-3} and rate of ceric ion disappearance is a function of feed molarity and reaction time [8].

Grafting of methyl methacrylate onto α-cellulose extracted from Hibiscus Sabdariffa and Gmelina arborea was carried out using ceric ion redox initiator under different reaction conditions. The grafted cellulose was characterized by IR showing presence of PMMA functional groups , SEM analysis confirmed deposition of PMMA on cellulose surface and TG,DTG detecting a major loss of mass around 410 ^{0}C and 310 ^{0}C for grafted cellulose. water sorbency and ion exchage capacity increases considerably for grafted cellulose [9]. The optimization of grafting of a cationic polymer onto cellulose has been investigated in order to establish the conditions for synthesis of cellulose graft cationic copolymers with a low percentage of grafting. Out of two matrixes Hadamard matrix gave evidence of important of several factors and the fractional factorial matrix showed the influence of other parameters not disclosed in the first experimental design.so from both matrices the significant parameters having major effects on percent of grafting have been deduced [10].

An UV curable surface coating was synthesized by grafting Glycidyl methacrylate (GMA) onto sodium carboxy methyl cellulose (SCMC) polymer chain using CAN as initiator in a homogeneous medium where acrylate groups involved in grafting while glycidyl groups available as pendant groups for a subsequent reaction induced by cationic photo initiator and UV light. The grafted produc t was characterized by FT-IR spectra .CMC was found hydrophobic on account of grafting confirmed from it's core shell configuration and exhibits pseudo plastic behaviour with a hysterisis suggestive of thiotropicity , a property favourable to surface coating in cycloaliphatic diepoxide system [11]. Thermo responsive graft copolymers were synthesized by grafting the CMC sample with amino terminated poly (N-isopropyl acrylamide) side chains of relatively low molecular weight. The product was characterized by IR ,1H-NMR spectroscopy , elemental analysis , TG , DTG , DSC , turbidimetry , viscometry , fluorescence probing rheology measurement and polymer solution preparation in citrate phosphate buffers in 0.1 M NaCl .The ionic strength of sodium was estimated to be 0.15 to 0.17 M [12].

Graft copolymerization of ethyl acryl ate (EA) and dim ethyl amino ethyl methacrylate (DMAEMA) monomer mixture onto water soluble hydroxyl propyl cellulose was carried out using potassium per sulfate (KPS) as initiator in aqueous medium. The graft copolymer was characterized by FT-IR spectra , elemental analysis , NMR , transmission electron microscopy and dynamic light scattering method suggesting that the introduction of DMAEMA monomer accelerates the initial rate of grafting where as increasing amount of monomer grafting parameters decreased significantly due to it's large size , redox reaction with KPS , hydrophilicity nature and chain transfer effect but % of humidity absorption increases due to hydrophilicity of grafted PDMAEMA chains.The graft copolymer is soluble in stimulated gastric fluid due to ionic repulsion of the protonated amine groups of PDMAEMA chains and could be used as a latex coating for gastric solubility tablets [13].

Starting from cellulose macroinitiator synthesized by direct acylation of cellulose with 2-bromo propionyl bromide in a room temperature ionic liquid (RTIL) , 1-allyl-3-methylimidazolium chloride , grafted copolymers were obtained via atom transfer radical polymerization (ATRP) of N,N-dimethylamino-2-ethyl methacrylate (DMAEMA) with CuBr/penta methyl diethylene triamine(PMDETA) as catalyst in dimethyl formamide(DMF).The grafted copolymer was characterized by ^{1}H –NMR, FT-IR and TGA measurements confirming covalent bond of PDMAEMA with cellulose backbone. The aggregates formed by cellulose-g-PDMAEMA copolymers in water was studied at various concentrations ,temperatures and PH values by means of UV,DLS,TEM and AFM indicating similar PH and temperature responsive properties to that of PDMAEMA .The synthetic strategy could be employed in the preparation of other novel bio materials from a variety of polysaccharides [14].

Cellulose fibers in form of filter paper have been modified by reaction of hydroxyl groups of the fiber with 2-bromo isobutyryl bromide followed by grafting of methyl acrylate (MA) via ATRP conditions. The papers were characterized by gravimetry, FT-IR, ESCA, and AFM. A block copolymer graft from the fiber was prepared by grafting poly (2-hydroxy ethyl methacrylate (PHEMA) a hydrophilic polymer upon the PMA layer confirmed from contact angle measurement and FT-IR showing a large increase in carbonyl content due to attach of PHEMA to PMA layer and consequently the hydrophilic/hydrophobic behaviour of cellulose surface tailored by using "living"/controlled radical polymerization methods such as ATRP [15].

High α-cellulose-g-PMMA copolymer was synthesized in (LiCl/DMAc) solvent system using BPO as radical initiator under N_2 atmosphere. The rate of grafting is a function of concentrations of monomer and initiator , reaction time and temperature[2].The grafted product was characterized by infrared spectroscopy where as thermal decomposition of was studied by TG,DTG and DSC technique at a heating rates of 10 ^{0}Cand 20 ^{0}C /min in N_2 atmosphere in the range of room temperature to 650 ^{0}C.The thermal stability of the grafted product increased and peak intensity of wide angle X-ray diffraction patterns decreased with increase of graft yield [16]. A sterically stabilized aqueous suspension of rod like cellulose micro crystal was prepared by combination of acid hydrolysis of native cellulose , oxidative carboxy methylated microcrystals and grafted poly(ethylene glycol)having a terminal amino group on one end(PEG-NH_2,MW=1000) using water soluble carbodiimide.[30]PEG grafted cellulose micro crystals showed dispersion stability towards 2M sodium chloride and redispersion into either water or chloroform from freeze dried state. The

concentrated aqueous suspension of the gragted micro crystals formed a chiral nematic mesophase through a phase separation similar to that of ungrafted sample but with a reduced spacing of finger print pattern.The grafted micro crystal was characterized by thermogravimetry and infrared spectroscopy [17]. Fibers isolated from Agaves lechuguilla and fourcroydes containing about 80% cellulose, 5% hemi cellulose and 15% lignin on treatment with n-octanol/aqueous NaOH leads an activated expanded gel like material with enhanced accessibility. Carboxymethylation, sulfation, acetylation and tritylation reactions as well as subsequent carboxymethylation of the trityl derivatives and selective oxidation of the primary hydroxyl function of methylated products with TEMPO/NaBr/NaClO were carried out under typical conditions for cellulose modification.The products were characterized by means of 13C-NMR and 1H-NMR spectroscopy and HPLC after complete depolymerization by GPC and determination of solubility [18].

Radiation induced graft copolymerization of styrene , mixture of styrene and acrylonitrile to cellulose and polyethylene in presence of methanol as solvent was carried out by Co-60 in Gamma cell 220 at a dose rate of 7.2 K gy /h .Higher graft yield obtained at low dose rate due to lesser termination of free radicals with the polymer growing radicals and recombination of primary radicals resulting in a longer chain length of the grafted copolymer.In styrene ,acrylonitrile copolymer technique styrene controls the homopolymer formation during grafting and water uptake of cellulose decreased on increased graft yield and a new transparent material is obtained on moulding the graftedCellulose.High degree of cross linking on radiation grafting of styrene was observed on grafting of styrene, acrylonitrile to low density polyethylene [19].

Acrylamide (AAm) , acrylic acid(Aac),2-hydroxy propylacrylate(HPA) ,2-hydroxy propyl methacrylate (HPMA) and N,N-methylene bis acrylamide(BAAm) were grafted to cotton cellulose by preirradiation method using Co-60 Gamma ray at a dose rate of 15 kGy/h .The grafted product was characterized by ESR , degree of polymerization (DP) , tensile strength measurement , FT-IR , gravimetry , X-ray diffraction and iodine sorption . The graft yield was highest for HPMA, medium for HPA and low for others.Highest swelling was observed for samples grafted with Aac and BAAm having saturation about 270% at natural PH. For AAm, HPA and HPMA at low graft yield swelling increases and decreases for higher graft yield where as there is no connection between the graft yield and swelling properties [20].

As mobility of the molecular chain play an important role in cross linking, it was improved by applying a coating of water soluble carboxy methyl cellulose on the surface of swelled and carboxy methlated cellulose and then irradiated with 5 kGy/h dose rate by a Co-60 γ-source for 2 hrs in a closed plastic bag.The modified product was characterized by SEM, molecular weight determination by viscometry and FT-IR spectra [21]. Effect of monomer(esters of MA and VA) structure in photo grafting of charge transfer (CT) complex [maleic anhydride (MA) with tri ethylene glycol divinyl ether (DVE-3)] to typically substrates like wool, cellulose, and poly propylene was studied in various solvents e.g. DCM, CCl_4, EtAc-CAN, THF, and acetone with a 90 W medium pressure mercury lamp at room temperature at a dose rate of $36Jh^{-1}$.DCM was effective for enhance grafting with out PI and polar solvents dissolved the homopolymers formed facilitating the removal of grafted substrate. Certain solvents precipitates homopolymers leading turbidity thus restricting transmission of UV and terminating the polymerization process. The graft yield was higher incase of cellulose having easily removable acetal hydrogen than wool which has extensive interlinkages leading rigid structure [22]. Graft copolymerization of acrylonitrile onto cellulose filter paper was carried out in DMF using gamma rays from Co 60 source at a radiation dose rate of 4 kGy/h in presence of styrene as homopolymer suppressor. Addition of $FeCl_3$ decreased both homopolymerization and graft polymerization where as inclusion of a low rate styrene with acrylonitrile leads successful grafting with little homopolymer formation and increased thermal stability of cell-g-PAN copolymer .The total ion current (TIC) generated by heating in the solid probe of a mass spectrometer equipped with a GCM data system showed that the degradation of the graft copolymer follows a two step pyrolysis [23].

The grafting order on cellulose by means of a Ce^{4+} initiation is methyl acrylate > ethyl acrylate > butyl acrylate > methyl methacrylate. They offered an explanation of reactivity in terms of steric and polar effects. It was also

proposed that grafting depends upon the stability of the radical. The polymer radical that is formed in case of methyl methacrylate is relatively stable, whereas in case of methyl methacrylate, which is the most reactive, the corresponding polymer radical is probably stable. It has also been reported by Dworjanyn and Garnett that during radiation grafting certain substituent activate monomers, whereas others deactivate, e.g.relative to styrene, 2-vinyl pyridine is strongly deactivated whereas o-methyl styrene is strongly activated to cellulose [24].

Grafting of methyl methacrylate (MMA) to backbone of cellulose and poly propylene in presence of additives such as mineral acids, photo initiators, vinyl ethers, oligomers , multifunctional acrylates(MFAs) was carried out using ionizing radiation and UV as initiating sources. Grafting was easier on cellulose backbone than PPE for it's polar nature ,UV sensitivity, and swelling behaviour in polar solvents thus diffusing monomers towards grafting site. Additives increased the concentration of monomers at the grafting site thus facilitating grafting process [25]. The effects of complexing agents, such as ascorbic acid, potassium fluoride and EDTA, on the grafting efficiency of PEA onto cellulose have been studied [51]. All of these additives reduced the grafting of poly (ethyl acrylate) on cellulose. With KF as a complexing agent, however, the decrease in percentage of grafting was much less, and grafting occurred without homopolymer formation. With Fenton's reagent initiated grafting, the primary radical $OH^{\cdot}$ responsible for the generation of active sites oncellulose is destroyed by reaction with Fe^{3+} formed during the reaction of H_2O_2 and Fe^{2+}. Consequently, grafting may be favored by complexation of Fe^{3+} by asuitable agents (e.g. ascorbic acid, KF or EDTA). It is also observed, however, that further increase in the concentration of KF considerably reduces grafting of ethyl acrylate, and similar behavior was seen in the grafting of vinyl acetate in the presence of Fenton's reagent. This may indicate that whereas at a lower concentration KF reduces Fe^{3+} by complex formation, promoting grafting, at higher concentration of KF, oxidized KF to elemental fluorine derived by the oxidation of KF by H_2O_2 may add to a vinylmonomer, with a consequent decrease in percent grafting. Thus, the addition of KF did not improve the percentage of grafting of VAc to cellulose [26,27].

L-Threonine possess -OH, $-NH_2$ and –COOH groups capable of forming complexes with Ce^{4+} . In general, the efficiency of grafting of methyl acrylate on cellulose was found to increase with increasing L-threonine concentration, but at higher concentration of L-threonine, the complex formation is reduced through competition by an enhanced rate of abstraction of H-atom from L-threonine by the growing grafted chains:

$$R_{poly}O(M_n)^{\cdot} + RNH_2 \longrightarrow R_{poly}O(M_n)\text{-}H + RNH^{\cdot}$$

$$R_{poly}O(M_n)^{\cdot} + ROH \longrightarrow R_{poly}O(M_n)\text{-}H + R\text{-}O^{\cdot}$$

$$R_{poly}O(M_n)^{\cdot} + RCOOH \longrightarrow R_{poly}O(M_n)\text{-}H + R\text{-}COO^{\cdot}$$

Grafting of methyl acrylate on cellulose was suppressed by 5-hydroxytryptophane and 5-hydroxy tryptamine additives. Apparently, the phenolic –OH groups present in these additives inhibit both polymerization and grafting. This may indicate that radio-protecting agents involve a free-radical mechanism in their mode of action [28]. Itaconic acid was grafted onto cellulose fibers using potassium persulfate as initiator and dyeing of the grafted fibers with methylene blue and remacryl rot shows good fastness towards UV light. The grafted product could be characterized by IR spectra signify the existence of carbonyl group of Itaconic acid at $1731cm^{-1}$, X- ray diffraction analysis showed a remarkable decrease in degree of crystallinity with in the percentage of grafting due to increase in the intermolecular distance between the cellulose chains which consequently lowers the degree of H-bonding between the chains , thus increasing the amorphous character. Thermogravimetry reveals a increase in percentage of grafting due to low thermal stability of poly itaconic acid, scanning electron microscopy analysis revealed a pronounced swelling effect and thicking of the diameters of fibers with increase in degree of grafting. More over appearance , softness , and ironing properties of cellulose improved after grafting [29]. Conversion of the hydroxyl groups of cellulose thio carbonyl-thio chain transfer agents , mediated the reversible addition – fragmentation chain transfer (RAFT) polymerization of styrene onto cellulose .The graft copolymers were characterized by gravimetry, attenuated total reflectance fourier –transform infrared spectroscopy(ATR-FTIR) , fourier transform Raman spectroscopy (FT-

Raman) , contact angle measurement , scanning electron microscopy , differential scanning calorimetry and thermogravimetry.Size exclusion chromatography of poly(styrene) chains cleaved from cellulose backbone showed narrow polydispersity [31]. Taste sensor material is prepared by grafting of poly acrylic acid (PAA) onto cellulose using CAN as initiator in acidic media under N_2 atmosphere and reaction of basic five taste substances NaCl, HCl, Q-HCl, sucrose and mono sodium glutamate (MSG) as shown in the fig – 1.The grafted membrane was characterized by FT-IR spectra , indicating presence of –CHO ,–COOH and –C-CHO linkage.SEM shows the surface morphology after grafting. Sensor materials prepared from grafted membrane showed distinct response patterns for different taste substance in terms of membrane potential which is a function of threshold concentration of PAA-g-cellulose membrane for NaCl , HCl , Q-HCl , MSG ,and sucrose as 0.01mm , 0.001mm, 0.08mm, 0.08mm, and 0.01mm respectively [32].

An oxidative of cellulose with sodium metaperiodate was performed where the oxidized groups were decomposed into free macro radicals and these reactive sites become the starting point for the graft copolymerization of cellulose substrate in presence of acrylic monomers in vapour phase. The graft yield is a fuction of polymerization time and oxidative degree of cellulose .The grafted polymer was characterized by DSC, GPC, viscosity, FT-IR and ^{13}C CP-MAS. They are suitable for consolidation and protection of precious cellulose based materials [33]. An oxidative reaction of cellulose with metaperiodate was performed where the oxidized groups were transformed into free macro radicals by treatment with UV light and become starting point for the graft copolymerization of methyl methacrylate and ethyl acrylate onto cellulose. The product was characterized by DSC, and TGA showing increased thermal stability in presence of acrylic polymers [34]. Grafting polymerization of methyl methacrylate and ethyl acrylate onto lilen and cotton was carried out in order to reinforce these materials when they underwent degradation. Taking this into account an artificial ageyinjg was performed onto cellulose based textile by metaperiodate oxidation where carbonyl groups were introduced in cellulose and used as photo sensitive agents allowing the formation of radical sites during polymerization reaction that started by irradiating the substrate with UV light. The product was characterized by FT-IR ,DSC, and SEM analysis [35].

Grafting of methyl methacrylate and ethyl acrylate onto cellulose chains of textiles with oxidized sites has been carried out where carboxyl and carbonyl groups have been introduced by oxidation of the cellulose and used as photo sensitive agents allowing formation of radical sites and copolymerization started by irradiating the substrate with UV light. With the grafting of acrylic monomers the mechanical strength, thermal stability, and resistance to chemical and biological agents of cellulose improved.The sample was characterized by ^{13}C solid state NMR spectroscopy, cross polarization dynamic process and direct integration of resonance process in ^{13}C single pulse excitation spectra [36]. Mono chlorotriazinyl-β-cyclodextrin(MCT- β-CD) and β-cyclodextrin (β-CD) was grafted to filter paper using 1,4-butanediol di-glycidly ether as the crosslinking agent.The untreated and treated filter paper was characterized by differential scanning calorimetry (DSC) and thermogravimetric analysis(TGA) demonstrating the covalent binding of cyclodextrins to filter paper.The quantification of β-CD and MCT- β-CD was determined by the dye extinction method with the inclusion of phenolphthalein.The final β-CD content amounted to 15.9 μmol and 72.8 μmol per gram of support(1.8% and 11.3% by weight) [37].

In order to improve the dispersibility of cellulose nano crystals (CNC) particles three different grafting reactions of acetylation, hydroxylation, and hydroxypropylation were introduced to modify the CNC surface.The properties of modified CNC were characterized by means of FT-IR, 13C –NMR, transmission electron microscopy (TEM), and thermogravimetric analysis (TGA).The results indicated that after desiccation, the modified products could be dispersed again in the proper solvents by ultrasonic treatments and the diameter of their particles had no obvious changes but their thermal degradation behaviour were quite different where initial decomposition temperature of the modified product via hydroxyethylation or hydroxypropylation was lower than that of the modified product via acetylation .Solvents are easily aggregated during the drying due to great number of hydroxyl groups on the surface.This shorting coming limited the application of CNC as reinforcing filler in nano composite materials [38]. A new low-density lipo protein (LDL) adsorbent with good adsorption performance has been obtained by graft copolymerization of acrylic acid (AA) onto microporous cellulose beads with ceric ammonium nitrate (CAN) as a

redox initiator.The initiator,monomer concentrations and reaction time has an adverse effect on PG and GE. Vitro study showed that adsorbent could remove total cholesterol(TC), low density lipoprotein-cholesterol (LDL-C), and triglyceride (TG) upto 5.55, 4.46, and 2.48 mg g-1, respectively from human plasma without substantially affecting high density lipoprotein-cholesterol(HDL-C) and total protein(TP).The adsorbent prepared might be useful for potential clinical application [39]. Graft copolymerization of ethylacrylate onto water soluble hydroxyl propyl methyl cellulose (HPMC) was investigated with potassium persulfate (KPS) as initiator in aqueous medium.The effect of monomer ,initiator, matrix concentrations, reaction time and reaction temperature on % grafting and grafting efficiency (GE) are discussed. The graft copolymers were characterized by FT-IR ,SEM, TEM, XRD and DSC. In addition equilibrium humidity adsorption behaviour of the pure grafted copolymers were studied [40]. Temparature induced copolymers of poly(N,N-dimethyl aminoethyl methacrylate) – grafted – celluloase nao crystals (PDMEMA-grafted-CNC) were synthesized by surface initiated atom transfer radical polymerization(ATRP).The grafted copolymers were characterized by TGA, FT-IR, and gel permeation chromatography (GPC).The size of the original CNC was 10-40 nm in width and 100-400 nm in length as characterized by atomic force microscopy(AFM).The liquide crystalline properties of the frafted copolymers were investigated using polarizing optical microscopy(POM).The graft copolymers exhibited fingerprint texture in lyotropic state. The temperature induced fingerprint texture changes of PDMAEMA –grafted –CNC aqueous suspensions were investigated at various temperatures. With increasing temperature , the spacing of the finger print lines decreased [41].

Graft copolymerization of methacrylic acid (MAA) onto cotton fibric using tetravalent ceric ion (Ce IV) – cellulose thiocarbonate redox system was investigated under different conditions including PH of the polymerization medium, ceric sulfate (CS) concentration (4-20 m mol/l), MMA concentration (1%-6%), polymerization time (1/4-2 h) and polymerization temperature (50-700C).The optimal conditions for grafting onto cotton fabric using the said redox system consisted of [CS] 20m mol/l ; [MMA] 4% ; PH of the medium 2 ; time 2 h ; temperature 600C keeping material-to-liquior ratio at 1:50.Applying ptimized conditions to different monomer namely acrylic acid(AA), methacrylic acid (MAA), acrylamide (Aam), acrylonitrile (AN), butylacrylate (BUA), methylmethacrylate (MMA), ethyl methacrylate (EMA), and gylcidyl methacrylate (GMA) onto the same substrate , the rates of grafting followed the order GMA>> MMA> AA > MAA > Aam > EMA > AN > BUA [42].

Copolymers of ethyl cellulose (EC) with polystyrene (PSt) were synthesized through atom transfor radical polymerization (ATRP) .The molecular weight of graft copolymers increased without any trace of the EC macro-initiator, and the polydispersity of the side chains increased with monomer conversion .kinetic study indicated that the polymerization was first order.The micelle characterization of the graft copolymers in acetone were investigated using dynamic light scattering (DLS), atomic force microscopy (AFM) and transmission electron icroscopy (TEM).With increasing concentration, micelles were gradually formed from the solution .The TEM and AFM images indicated that the micelles had spherical shape and showed core – shell structure [43].

Nanosized copolymer latrex of hydroxypolymethyl cellulose (HPMC) grafted with ethyl acrylate (EA) and dimethylaminoethylmethacrylate (DMAEMA) has been prepared by acidifying submicron-sized latex particles synthesized by soap-free emulsion graft copolymerization using potassium persulfate (KPS) as initiator. The effects on the diameter of the latex particles of different conditions such as DMAEMA concentration, amount of HPMC, and ratio of HCL to DMAEMA for acidification were investigated.Increasing the mole ratio of HCL to DMAEMA content decreased the particle diameter where as increasing the amount of HPMC increased the particle size. Measurement by dynamic light scattering (DLS) revealed the diameter of the latex particle was > 200 nm before acidification and < 100 nm after acidification.Evidence of grafting was obtained by use of FT-IR spectroscopy. Transmission electron microscope (TEM) was used to characterize the morphology of the copolymer particles before and after acidification [44]. Native cellulose was oxidized with catalytic amounts of 2,2,6,6-tetramethylpiperidine -1- oxyl radical (TEMPO), sodium hypo chlorite and sodium bromide in water. The primary alcohol moieties were selectively oxidized into carbonyl groups, then the oxidized cellulose was coupled with amine derivatives by a peptidic reaction by using carbodiimide and hydroxyl succimide as catalyst and amidation agent. The obtained coupled cellulose showed low polarity, with stability in non polar solvents. The products were characterized by FT-IR, 13 C-NMR, rheology and

conductometric titration as well as transmission electron microcsopy.Their hydrophilic character was evaluated by observing their behaviour in polar and non polar solvents [45]. Chemical grafting of β-cyclodextrin derivative (β-CD) onto fibers followed by inclusion of benzoic acid in the grafted CD cavities as a probe chemical. Physiochemical properties and performances of the untreated and treated fibers have been determined with infrared spectra, microscopy, swelling measurements, antimicrobial finishing tests, and dye adsorption. The results showed that cellulose fibers can be efficiently modified with no significant changes in it's structural and surface properties ; the treated fibers show an attractive behaviour in swelling ,dye adsorption and antibacterial activity [46]. Graft copolymerization of ethylacrylate (EA) and dimethyl aminoethyl methacrylate (DMAEMA) monomer mixture onto water soluble hydroxyl propyl methyl cellulose was investigated with potassium persulfate (KPS) as initiator in aqueous medium.The graft copolymer was characterized by FT-IR spectra,elemental analysis, nuclear magnetic resonance, transmission electron microscopy, and dynamic light scattering methods.The results suggest that the introduction of DMAEMA clearly accelerates the initial rate of the graft copolymerization where as the grafting parameters decreased significantly with increasing amounts of DMAEMA due to relatively large size of the DMAEMA molecule, it's redox reaction with KPS, it's hydrophilicity in water and it's chain transfer effect.The equilibrium humidity adsorption behaviour and acid solubility of graft copolymer films were studied [47].

To develop low cost and environmentally friendly polymeric materials for enrichment separation and remeriation of metal ions from water, novel reactive graft copolymers based on cellulose extracted from pine needles were synthesized by grafting of poly(glycidyl methacrylate) alone and with comonomers acrylic acid ,acryamide and acrylonitrile by benzoyl peroxide initiation.The graft copolymer was characterized by elemental analysis, FT-IR, and solvent uptake behaviour.An attempt has been made to study sorptions of Fe^{2+} , Cu^{2+} and Cr^{+6} on candidate graft copolymers by an equilibration method and to investigate the structural aspects of graft copolymers and establish a relationship between the structural aspects of graft copolymers and metal ion uptake efficiency and selectivity [48].

Crossedlinked hydroxyethyl cellulose-g-poly(acrylic acid) (HEC-g-PAA) graft copolymer was prepared by grafting of acrylic acid (AA) onto hydroxyl ethyl cellulose (HEC) using ceric ammonium nitrate (CAN) / HNO3 initiator system in presence of poly (ethyleneglycol diacrylate) (PEGDA) crosslinking agent in 1:1 (v/v) mixture of methanol and water at 30 ^{0}C.Carbonyl content of polymer was determined by neutralization of –COOH groups with NaOH solution and sodium salt of copolymer (HEC-g-PAANa) was swelled in distilled water in order to determine the equilibrium swelling value of copolymer.Both dry HEC-g-PAA and swollen HEC-g-PAANa copolymer s were used in the heavy metal ion removal from three different aqueous ion solutions as follows: a binary ion solution with equal molar contents of Pb^{2+} and Cd^{2+} , a triple ion solution with molar contents of Pb^{2+} , Cu^{2+} and Cd^{2+} and a triple ion solution with twice Cu^{2+} molar contents of Pb^{2+} and Cd^{2+}.Higher removal values on swollen HEC-g-PAANa were observed in comparision to those on dry polymer.The presence of Cu2+ decreased the adsorption values for Pb2+ and Cd2+ ions on both types of HEC copolymer.However with further increase in Cu2+ content , both dry and swollen copolymers became apparently selective to Cu2+ and Cu^{2+} values exceeded the sum of adsorption values for Pb^{2+} and Cd^{2+} .Maximum metal ion removal capacities were 1.79 and 0.85 m mol Me^{2+} / g polymer on swollen HEC-g-PAANa and dry HEC-g-PAA, respectively [49].

Acryl amide was grafted onto cellulose powder and flat membranes followed by activation with glutaraldehyde in order to provide supports for the enzyme immobilization. The grafting degrees of acrylamide on cellulose acetate flat membranes increased almost linearly with the initiator /membrane ratio, polymerization time and monomer /membrane ratio,where as the activation time had a more complex influence.The immobilization of xylanase was successfully occurred on the acrylamide grafted CA membranes and showed biocatalytic activity in beech wood xylan solution,after subsequent incubations at 50^0 C, lasting 7 hrs altogether. The immobilized enzyme was more resistant to activation by heat than the soluble enzyme. The grafted product was characterized by FT-IR and determination of nitrogen content by cellulose acetate material [50].

CONCLUSIONS

The discussion above shows that, through grafting, a beautiful level of control on both structure and function of cellulosic materials can be implemented. In this report, we have sketched different mechanistic approaches for grafting by chemical method, radiation technique, photochemical and enzymatic techniques. Apart from the conventional grafting process, living radical polymerization and ring-opening polymerization are also focused. Different factors that control grafting, like the nature of the backbone, initiator, monomer etc. have also been discussed. Fortunately, the grafting process is now expanding rapidly through electron beam curing processes that can be achieved in a fraction of a second, and yield products in one step without further purification. Apart from the various advantages of the grafting, research takes step towards 'bio degradability'. It may solve some of the problems of environmental pollution caused by components that resist bio-degradation and will play a major role in good health and well being of society.

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RESEARCH ARTICLE

Lipid Mediate Apoptosis in Yeast *Saccharomyces cerevisiae*

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ABSTRACT

Accumulation of fatty acids trigger apoptosis termed as lipo-apoptosis. Yeast due to its ease of studying at biochemical and genetic level, low doubling rate, ease of cultivation has been used as a standard model to study various fundamental cellular processes and also good health and well-being. Understanding the interconnection between evolutionarily conserved, stress response mechanisms such as lipotoxicity and apoptosis in yeast strains undergoing apoptosis has been a subject of intense study in recent years. Recent advances in lipoapoptosis have shed light on the role of free fatty acid, sphingolipids, cardiolipin and lipid peroxidation in the mitochondrial-mediated intrinsic model of programmed cell death. The future studies address several questions pertaining to apoptosis and lipid dysfunction.

Keywords: PCD, Lipoapoptosis, fatty acids, phospholipid, Good health and well-being

INTRODUCTION

Ever since apoptosis discovered in yeast (*Saccharomyces cerevisiae)* and bacteria such as *Xanthomonas campestris pv. glycines*, *Bacill*us sp. and *Bordetella bronchispetica*, yeasts has become an attractive model system in biomedical research for studying many conserved cellular processes such as apoptosis, mRNA decay or lipid metabolism which cannot be studied in prokaryotes and also aspects of good health and well-being [1-6]. Apoptotic studies in yeast strains defective in cytoplasmic deadenylases or mRNA decay suggested interconnecting mechanism between mRNA metabolism and apoptosis [7]. Central mechanisms of lipotoxicity are conserved from yeast to mammals and different lipid species like ceramides, free fatty acids (FFA), diacylglycerol (DG), spingolipids or cholesterol are known to induce apoptosis (also termed lipoapoptosis) [8].

Alterations of lipid metabolism can trigger cell death and yeast can be used to address questions pertaining to lipid-associated aspects pertaining to good health and well-being in humans. Mitochondrial retrograde (RTG) signaling, activated in response to metabolic stress and during replicative aging in rho+ yeast cells, extends the replicative life

span in respiratory deficient yeast cells. Another conserved mechanism connected to retrograde signaling is target of rapamycin (TOR) signaling that regulate growth and metabolism in response to nutrient sensing. In higher eukaryotes mammalian TOR (mTOR) signaling regulates cancer cell motility and metastasis. TOR kinase inhibitors that inhibit mTOR pathway are currently in pre-clinical and clinical development stage as potential cancer therapeutic drugs [9, 10]. Cellular mechanisms such as apoptosis, retrograde signaling, TOR signaling and mRNA perturbations are influenced by environmental cues [11, 12].

Lipid metabolism and apoptosis

The goal of apoptotic research in yeast systems is to determine alterations in lipid metabolism and its causal link to apoptosis in strains defective in mRNA decay. Numerous studies on good health and well-being provided connection between lipid metabolism, chronological life span and apoptosis in the budding yeast *Saccharomyces cerevisiae*.

Lipid metabolism generates various bioactive metabolites known as signaling molecules such as fatty acid, eicosanoids, diacylglycerol, phosphatidic acid, lysophophatidic acid, ceramide, sphingosine, sphingosine-1-phosphate, phosphatidylinositol-3 phosphate, and cholesterol that are known to activate mitochondria mediated cell intrinsic pathway and thereby promote caspase dependent apoptosis. Understanding the causal link between apoptosis and lipid metabolism might provide a rational for discovery of new drug targets [13]. The exogenous addition of palmitoleic acid results in lipid toxicity and lipid remodeling in endoplasmic reticulum, mitochondria, and palsm membrane that causes the cells to initiate regulated mode of cell death termed liponecrosis. Understanding regulated mode of cell death helps in understanding various human diseases that are linked to dysregulated lipid metabolism such as liver cirrhosis, obesity, metabolic syndrome, type 2 diabetes, cardiovascular diseases, and cancer [14].

Very recently Kuo's team for the first time show a positive correlation between tri acyl glycerol (TAG) content and chronological lifespan in budding yeast. This cellular pro-longevity function of TAG content provides support to the obesity paradox theory [15]. Suppression of apoptotic phenotypes by over expression of NEM1 in *Kllsm4*Δ1 strain suggesting a link between apoptosis in strains defective in mRNA degradation and phospholipid homeostasis [16].Yeast mutants defective in the major cytoplasmic deadenylase (*CCR4*) were reported to have reduced *INO1* expression [17]. It is suggested that elevated levels of Phosphatidylethanolamine (PE) promote autophagic capacity and increases longevity in *S. cerevisiae* [18].

Based on these reports, we hypothesize mutants defective in mRNA decapping activation factors (*LSM1*), cytoplasmic deadenylases (double deletion of *CCR4* and *PAN2*) have reduced *INO1*, *INO2*/*INO4* transcript levels, elevated expression of *OPI1* (negative regulator of phospholipid biosynthesis), and consequent TAG accumulation (Fig. 1). Expression levels of *INO1*, *INO2*/*INO4* and *OPI1* as well as correlation of transcriptome with lipidome will reveal expression levels of large number of phospholipid biosynthetic genes and quantitate individual lipid species (TAG, DAG, PA, PE, sphingolipids and free fatty acid levels) under apoptotic and non-apoptotic conditions. There is a complex interplay between lipid catabolism and autophagy as any disfunction in autophagy mediated lipid catabolism leads to host of various diseases and therefore targeting autophagy pathway has gained significance in lipid mediated disorders [19].

CONCLUSION

Quantitation of phospholipids using liquid chromatography mass spectrometry and trancriptome analysis using yeast microarray to better understand whether changes in lipid metabolism or lipid profile causally linked to apoptosis in yeast.

Studying these conserved processes in yeast leads to:

- Better understanding on the roleof signaling systems (RTG/TOR signaling) and lipid metabolism in yeast apoptosis.
- Better understanding on pharmacological induction of yeast apoptosis towards combatting yeast and fungal infections

Studying these complex cellular processes in human cell lines is always challenging due to lack of consistency in research results and therefore necessitates the need of an easier system such as yeast.

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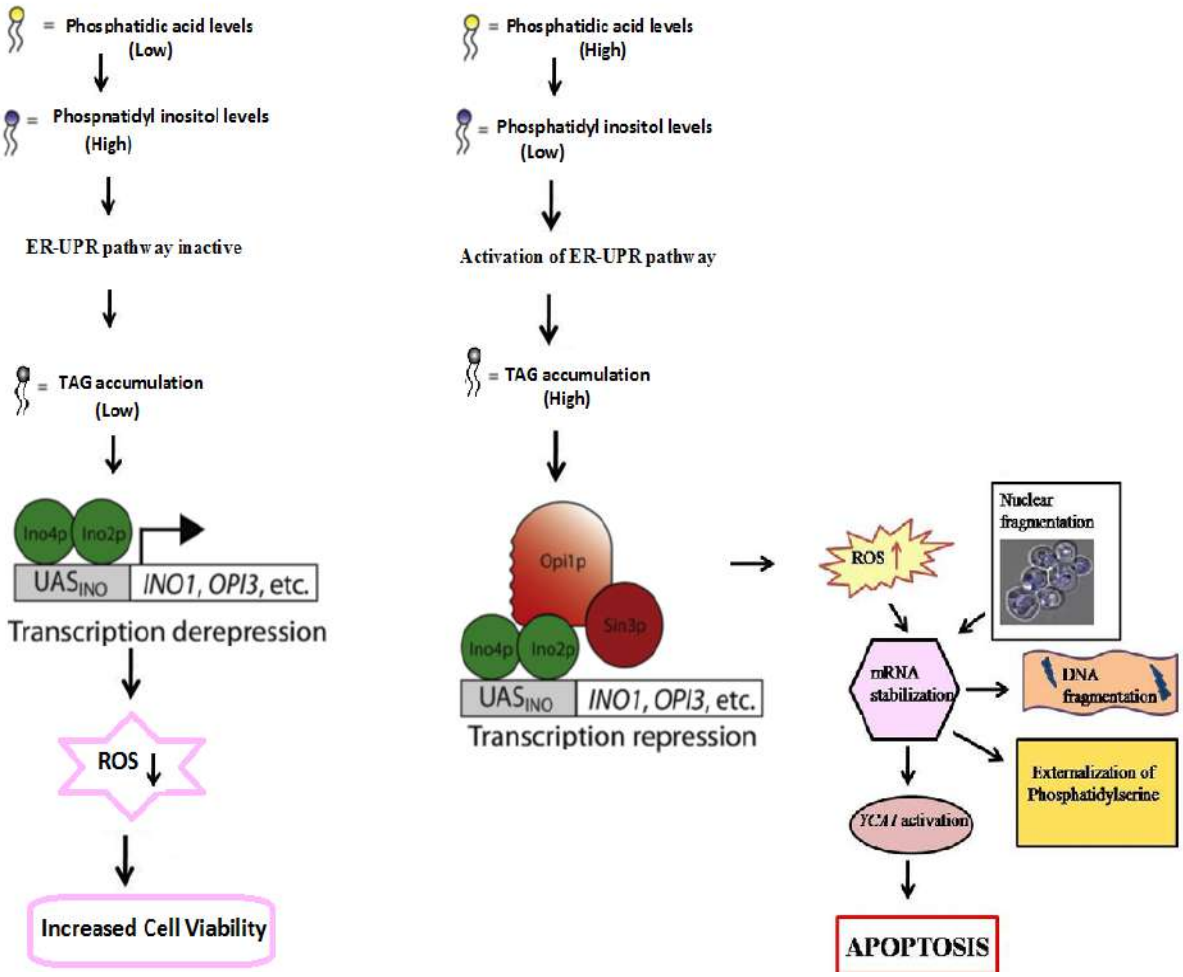

Fig.1: Speculative model showing reduced transcription levels of *INO1*, *INO2*/*INO4* contributing to apoptosis in mutants defective in mRNA decay factors. In yeast a high INO level (*INO2*/*INO4*) enhances expression of genes involved in phospholipid biosynthesis (Phosphtidyl choline and phosphatidyl inositol), myoinositol biosynthesis and transport, fatty acid metabolic processes and ribonucleoside synthetic process. At low INO levels aminoacids are down-regulated; promote triacyl glycerol (TAG) biosynthesis and accumulation via ER stress and activation of the unfolded protein response (UPR) [20].

REVIEW ARTICLE

A Brief Overview of Omicron Virus Including its Severity, Transmissibility, Genomic Evolution and its Impact on Vaccinated Population.

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ABSTRACT

Two years after the appearance of the severe acute respiratory syndrome-CoronaVirus-2 (SARS-CoV-2) in Wuhan Province in China, on November 24, 2021, another novel variant of the virus was reported in South Africa. The World Health Organization (WHO) announced it as the Omicron (B.1.1.529) variant, which belongs to the variant of concern (VOC). Following Alpha, Beta, Gamma, and Delta VOCs, Omicron is the fifth mutation of SARS-CoV-2. Today, this highly mutated variant is spreading rapidly around the globe, while the world is exhausted by the pandemic and is still struggling with the widespread negative social, psychological, and economic effects of the COVID-19. Omicron genome carries atleast 50 new mutations with 30 located in these quence of the viral Spike protein,which has been the target of developed vaccines. Key Amino Acid Substitutions in Spike Protein (RBD substitutions in bold type): A67V, T95I, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F. This brief article focused on Omicron as a novel variant in the current pandemic. As a result, the current work intends to give thorough information regarding the novel covid-19 variant's emergence, effect, genomic evolution, and therapeutic implications (SARs-COv-2). This brief article focused on Omicron as a novel variant in the current pandemic.

Keywords: Omicron, COVID-19, VOC, SARs-COv-2.

INTRODUCTION

Severe acute respiratory syndrome corona virus-2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19), emerged in Wuhan, China in December 2019, and has since spread around the world. By mid-May 2020, more than 90 million people had been tested, more than 4.5 million people had been infected, and there had been more than 300,000 deaths globally. While the USA has experienced the greatest numbers of cases and deaths, new epi-centres of the pandemic are emerging, such as Russia, Brazil and India, and it is highly likely that furthere picentres will emerge. On Nov 25, 2021, a new SARS-CoV-2 variant of concern (VoC), omicron-2 was reported. It triggered an urgent WHO meeting on 26 November 2021 to critically assess the various aspects of the variant reported by South Africa.[1,2] The first sequenced omicron case was reported from Botswana on Nov 11, 2021, and a few days later another sequenced case was reported from Hong Kong in a traveller from South Africa. Omicron emerged in a COVID-19-weary world in which anger and frustration with the pandemic are rife amid widespread negative impacts on social, mental, and economic wellbeing. Although previous VoCs emerged in a world in which natural immunity from COVID-19 infections was common, this fifth VoC has emerged at a time when vaccine immunity is increasing in the world.[3,4,5,6]SARS-CoV-2 is a single-stranded-RNA virus with a genome that is proneto mutations in relatively short periods of time. Millions of sequences have shown that only few mutations effectively cause amore severe disease with high transmissibility and infectivity. The viral genetic variations have affected the pandemic course in 2021. The new variants have caused new peaks of infections globally. The initial patient clusters infected were, however, identified by sequencing in Botswana, confirming that the dominating variant was not Delta. According to the latest news, at least 50 countries have confirmed Omicron cases. The rapid spread of Omicron in South Africa is concerning because of its many mutations. The Omicron genome carries atleast 50 new mutations with 30 located in these quence of the viral Spike protein, which has been the target of developed vaccines**.**[7]Key Amino Acid Substitutions in Spike Protein (RBD substitutions in bold type): A67V, T95I, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F. After initial identification that the new variant was associated with an S-gene target failure on a specific PCR assay because of a 69–70del deletion, similar to that observed with the alpha variant. The earliest known case of omicron in South Africa was a patient diagnosed with COVID-19 on Nov 9, 2021, although it is probable that there were unidentified cases in several countries across the world before then. In South Africa, the mean number of 280 COVID-19 cases per day in the week before the detection of omicron increased to 800 cases per day in the following week, partly attributed to increased surveillance. COVID-19 cases are increasing rapidly in the Gauteng province of South Africa; the early doubling time in the fourth wave is higher than that of the previous three waves.

Classification of Omicron Variant

According to WHO, we can classify Omicron variant in to two category. One is SARS-CoV-2 Variant of Interest (VOI) & another one is Variant of Concern (VOC). [8]

A SARS-COV-2 VOI IS A SARS-COV-2 Variant

A variant with with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND that has been identified as causing significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health. [9,10,11]

Possible attributes of a Variant of Interest:

- Specific genetic markers that are predicted to affect transmission, diagnostics, therapeutics, or immune escape.
- Evidence that it is the cause of an increased proportion of cases or unique outbreak clusters.
- Limited prevalence or expansion in the US or in other countries.
- A Variant of Interest might require one or more appropriate public health actions, including enhanced sequence surveillance, enhanced laboratory characterization, or epidemiological investigations to assess how

easily the virus spreads to others, the severity of disease, the efficacy of therapeutics and whether currently approved or authorized vaccines offer protection.[12,13,14,15]

- Currently, no SARS-CoV-2 variants are designated as VOI.

A SARS-COV-2 VOC IS A SARS-COV-2 Variant: A variant for which there is evidence of an increase in transmissibility, more severe disease (for example, increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures. [16,17,18]

Possible attributes of a variant of concern: In addition to the possible attributes of a variant of interest

- Evidence of impact on diagnostics, treatments, or vaccines
- Widespread interference with diagnostic test targets
- Evidence of substantially decreased susceptibility to one or more class of therapies
- Evidence of significantly decreased neutralization by antibodies generated during previous infection or vaccination
- Evidence of reduced vaccine-induced protection from severe disease
- Evidence of increased transmissibility
- Evidence of increased disease severity
- Variants of concern might require one or more appropriate public health actions, such as notification to WHO under the International Health Regulations, reporting to CDC, local or regional efforts to control spread, increased testing, or research to determine the effectiveness of vaccines and treatments against the variant. Based on the characteristics of the variant, additional considerations may include the development of new diagnostics or the modification of vaccines or treatments.
- Current variants of concern in the United States that are being closely monitored and characterized are listed below. This table will be updated when a new variant of concern is identified.

According to CDC ,we can classify Omicron variant in to four category. One is SARS-CoV-2 Variant of Interest (VOI) one is Variant of Concern (VOC)., Variants being monitored (VBM), Variant of high consequence (VOHC).[19,20,21,22,23,24]

Variants Being Monitored (VBM): CDC monitors all variants circulating in the United States. Variants designated as VBM include those where data indicates there is a potential or clear impact on approved or authorized medical countermeasures or that have been associated with more severe disease or increased transmission but are no longer detected, or are circulating at very low levels, in the United States. These variants do not pose a significant and imminent risk to public health in the United States.[25,26]

- A Variant of Interest or a Variant of Concern may be downgraded to this list after a significant and sustained reduction in its national and regional proportions over time, or other evidence indicates that a variant does not pose significant risk to public health in the United States. [27,28,29,30,31]
- These variants continue to be closely monitored to identify changes in their proportions and new data are continually being analyzed. If the data indicate that a VBM warrants more concern, the classification will be changed based on the SIG assessment of the attributes of the variant and the risk to public health in the United States.[32,33]

Variant Of High Consequence (VOHC): A VOHC has clear evidence that prevention measures or medical countermeasures (MCMs) have significantly reduced effectiveness relative to previously circulating variants. Possible attributes of a variant of high consequence:

In addition to the possible attributes of a variant of concern[34,35,36,37,38]

- Impact on MCMs.
- Demonstrated failure of diagnostic test targets.
- Evidence to suggest a significant reduction in vaccine effectiveness, a disproportionately high number of infections in vaccinated persons, or very low vaccine-induced protection against severe disease.

- Significantly reduced susceptibility to multiple EUA or approved therapeutics.
- More severe clinical disease and increased hospitalizations.
- A variant of high consequence would require notification to WHO under the International Health Regulations, reporting to CDC, an announcement of strategies to prevent or contain transmission, and recommendations to update treatments and vaccines.
- Currently, no SARS-CoV-2 variants are designated as VOHC.

Severity Of Omicron: While the omicron variant's abnormally large number of mutations is remarkable, the development of yet another SARS-CoV-2 variation is not.[39,40,41,42] According to the World Health Organization (WHO), It is unclear whether Omicron infection causes more severe disease than infections caused by other variations, such as Delta. According to preliminary data, hospitalisation rates are rising in South Africa, however this could be due to an increase in the general number of persons becoming infected rather than a specific Omicron illness. [43,44,45,46,47]

- According to the statistics, this new variety affects previously covid infected patients as well as vaccinated people. [48]
- Young people are more likely to be infected with omicron, and it spreads more swiftly than other covid types, according to some reports. As a result, it is classified as a VOC [Variant of Concern], and the severity of this variant is greater than that of other variants.[49,50]

Transmissibility Of Omicron: WHO has stated that It's unclear whether Omicron is more transmissible (i.e., easier to transfer from person to person) than other variations, such as Delta. In areas of South Africa affected by this variation, the number of people testing positive has increased, but epidemiologic studies are planned to determine if this is due to Omicron or other factors. South African scientists have discovered that the omicron variation of the coronavirus spreads more than twice as fast as the delta variant in that country. "It appears to be more transmissible than delta," Juliet Pulliam, director of the DSI-NRF Centre of Excellence in Epidemiological Modelling and Analysis at Stellenbosch University, stated. According to the CDC, alterations in the spike protein suggest that the Omicron version is more transmissible than the original SARS-CoV-2 virus, but it's impossible to say whether it's more transmissible than Delta.[51,52]

- N501Y increases ACE2 receptor binding, which may boost transmission, and the combination of N501Y and Q498R may increase binding affinity even more; nevertheless, other Omicron spike protein changes are likely to diminish ACE2 receptor binding. As a result, the whole range of spike protein changes present in the Omicron variation must be used to determine receptor binding affinity. [53,54]
- H655Y is close to the furin cleavage point, it may accelerate spike cleavage, aiding transmission. [55]
- N679K is close to the furin cleavage site and contributes to its polybasic character, which may enhance spike cleavage and help transmission. [56,57]
- P681H has been proven to improve spike cleavage, which may help with transmission. This mutation is found in Alpha, but a different mutation (P681R) is found in Delta. [58]

Effect of Omicron on Prior Sars-Cov-19 Patients: According to the Scientists of South Africa and WHOpeople who already had COVID-19 could be more vulnerable to a second infection from this new variant. [59]

- According to virologist Paul Bieniasz at Rockefeller University in New York says that Omicron carries many mutations that likely help the variant evade the immune system.
- Bieniasz and his colleagues have already conducted lab research on key mutations that show up in omicron and found that they can help prevent antibodies from killing the virus. Information is limited. More information on this will become available in the coming days and weeks.

Effect of Omicron on Vaccines: WHO is working with technical partners to understand the potential impact of this variant on our existing countermeasures, including vaccines. Vaccines remain critical to reducing severe disease and death, including against the dominant circulating variant Delta. Current vaccines remain effective against severe disease and death. [60]

- According to Australian Govt. There is no evidence to date that the vaccines Australians have been given are any less effective at preventing severe illness, hospitalisation or death from Omicron.They working on that to find out how effective vaccines currently approved for use in Australia are at protecting people against the effects of this variant. According to CDC there are no data available to assess the ability of sera from vaccinated persons or those with previous SARS-CoV-2 infection to neutralize the Omicron variant.

Common Signs & Symptoms Of Omicron: Symptoms for the new COVID Variant "Omicron" are given below.
Most common symptoms: Most common symptoms for the new COVID Variant "Omicron" are fever, cough, tiredness, loss of taste or smell. [61,62]
Less common symptoms: Less common symptoms for the new COVID Variant "Omicron" are sore throat, headache, aches, pains, diarrhoea, a rash on skin, discolouration of fingers or toes.red or irritated eyes.
Serious symptoms: Serious symptoms for the new COVID Variant "Omicron" are difficulty breathing or shortness of breath, loss of speech or mobility, or confusion or chest pain. [63,64]

Test Available for Detection Of Omicron: According to WHO RT-PCR tests can only confirm whether the person has an infection or not. They are not designed to determine which particular variant has infected the person. For that, a genome sequencing study has to be done. [65,66]

Diagnosis of Omicron: It is diagnosed with a medical history which includes any recent known exposure to COVID-19, and a physical exam to check for symptoms of COVID-19. Once the symptoms of the Omicron variant start appearing. "The symptoms of Omicron variant are mild, mostly asymptomatic. However, some cases have been reported where patients were suffering from fever, headache, nausea, body pain, etc. So, for patients who are experiencing any of the symptoms of Omicron, home isolation is a must, then for the conformation RT-PCR test carried out to diagnose the virus. Testing for variants requires genomic sequencing, which not all labs can do and it can be expensive. State health departments may run tests to help determine prevalence of a particular variant in that state, but it is unlikely individual patients would learn which variant they are infected with. Treatments for mild to moderate Omicron symptoms include [67,68]

- Home isolation
- Rest
- Drinking plenty of fluids
- Taking medicine used in previous covid variant treatment
- More severe cases may require hospitalization and treatments may include:

Corticosteroids

- Dexamethasone is preferred
- Prednisone, methylprednisolone, or hydrocortisone may be used if dexamethasone is not available

Immunotherapy

- Convalescent plasma
- Immunoglobulin products
- Interleukin inhibitors
- Interferons
- Kinase inhibitors
- Antiviral therapy with remdesivir
- Antithrombotic therapy: anticoagulants and antiplatelet therapy
- High-flow nasal cannula (HFNC) oxygen
- Ventilation

These are used for the treatment of Delta virus. It may be helpful in the case of Omicron variant.

Specifically according to the physician advice the person below 60age having mild symptoms, they can take Paracetamol, antibiotics, antiallergics and painkiller to treat fever and normal body pain.

- GSK, which is developing the Covid-19 antibody-based therapy with US partner Vir, said Preclinical data demonstrate sotrovimab(single monoclonal antibody and the drug works by binding to the spike protein on the outside of the Covid-19 virus) authorised in multiple countries around the world, retains activity against all tested variants of concern, including key mutations of Omicron. The tests are continuing to confirm the results against all of the Omicron mutations, with an update expected by the end of the year.[69]
- Pfizer developed a Covid treatment pill Paxlovid is effective against the omicron variant. The pill blocks an enzyme the virus needs to replicate. It is used in combination with HIV drug ritonavir, which slows the human metabolism to allow the Paxlovidto remain active in the body longer at a higher concentration to combat the virus. [70]
- Gilead has conducted an analysis of genetic information currently available for the Omicron variant and found no additional prevalent mutations in the viral RNA polymerase compared to previous SARS-CoV-2 variants. This suggests that Veklury® (remdesivir) will continue to be active against the Omicron variant and Gilead will conduct laboratory testing to confirm this analysis. [71,72]
- In Nov 30,2021A Food and Drug Administration advisory committee voted Tuesday in favor of recommending molnupiravir, a new antiviral pill made by the drug companies Merck and Ridgeback Biotherapeutics for treating COVID-19. [73]

According to the physician Monoclonal antibody cocktail and a oral antiviral drug (molnupiravir) is given to the patient above 60age. Monoclonal antibody cocktail is more useful in those patient having previous history of Delta variant infection.

Precaution For Omicron: The rising cases of Omicron are increasing the threat of the third wave of COVID-19 pandemic. People are advised to not compromise the necessary precautions and guidelines issued by both the Central and state governments.The most important thing we can do is to reduce the risk of exposure to the Omicron virus. To protect ourself and ourloved ones, make sure to:

- Wear a mask that covers your nose and mouth. Make sure that your hands are clean when you put on and remove your mask.Keep a physical distance of at least 1 metre from others.
- Avoid poorly ventilated or crowded spaces.
- Open windows to improve ventilation indoors.
- Wash your hands regularly.
- Avoid unnecessary travelling and party.
- When it's your turn, get vaccinated. WHO-approved COVID-19 vaccines are safe and effective.
- If there is any symptoms shows we can go for home quarantine, testing is mandatory for the confirmation & for safety purpose and consult with the physician without any fail.
- If the test report is positive, we should follow all the instructions given by physician, taking proper medication and therapy and follow all the covid protocols. [74]

Effect Of Omicron On Worldwide: The Omicron coronavirus variant has already led to panic in many western countries, with experts expressing concern about its impact on global economic recovery. panic has spread across the world after the discovery of the Omicron variant of coronavirus, which has been classified as a 'variant of concern' by the World Health Organisation (WHO). Top scientists recently issued a warning against the virus, citing its high transmissibility and low vaccine penetration across the globe. The new Omicron variant of COVID-19 may pose a fresh risk to the ongoing global recovery. However, preliminary evidence suggests the Omicron variant is expected to be less severe in India with the increasing pace of vaccination, said the Finance Ministry in its Monthly Economic Report for November 2021. India's economic recovery is expected to gain strength in the remaining quarters of the financial year on the back of upbeat market sentiments, rapid vaccination coverage, strong external demand, and continuous policy support by the Reserve Bank of India (RBI) and the government, according to the report. The country's real gross domestic product (GDP) in the second quarter of the current fiscal grew by 8.4 per cent year-on-

year, recovering more than 100 per cent of the pre-pandemic output in the corresponding quarter of the financial year 2019-20. India has not only caught up with its pre-pandemic output of the second quarter but is also expected to do so for the whole year, according to the finance ministry's report.

The outbreak of Omicron, the new variant in the Covid-19 pandemic, is a further challenge that concerns not only a difficult health situation or a complex socio-economic framework, but also the role of Education, regarding secondary school, vocational education training institutes, and university students around the world, without forgetting all those who live the community dimension of the campus and, therefore, with a specific risk of infection. The Global Students Forum, the democratic, independent, and worldwide union of students demands the attention of CSOs and NGOs, trade unions, national and international policymakers, to share an inclusive and long-term strategy that safeguards the education sector against possible closures and against restrictions that could be dangerous for people disadvantaged in society.[75,76,77,78]

Similarities & Difference of Omicron virus with Delta virus:

Omicron Virus - Delta virus

1. The Omicron variant was first detected in Botswana (on November 11) and three days later in South Africa, which has since then reported an increasing number of cases caused by the new Covid-19 variant. 2. Researchers found 43 mutations in the spike proteins of the Omicron variant as compared to Delta. 3. A recent study released today showed that the Covishield vaccine was effective against the deadly Delta variant. vaccines have been able to counter Delta. 4. Experts reveal that fatigue, joint pain, cold and headaches are four common signs of omicron that are different from that of the Delta variant.	1.The Delta variant was first identified in India in December 2020 as it swept rapidly through the country before reaching the United Kingdom and the United States. 2. Researchers found 18 mutations in the spike proteins of the Delta variant as compared to Omicron. 3. Scientists speculate that Omicron could render vaccines less effective. However, this is still being researched. 4. Experts reveal that loss of smell and taste, which were common signs of Delta, were hardly seen in the case of the Omicron.

CONCLUSION

Here is some brief information about new variant. A large no of Omicron new cases has been emerge in all over world.Virus is circulating widely and causing numerous infections, the likelihood of the virus mutating increases. The more opportunities a virus has to spread, the more opportunities it has to undergo changes. New variants like Omicron are a reminder that the COVID-19 pandemic is far from over. It is therefore essential that people take this seriously and get the vaccine when available to them for their good health and well being.

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RESEARCH ARTICLE

Design of a Reconfigurable Ultra-Wideband (UWB) Antenna for Pattern Diversity Applications

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ABSTRACT

Across configuration of an ultra-wideband (UWB) directional antenna for multidirectional array functions has been proposed in this article. The CPW (Coplanar Waveguide) UWB prototype was originally designed as a basic antenna to obtain a virtually unchanged radiation pattern on a circuit board. This basic antenna is coupled to a similar antenna in a four-element cross configuration to perform an array function. The proposed structure provides high isolation of the intermediate element of 10 dB or more with a voltage-to-wavelength ratio (VSWR) of less than 2 in the 7.5 GHz to 10.7 GHz frequency range. The transmission characteristics and operating frequency range of the proposed antenna are investigated. The simulated result shows that the proposed antenna is suitable for UWB beam applications. The simulated directional UWB antenna is united with alike antennas printed on both sides of the substrate in a cross-symmetrical arrangement to achieve the characteristics of a multidimensional radiation pattern. The transient array is designed so that the antenna elements do not come into direct contact with the antenna.

Keywords: Ultra-Wideband (UWB) antenna, voltage standing wave ratio (VSWR), S11 Plot, Radiation Pattern.

INTRODUCTION

Ultra-wideband (UWB) communication systems are attracting much attention from researchers and industries due to their advantages of more data rates, compact dimensions and low energy consumption [1]. In such an environment, it is necessary to use antenna induction technology as it can improve transmission quality by reducing the bleaching of multiple layers. Antenna array technology can be implemented in a variety of ways, such as spatial diversity, polarization and pattern diversity. It was difficult to convert the antenna into a reconfigurable device using a variety of methods to change the internal structure of the antenna. There are many factors to consider, such as achieving good return, good efficiency, stable radiation pattern and good impedance matching under all antenna operating

conditions [2]. In recent years, UWB antennas having various antenna patterns are attracting much attention. The antenna has several radiating elements side by side, and the radiation pattern of each element is partially oriented in a different direction. Most of these array antennas have a bidirectional or partially circulating radiation pattern, so their gain is low. Radiation from highly expanded UWBs can be blocked by installing directional UWB antennas such as those provided in additional locations (opposite) [1, 3, 4]. However, these antennas are large or have an unstable radiation pattern across the entire UWB. This paper presents a UWB antenna with high insulation of multidimensional type and intermediate elements. The proposed antenna set includes a small directional antenna for fast configuration UWBs. The simulation is performed with HFSS (High-Frequency Structure Simulator) software. The group delay and antenna gain are reported.

ANTENNA DESIGN METHODOLOGY

The basic design is a directional antenna with a circuit board with an asymmetric CPW fed. This antenna has a 50-ohm flat circular monopole fed with printed lines of a 1.6 mm thickness FR4 substrate with $\varepsilon_r = 4.4$ and $\tan\delta = 0.025$. A planar prototype monopole is being designed here. First, the CPW line ground plane is adjusted to a half ellipse shape with an offset "S" from the feed position to increase the bandwidth of the impedance. Then, in the CPW, one side of the semi-elliptical ground plane expands into an asymmetric curve that acts as a reflector for the round monopoly, as shown in figure 1.

The directional UWB antennas described previously are combined with similar antennas printed on both sides of the board in a symmetric horizontal arrangement to perform the multivariate array function. The horizontal arrangement is done in such a way that the antenna elements do not come into direct contact with each other. The slot is used to fix the cross-link. Since none of the antenna elements is in direct contact with each other, the connection between successive antenna elements is expected to be very low. Simulate the distribution of surface currents at different frequencies for the antenna components connected to the gate. You can see that the amount of surface current flowing from port 1 to the other antenna element is very small. This indicates high insulation between successive antenna elements. When considering the ports associated with different antenna elements separately, there is a similar current distribution at different frequencies with high isolation between the elements.

To characterize the proposed antenna, a prototype was designed with a 1.6 mm thickness FR4 substrate ($\varepsilon_r = 4.4$ and $\tan\delta = 0.025$), which is shown in Figure 1. Each antenna component is connected to a coaxial cable 50 ohm. The S parameter is simulated when one port is active and the other goes up to 50 ohms.

S-PARAMETER RESULT ANALYSIS

The simulated reflection coefficient parameter, i.e., S_{11}, starts with the antenna component connected to port 1, and the remaining terminals remain closed with a load of 50 Ohm. The same process applies to all other ports. The interconnect measurement (Sab) starts at ports 1 and 2 (a = 2 and b = 1) and the other ports end with a load of 50 ohms. This procedure is recurring for all combinations of a and b. The simulated S parameter 2 shown in the figure indicates that the proposed antenna configuration offers an ultra-wide impedance bandwidth (S11 <-10 dB) for broadband applications from 7.5 GHz to 10.7 GHz. As can be seen in Figure 2, the isolation between successive antenna elements exceeds 10 dB over the entire impedance bandwidth. The cause for the high insulation is that the antenna elements do not come into straight connection with each other. It has been detected that the reflection parameters are the same for all antenna elements due to structural symmetry. However, it is not comparable to the second set of other S-parameter, due to differences in the location of successive antenna elements.

A similar technique was used based on the proposed UWB antenna (if printed on the same side of the substrate). It has been observed that the maximum insulation achievable with this method is around 15 dB at low UWB

frequencies. The 3D gain polar plot of the simulation results is shown in figure 3. It can be seen that the maximum gain of the proposed antenna is 6.05dB.

For lossless data transmission, the UWB antenna must offer a constant group delay and a constant transfer function response across the entire impedance band. The simulated group delay versus frequency is shown in figure 4. Figure 4 shows that the variation in the group delay response and the transfer function is within 1 ns and 6.4 dB over the entire impedance bandwidth, respectively. This indicates that the distortion in the impedance band is very low.

CONCLUSIONS

A cross configuration of a directional UWB antenna to characterize changes in multidirectional radiation patterns has been analysed. The proposed configuration with the UWB also includes low microwave bands such as industrial scientific and medical (ISM) band. The characteristics of the simulated radiation pattern indicate that the proposed antenna exhibits a multidirectional radiation pattern with a pattern that maintains its orientation in the impedance range. If the simulated envelope correlation coefficient (ECC) value is less than 0.1 over the entire impedance range, the proposed antenna shows good diversity performance. The group delay and transfer response measured with fluctuations across the entire impedance band within 1 ns and 10 dB, respectively, indicate that the proposed structure exhibits minimal transmission distortion. The small deviation in gain and high antenna efficiency means that the proposed antenna configuration can be used for a variety of UWB beam applications. The goal of this proposed work is to bring innovations into antenna design.

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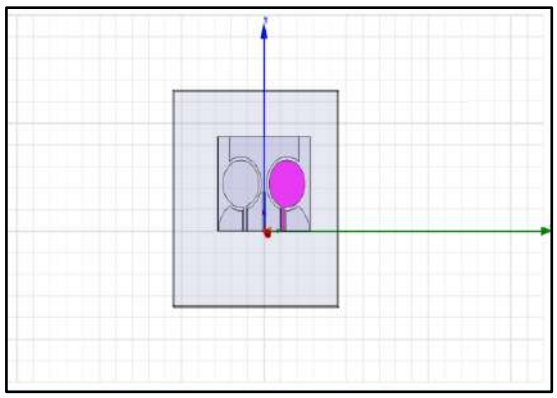

Figure 1. Proposed antenna design using HFSS software

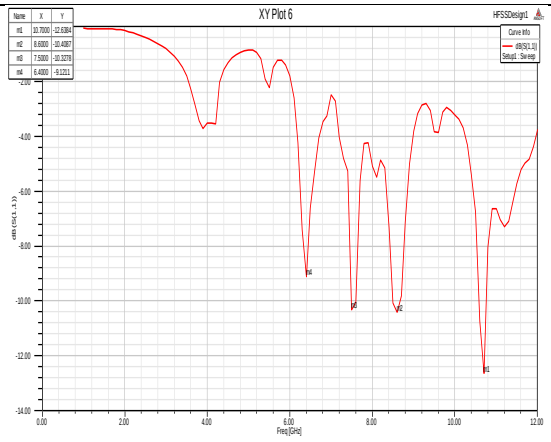

Figure 2. Simulated S_{11} Vs frequency plot

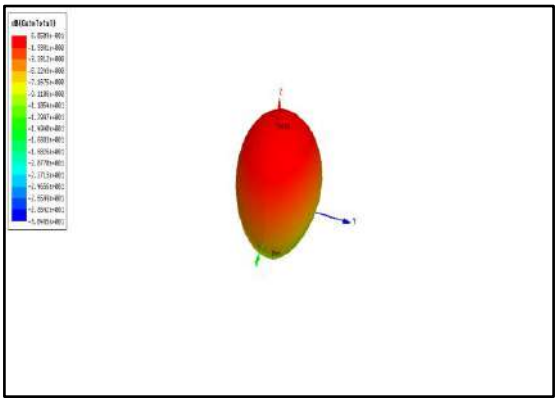

Figure 3. 3D polar plot

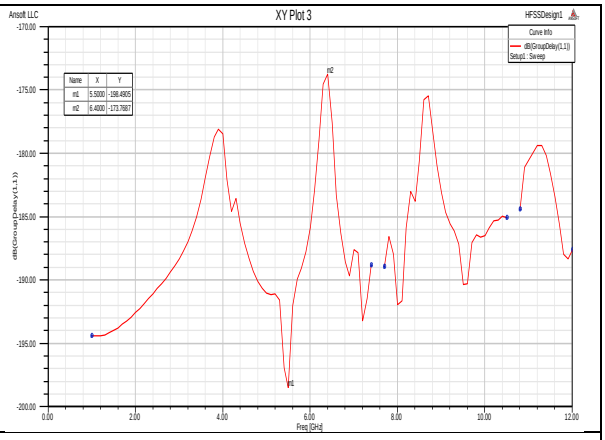

Figure 4. Simulated group delay Vs frequency plot

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RESEARCH ARTICLE

Effect of Selected Hydrophilic Polymers on the *In vitro* Dissolution Profile of Aceclofenac Crystals

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ABSTRACT

The objective of the present work was to investigate the effect of various hydrophilic polymers like hydroxypropylmethyl cellulose, methyl cellulose, carboxymethyl cellulose and poly vinyl alcohol on the *in vitro* dissolution property of Aceclofenac-crystal products produced from ethanol-water solution. Drug-crystal particles were produced by solvent-change technique in presence of polymeric solution. Results showed that in presence of polymers; crystal yield percentage was higher than in case of pure drug crystal (absence of polymer). A higher % of cumulative drug release was reported for the crystal formulation than plain Aceclofenac. Further *in vivo* studies are warranted before technology transfer of the formulation for its industrial scale production.

Keywords: Aceclofenac; Controlled crystallization; hydrophilic polymers; *In vitro* dissolution, Industry scale, Good health.

INTRODUCTION

An enhancement of dissolution rate for poorly water soluble drugs is the need of the hour in the formulation design of orally administered dosage forms to produce desired onset of action. Controlled crystallization of low aqueous soluble drugs from solutions in presence of hydrophilic polymer(s) is an emerging strategy to increase their solubility and dissolution rate[1]. Though several drug delivery techniques such as solid dispersion, salt forms, multiple emulsion, complexation etc. have been reported to improve the solubility and dissolution rate of poorly soluble drugs, crystallization method has been evolved as a simple, effective and industrially viable technique for this purpose [2]. Manipulation of crystallization process through the aqueous polymeric solution is comparatively less explored but a largely promising area of research in drug delivery. Crystalline products can be produced by

using several conventional techniques including solvent evaporation, pH change, thermal treatment, vapor diffusion, growth in presence of additives (surfactants/polymers) etc [3]. Among these, crystallization in presence of polymeric solution is being investigated widely to improve the solubility and dissolution rate of drug products. Presence of appropriate polymer(s) in desired quantity may assist in maintaining super saturation level of drug after dispersion into vehicle [4, 5]. Side by side polymers can also modify viscosity of the medium and affect nucleation phase during crystal formation, which results in alternation of polymorphic forms or crystal habits. Modification of crystal forms leads to amorphysation in the sample, which in turn leads to increased solubility and oral bioavailability [5].

Aceclofenac (ACE) is a non steroidal anti inflammatory drug and has been commonly recommended in the treatment of arthritis (rheumatoid/osteoarthritis/gout), spondylitis, inflammation, fever etc [6]. Its profound analgesic effect is mostly related to the inhibition of the enzyme cyclooxygenase-2[7]. However, being a BCS class II type drug, the main problem associated with its oral administration is the extremely low solubility in aqueous media (0.09 mg/ml) [6]. Thus, its dissolution in the gastrointestinal fluid is the major rate-limiting step for the absorption of the drug to achieve prompt onset of action. Several advanced formulation techniques have been reported to improve the solubility and bioavailability of ACE [8-11]. In a recent study, Yuliandra *et al*., 2018 reported the cocrystal formulation of ibuprofen with nicotinamide (as conformer) for improved solubility and *in vivo* analgesic activity. The cocrystal form of Ibuprofen as reported showed significant increase in solubility as compared to the physical mixture of drug/coformer and pure ibuprofen [12]. In another study by Hussain et al. 2018, solubility and dissolution properties of ibuprofen was found to be increased by co-milling with different polymeric excipients. As per the report, co-milling of ibuprofen with the polymer (Hydroxymethylpropyl cellulose) improved the kinetic solubility and dissolution rate of ibuprofen up to 4 fold than pure ibuprofen [13]. However; no such studies have reported the effect of different hydrophilic polymers on the physicochemical properties or dissolution rate of ACE crystals.

Hence, the present work was intended to study the effect of some selected hydrophilic polymers viz. hydroxypropylmethyl cellulose (HPMC), methyl cellulose (MC), carboxy methyl cellulose (CMC) and poly vinyl alcohol (PVA) on the physicochemical behavior and dissolution profile of ACE crystal products. Aceclofenac crystals were produced by controlled crystallization method using anti-solvent technique in presence of aqueous polymeric solution and evaluated for physicochemical and *in vitro* dissolution properties. This particular work to the best of our knowledge has not been reported so far.

Experimental

Materials

ACE was received as a free sample from Tejani life care, Cuttack, India. HPMC, CMC, MC and PVA were purchased from Merck Private limited, Mumbai, India. All other types of chemicals/solvents used during the experiment were of analytical grade.

Methods of Preparation

Briefly, about 2 g of ACE was taken in a beaker and was dissolved in ethanol (100 gm). The mixture was then poured inside a 1 L crystallization vessel with continuous agitation at a speed of 100 rev min^{-1} and maintained at 50 °C. Then the selected polymer at a low concentration (0.5 % w/w) was dispersed in 600 ml of water The prepared polymeric solution was then added slowly to the above drug solution (3.3 ml min^{-1}) [14]. Following this, simultaneous cooling was also applied to the above dispersion system (50 °C down to 10 °C) at a rate of 0.22 °C min^{-1} through an external probe. Four such batches were prepared separately with the above four polymers (viz. HPMC, MC, CMC, PVA) at constant drug-polymer concentrations.

Characterizations

Crystal yield

The percent crystal yield was evaluated from the weight expressed as the % of ACE dissolved initially in 50 ml of ethyl alcohol during first step of preparation to the amount of crystal products recovered at the end.

In vitro Dissolution Study

In vitro dissolution study was carried out using USP paddle type II dissolution apparatus (Dissolution tester (USP) DS8000, Labindia). For the study, double distilled water (at 37 °C) was used as the dissolution medium. Briefly, 100 mg of ACE and experimental crystal products (equivalent to ACE 100 mg) were placed in the above dissolution vessel (900 ml capacity) [17]. The samples were allowed to set at the bottom before rotation of the paddle (50 rpm). The temperature was maintained at 37 °C ± 0.5 °C throughout the experiment. The study was conducted for 2h. About 10 ml of samples were withdrawn from the dissolution chamber at regular time intervals (10, 20, 30, 45, 60, 75, 90, 120 min) through a syringe fitted with a membrane filter (0.25 µm) with simultaneous replenishment of fresh release medium. The collected samples followed by suitable dilutions were analyzed at 275 nm using a UV-Visible spectrophotometer (Labindia) against double distilled water as blank [15]. The studies were carried out in triplicate (N=3), and the mean values of cumulative drug release (%) were obtained.

RESULTS AND DISCUSSIONS

The study mainly focuses to understand the crystallization behavior and modification in dissolution profile of ACE crystal products in presence of hydrophilic polymers. Here ACE crystals were generated by using anti-solvent approach. Ethanol was used as the main solvent to solubilize ACE, where as aqueous solution of polymer was used as the anti-solvent. Polymers, as discussed previously tend to prolong the super saturation process and increase the viscosity of the medium to induce controlled crystallization. Total five sets of crystal product batches were reported, one for the pure re-crystallized drug crystal from ethanol (without any polymers), and rest four sets were in presence of the selected polymers (Table 1). The amount of polymers and drug were kept constant for each batch to compare the effects of selected polymer on the crystal property as well as dissolution behavior of ACE.

Percentage (%) Yield

Results showed that yield % of ACE crystal was affected by the presence of polymers (Table 1). Among various polymers, HPMC resulted highest crystal yield (95.51%). In case of pure ACE crystals (without polymers), the yield was 80.52%. Presence of polymers clearly affected the crystallization process as depicted from the results as the overall yield % of crystal products increased in presence of polymers than without polymer.

Dissolution of Drug

Drug dissolution is the most important evaluation parameter of the recrystallized products. The result of dissolution data is inevitable to establish *in vitro-in vivo* correlation, which is again essential for clinical translation of the formulations from bench to bed side. A higher dissolution rate signifies higher rate of absorption, faster onset of action along with increased bioavailability.[19,20] In the present work, in vitro dissolution study of pure drug, drug crystal and polymer treated crystal products were carried out in double distilled water at 37 ± 0.5 °C in USP type II dissolution apparatus (Figure 1). In view of the very low solubility nature of ACE in aqueous medium, double distilled water was used as the release medium during the study. Similar reports for the use of water as release medium for poorly soluble drugs have already been reported. From the data, it was observed that dissolution rate of all experimental polymer treated crystal products was higher than that of plain ACE and ACE pure crystals during 120 min experimental study period. Clearly, presence of polymers during crystallization affected the dissolution profile of ACE. Further, among the four selected polymers, HPMC improved the drug dissolution to the extent (95%) as compared to the other polymers. The order of dissolution was observed as $ACE<ACE^{0}<ACE^{1}<ACE^{2}<ACE^{3}<ACE^{4}$. Reduced crystalline intensity of ACE to the maximum extent in presence of HPMC could result in maximum dissolution of drug and the result was also supported by XRD and SEM data. A significant improvement in dissolution of ACE^{4} would be helpful for further *in vivo* studies to gather data for its future clinical translation.

CONCLUSIONS

The work investigated the effect of hydrophilic polymers on the crystallization behavior and dissolution profile of ACE. In presence of polymers, the crystal yield % was increased, probably due to interference of polymers during nucleation phase or in attaining supersaturaion during crystal formation. A significant improvement in rate of dissolution was reported for the experimental ACE crystals produced in presence of polymers than the free ACE or pure ACE crystal. For pure ACE, about 33.5% cumulative drug This study overall reported that presence of inert hydrophilic polymers could effectively enhance the dissolution rate of ACE. Further *in vitro* and *in vivo* studies are hereby warranted to establish the optimized drug crystal for its future technology transfer at industrial scale.

ACKNOWLEDGEMENT

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Conflicts of Interest

The authors of the article have no conflicts of interest to declare.

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Table 1 Formulation of experimental Aceclofenac rerystallized from aqueous polymeric solution

Formulation code	Polymer	Polymer concentration (% w/w)	% yield
ACE^0	None	--	80.52 ± 0.644
ACE^1	CMC	0.5	91.95 ± 0.818
ACE^2	PVA	0.5	86.45 ± 0.708
ACE^3	MC	0.5	88.38 ± 1.310
ACE^4	HPMC	0.5	95.51 ± 2.046

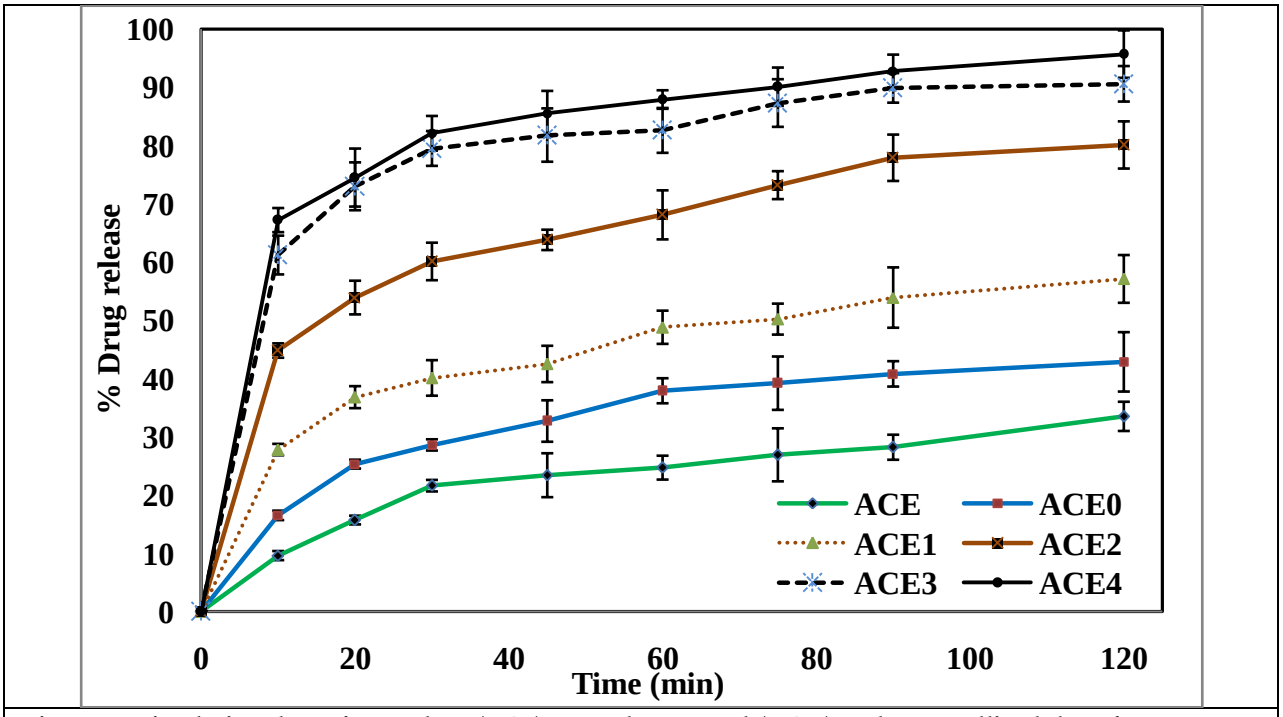

Figure 1: Dissolution data of pure drug (ACE), pure drug crystal (ACE^0) and recrystallized drug from aqueous polymeric solution (ACE^1, ACE^2, ACE^3 and ACE^4) in double distilled water for 120 min. All set of experiments were performed in triplicate. Data show mean ± SD (n =3). Error bars indicate standard deviation values

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RESEARCH ARTICLE

Adsorption of Copper Ion by Graphene Oxide / Cellulose Hydrogel Prepared from NaOH / Urea Aqueous Solution

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ABSTRACT

By taking advantage of cellulose, graphene oxide (GO), and the process for cross linking using glutaraldehyde, we propose a simple and novel method to prepare GO/cellulose hydrogel with good potential to adsorb metal ions. GO nano sheets containing carboxyl and hydroxyl groups were introduced into the surface of the cellulose hydrogel with retention of the gel structure and its nanoporous property. Due to the introduction of GO, the GO/cellulose composite hydrogels exhibited good compressive strength. Adsorption capacity of Cu^{2+} significantly increases with an increase in the GO/cellulose ratio and GO/cellulose hydrogel showed high adsorption rates. The calculated adsorption capacities at equilibrium (q^{cal}_e) for GO/cellulose hydrogel (GO:cellulose = 20:100 in weight) was up to 94.34 $mg.g^{-1}$, which was much higher than that of the pristine cellulose hydrogels. GO/cellulose hydrogel exhibited high efficient regeneration and metal ion recovery, and high adsorption capacity for Cu^{2+} ion for water sustainability.

Keywords: cellulose, graphene oxide (GO), crosslinking, glutaraldehyde, Adsorption, hydrogels, sustainability.

INTRODUCTION

Due to the rapid modernization and industrialization, the effect of heavy metal ions to the environment is a particular concern worldwide. Heavy metals are among the most common pollutants found in wastewater and can be gathered in the environment and living tissues, causing various diseases and disordering of living organisms even at a trace level. Due to the discharge of large amounts of metal-contaminated wastewater, industries bearing heavy

metals, such as Cd, Cr, Cu, Ni, As, Pb , and Zn, are the most hazardous among the chemical-intensive industries because of their high solubility[1]. Particular focus is given to innovative physico-chemical removal processes such as; adsorption on new adsorbents, membrane filtration, electrodialysis, and photocatalysis. Application of polymeric membranes for the adsorption of hazardous pollutants may lead to the development of next generation reusable and portable water purification appliances. Adsorption process being very simple, economical ,effective and versatile has become most prefered method for removal of toxic contaminants from wastewater. Bioadsorption is considered to be a potential alternative to conventional technologies for the adsorption of metal ions from aqueous solutions. A great deal of attention has been diverted toward the production of bioadsorbents from renewable resources, such as cellulose, starch, lignin, and agricultural wastes. These bioabsorbents have many advantages over conventional adsorbents, such as low cost, are biodegradable, eco-friendly, and highly efficient [2].Especially, the hydrogels obtained from cellulose have spurred great interest in the adsorption of heavy metal ions from aqueous solutions, because of their particular physicochemical properties, such as the facility of the incorporation of different chelating groups into the polymeric networks, the internal porous structure, are eco-friendly, cost-effective, and have a high specific surface area [3]. The new mixture solvent of NaOH/urea aqueous systems makes it easy to prepare cellulose-based hydrogel have wide application in dye removal, adhesion, and ion adsorption [4,5].This solvent has been suggested as an environmentally friendly system [6]. Nevertheless, most of the hydrogels suffer from a lack of adsorption capacity and mechanical performance. The poor adsorption and mechanical property of hydrogel has limited its further industrial applications [7].GO is an extremely oxidative form of graphene acquired by graphite chemical exfoliation [8]. There are adequately oxygen having functional groups in its graphitic back: carbonyl and at the layer ends and hydroxyl and epoxy groups on the base plane [9],[10]. Similar to graphene, GO may also be used as an adsorbent due to its big theoretical surface area, high water solubility and oxygen containing surface functionalities [11], [12]. For instance, it has been employed for efficient removal of potentially toxic elements [13] from contaminated aqueous media. The oxygen containing groups allow for binding and positively charged organic molecules via electrostatic interaction and coordination [14] The sorption features of rGO have also been considered and showed to be very real low cost water treatment materials 15], [16], [17], [18].However, despite its unique properties, graphene forms irreparable collections or even rolls to form graphite via π–π stacking and van der Waals interactions; if the layers are not well divided from each other, thereby, limiting its application in the area of ecological preservation [19],[20],[21]. The aggregation of graphene layers can impede the rapid mass transport, reduce the specific surface area and impact the material performance [22]. For GO, it has frail bonding affinity for anionic molecules due to robust electrostatic repulsion among them. These drawbacks of graphene may be overwhelmed by non-covalent or covalent functionalization with dissimilar compounds and other molecules [23], which augments their limit of detection, selectivity and sensitivity, thereby, opening up new chances to further investigate the possible applications of these compounds in the industrial wastewater treatment [24],[25].Besides, different nanocomposites based on graphene (rGO and GO) have been effectively produced and lengthily studied as sorbents for water treatment purposes [26],[27],[28],[29],[30].By taking advantage of cellulose, graphene oxide(GO),and the process for cross linking using glutar aldehyde ,we propose a simple and novel method to prepare GO/cellulose hydrogel with good potential to adsorb metal ions from industrial waste discharge stream leading to clean water and sanitation

MATERIALS AND METHODS

Materials

Cellulose with DP of 385 (cotton linter pulp) was supplied by sigma aldrich Ltd. The α-cellulose content in cotton linter pulp was more than 95%. Length and width of cellulose fiber were measured from 362 to 619 μm and 18 to 36 μm, respectively. All cellulose samples were shredded into pieces and distributed, and vacuum dried at 60 ˚C for 24 h to remove adsorbed water before use. All chemicals of analytical grade were obtained from sigma and pallav chemicals and used without further purification. The standard solutions (1000 μg/mL) of Zn (II), Fe (III), and Pb (II) were collected from different industrial water. The graphene oxide is purchased from Shilpent Enterprises.

Preparation of GO / Cellulose Hydrogel

A solution of 4.0 wt % cellulose in NaOH/urea aqueous solution was prepared according to the previous work [63]. GO was dispersed into the 7.0 wt % NaOH/12.0 wt % urea aqueous solution precooled to ´12.6 ˝C for further ultra-sonication for 1 h. Cellulose (2 g) was added in the suspension (50 mL) and stirred for 15 min at 5000 rpm. Then, 6 mL glutaraldehyde , as a crosslinking agent, was added drop wise to the GO/cellulose mixture. After completion of glutaraldehyde feeding, the resultant mix Shiptures were stirred at 25 ˝C for 30 min to obtain a homogeneous solution, and then kept at 25 ˚C for 48 h in a water bath to transform into hydrogels. Finally, the crosslinked hydrogels were immersed in water for three days to remove any remaining residue. A series of GO/cellulose hydrogels were obtained with various GO weight contents (GO:cellulose = *x*:100, where *x* = 2.5, 5, 10, 20, and 30). The resultant hydrogels were labeled as GO(*x*)/cellulose(100).

Characterizations

Fourier transform infrared (FTIR) spectra of the dried hydrogels were recorded with a Thermo Scientific Nicolet iN 10 FTIR Microscopy instrument equipped with a liquid nitrogen-cooled mercury-cadmium-teluride (MCT) detector. The scan range was 600–4000 cm^{-1}, and the distinguishability was 2 cm^{-1}. X-ray diffractograms were collected on an XRD-6000 instrument with an incident wavelength of 1.54 Å (Cu Kα radiation) and a detector at a scanning rate of 1 min^{-1} over the 2θ range, from 5^0 to 45^0. Cellulose hydrogels were weighed (M_h) and then dried at 105 ˚C to a constant weight. The dried sample was cooled down in a desiccator to room temperature and weighed (M_d). The water content (W_c) can be calculated as:

$$W_c = 100 - (M_d/M_h)*100 \quad (5)$$

The compressive test was performed on cellulose hydrogels at a rate of 5 mm¨min^{-1} by a CMT6503 Test Machine. The un dried hydrogel samples were cylindrical hydrogel 5.0 mm in diameter and 5.0 mm in thickness.

The Brunauer-Emmett-Teller (BET) was measured with a Tristar II 3020 instrument using the adsorption of N_2 at the temperature of liquid nitrogen. Prior to measuring, all of the samples were degassed at 393 K for 16 h and finally out gassed to 10^{-3} Torr. All of the samples were tested three times and the the average value was used. The morphologies of hydrogels were examined using scanning electron microscope (SEM) instrument. All hydrogel samples were immersed in distilled water at room temperature and allowed to swell to equilibrium, then fast-frozen in liquid nitrogen, and freeze-dried before SEM observation.

The method for determination of the point of zero charge (pH_{pzc}) was proposed by Balistrieri and Murray. Accordingly, to a series of well-stoppered 100 mL polyethylene bottles containing 40 mL of aqueous sodium nitrate solutions, different amounts of either 0.1 M HCl or 0.1 M NaOH solution were added in order for the pH of the samples. The bottles were filled to 50 mL with the aqueous sodium nitrate solutions. After 2 h of equilibration the pH values were noted as pH_i. A known amount of hydrogel was added in each bottle and left at 30 ˚C for 72 h with shaking. The pH values of the supernatant liquid in each bottle was noted as pH_f.

Adsorption Studies

Preparation of Cu^{2+} Solution

Cu^{2+} solutions (500 mg¨L^{-1}) were prepared by dissolving 1.9644 g solid $CuSO_4.5H_2O$ in 1000 mL of deionized (DI) water. The other solutions of different concentrations were adjusted by serial dilution.

Adsorption Procedures

Unless otherwise stated, batch experiments were carried out (at 298 K) by agitating a fixed mass of dry hydrogel (10 mg, the GO(20)/cellulose(100)) in 50 mL of metal solutions (initial Cu concentration of 200 mg/L, initial pH of solution 5.3) at 100 rpm for 120 min. The adsorbent/heavy metal ion solution mixtures were shaken in a thermostatic oscillator . The supernatant was transferred for determination of Cu^{2+} concentration by measuring the absorbance at 810 nm (Abs_{810}) [37] using a UV 2300 spectrophotometer . Preliminary experiments showed a linear correlation between Abs_{810} and Cu^{2+} concentration. All of the samples were tested three times and the the average adsorption

intensity was used to estimate Cu^{2+} concentrations. The equilibrium absorption amount of metal ions absorbed on the bioadsorbent, q_e(mg/g), was calculated using Equation (6):

$$q_e = (C_0 - C_e)V/m \quad (6)$$

where C_0 is the initial metal ions concentration (mg/L), $C_e$is the equilibrium metal ions concentration in solution (mg/L), m is the weight of the dried hydrogel used (g), and V is the volume of the metal ions solution (L). Kinetics experiments were carried out with different initial Cu(II) concentrations (50 and 100 mg/L), and the mixture was agitated continuously for 3–150 min. To study the effect of temperature, isothermal experiments were conducted at 293, 298, and 303 K. In this group of experiments, the initial Cu(II) concentration was varied from 50 to 400 mg/L.

Desorption and Reusability Behaviors of GO/Cellulose Hydrogel

After the attainment of equilibrium, the Cu^{2+}-loaded hydrogel was filtered from the solution and washed several times with distilled water to remove any unabsorbed Cu^{2+}. Thereafter, the bioadsorbents were immersed into 0.1 M HCl solution (50 mL) for 2 h to remove the adsorbed Cu^{2+} from the hydrogel and then regenerated with 0.1 M NaOH for 1 h. Finally, the hydrogel particles were thoroughly washed with deionized water to reach a neutral pH and again used in the adsorption experiment. The desorption efficiency was calculated according to Equation (7):

$$\%of desorption efficiency = \frac{amount of Cu\ \ (II) desorbed}{amount of Cu\ \ (II) absorbed} x100 \quad (7)$$

Adsorption of Other Hazardous Metals

Ten milligrams of dried hydrogel were soaked in 50 mL of 100 mg/L multi-metal (Zn + Fe + Pb) solutions. The mixtures were shaken in a thermostatic oscillator at 100 rpm for 120 min at 298 K. The heavy metal ion concentration of the supernatant liquid was determined using an inductively coupled plasma optical emission spectroscopy for Zn^{2+}, Fe^{3+}, and Pb^{2+}.

RESULTS AND DISCUSSION

FTIR analysis

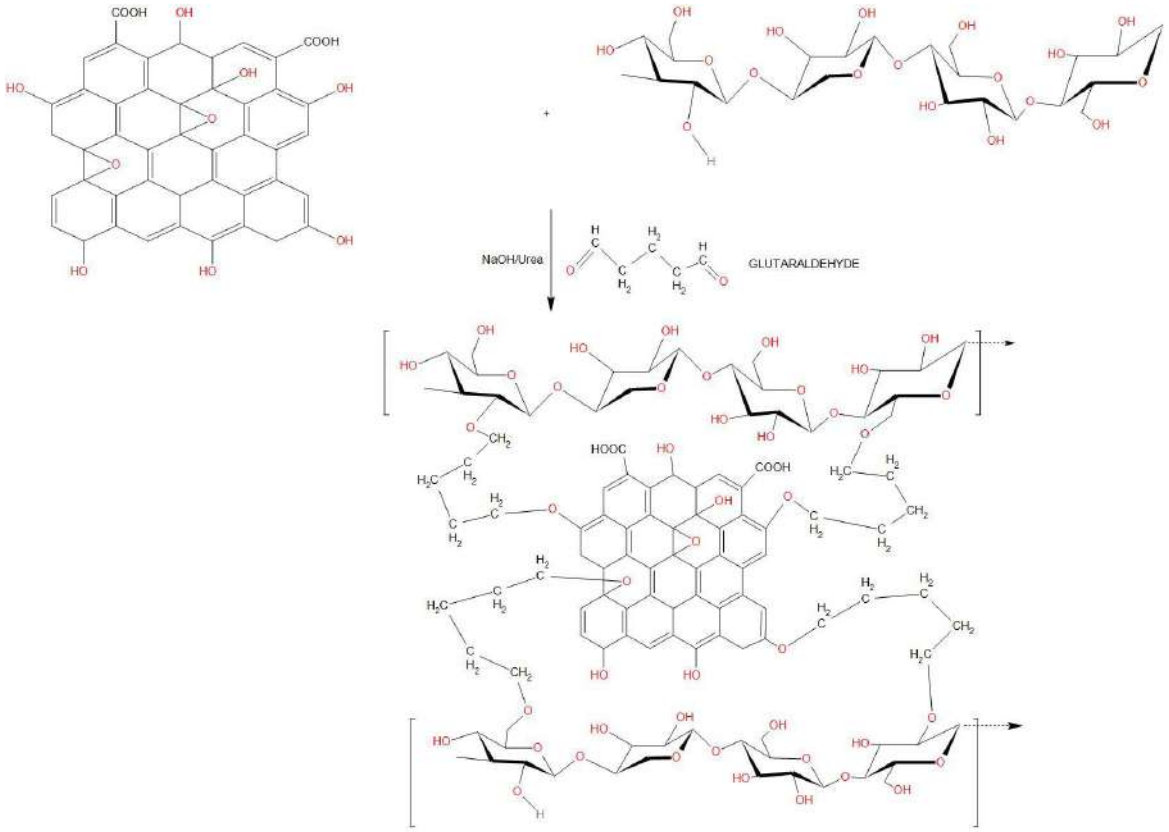
FTIR was used to expound the characteristics of GO, GO/cellulose hydrogel, cellulose hydrogel, and Cu(II)-loaded GO/cellulose hydrogel, as shown in Figure 1. GO exhibited a strong absorption band at 3381 cm^{-1}, which corresponds to a characteristic band of –OH. The absorption band at about 1596 cm^{-1} is assigned to the aromatic C=C, while the absorption bands at 1720, 1231, and 1041 cm^{-1} are assigned to the stretching vibrations of carboxy (C=O), epoxy (C–O–C), and alkoxy (C–O) groups, respectively [31]. In the spectrum of GO/cellulose, the absorption band attributed to epoxide groups disappeared, while the absorption intensity for alkoxy groups at 1041 cm^{-1} increased, suggesting the successful conversion of epoxide groups into alkoxy groups. The intensity of absorption peaks at 3381 cm^{-1} was diminished due to the decrease of hydroxyl groups when compared to that of GO. The results indicated that the crosslinking reaction of cellulose and GO in NaOH/urea aqueous solution with Glutaraldehyde occurred. The symmetric stretching vibration of CH_2 is visible at 2923 cm^{-1} and 2873 cm^{-1} (spectra b, c and d), in agreement with the literature data [32]. Compared with the cellulose hydrogel without GO (spectrum c), two distinct band observed at 1605 cm^{-1} and 1344 cm^{-1} in the GO/cellulose hydrogel (spectrum b) can be attributed to COO^- stretching and bending, respectively [33]. Here, we present evidence for the existence of the carboxyl groups of GO in the hydrogels. After copper ion adsorption on the GO/cellulose hydrogel (GO/cellulose hydrogel + Cu^{2+}, spectrum d), the absorption bands of COO^- groups at around 1605 cm^{-1} shift to 1579 cm^{-1}. This can be attributed to the formation of the coordinated COO^- and Cu^{2+} complexes [34]. The O–H band absorption peak was observed to shift to 3386 cm^{-1} when the GO/cellulose hydrogel is loaded with Cu^{2+}. It seems that this functional group participates in metal binding [35].

XRD analysis

To obtain information about the crystalline structure of the GO, cellulose hydrogel and the GO/cellulose hydrogel, the x-ray diffraction (XRD) patterns of these samples were measured and are shown in Figure 2. GO exhibits a characteristic diffraction peak at 2θ = 11.4˝, resulting from its (002) crystal planes [36]. The XRD pattern of GO contains a peak at around 41˝, which is related to the (100) plane of the graphite [37]. Cellulose hydrogel displays the diffraction peaks at 2θ = 20.1˝ and 22.5˝, which correspond to the (110) and (200) planes of cellulose II crystalline form, respectively. GO/cellulose hydrogel exhibits three distinct peaks at 2θ = 14.1˝, 20.1˝, and 22.5˝, which are assigned to the (110), (110), and (200) planes of crystalline form of cellulose II, respectively [38]. However, the peaks of GO/cellulose hydrogel moved from 12.1˝ to 14.1˝. The cross-linking reaction of Glutaraldehyde with GO and cellulose may be due to shrinkage of the (110) planes causing this peak to move to higher angles [39]. The results indicate that the structure of cellulose I was destroyed in aqueous NaOH/urea and transformed into cellulose II. In contrast, the GO/cellulose hydrogel generates only the characteristic peaks of cellulose with no characteristic peak of GO. These findings can be explained as the high dispersibility of the GO sheets in the GO/cellulose hydrogel due to the bond interactions between the cellulose molecules and the GO sheets, so that the periodic interlayer spacing between the GO sheets disappeared [40].

Reaction Mechanism

To sum up, the mechanism for cross-linking reaction of Glutaraldehyde with GO and cellulose in NaOH/urea solution is schematically illustrated in Figure 3. The hydroxyl groups of the cellulose were cross-linked covalently with epoxy and hydroxyl groups of the GO through nucleophilic attack of the alcoholate anion to form a monoethers of chloropropanediols and a new epoxide formed by chloride displacement, leading to the completion of the cross-linking .[41]



(Reaction scheme of interaction cellulose with graphene oxide and glutaraldehyde)

As can be seen in Table 1, the samples with different content of GO showed similar water content. The compressive modulus of the hydrogels increased to a maximum and then decreased, with the GO/cellulose ratios increasing from 2.5/100 to 30/100. At lower concentrations, this dependence of the compressive modulus on the content of GO is perhaps due to the chemical bond between the cellulose fibers and the surface of GO. However, GO also reduces macromolecular interactions which decrease the compressive strength . So the GO(5)/cellulose(100) hydrogel possessed the higher compressive modulus. The value is much higher than those of cellulose-alginate hydrogel (30.9 kPa) [42], pure cellulose hydrogel (48 kPa) and cellulose/poly(*N*-isopropylacrylamide) hydrogel (58 kPa) [43]. The GO/cellulose hydrogel, in general, has a large specific surface area. Furthermore, it can be seen that, with increasing GO content, the Brunauer-Emmett-Teller (BET) surface areas and pore volume of the samples resulted in an obvious enhancement. This indicated that the electrostatic repulsions caused by the ionic character of the carboxylate anions (COO^-) in GO had enlarged the space in the networks of hydrogels [41]. Compared with the GO(10)/cellulose(100) sample and the GO(30)/cellulose(100) sample, a notable reduction of the specific surface area, pore volume, and average pore size of GO(20)/cellulose(100) hydrogel was observed. One possible explanation was the formation of GO sheets on the surface and inner of GO(20)/cellulose(100) hydrogel, leading to the block of some pore structures [44]. Another possible explanation was the agglomeration of the graphene oxide sheets [45].The surface of GO/cellulose hydrogels showed smooth morphology, which also indicated that the cellulose was miscible with GO. As shown in Figure 3, there was a distinct common point of intersection at the ΔpH = 0 line at pH_i= 6.5, which was the $pH_{pzc}$of the GO/cellulose hydrogel. Hence, the hydrogel is positively charged at a pH below $pH_{pzc}$and negatively charged at a pH above pH_{pzc}. The above results suggest that the electrostatic attraction between metal ions and the hydrogel surface should increase with increasing solution pH [46].

Adsorption Measurements

The effect of GO/celluloses ratio on Cu^{2+} uptake is shown in Figure 4. The adsorption capacity of Cu^{2+} was 47.5 mg/g at a GO/cellulose ratio of 0:100, and then increased to 88.5 mg/g as the ratio increased to 30:100. The adsorbent has a heterogeneous distribution of GO on the surface. The amount of sorbate which is adsorbed per unit weight of adsorbent at a given solution concentration is not proportional to the surface area, indicating that the characteristics of the surfaces of the GO/cellulose hydrogels are different in each case. This phenomenon should be attributed to more oxygenous functional groups being incorporated into the hydrogel as the GO/celluloses ratio increases,which increase the surface complexation, electrostatic attraction, and ion-exchange capability of bioabsorbent [47]. One problem with GO(30)/cellulose(100) hydrogel is incomplete cross-linking, probably because of the high ratio of GO/ Glutaraldehyde. Thus, GO/cellulose hydrogel with a ratio of 20:100 was chosen in the following experiments. As shown in Figure 5, the experiments were carried out in the pH range 1.0–7.5. The adsorption capacities of Cu^{2+} increased as pH increased from 1.0 to 5.3. This is because the pH value affects the surface charge of the adsorbent. When the pH value increased, the negative charge of the adsorbent increased [48]. Above pH 5.3, the solution became turbid. Meanwhile, the GO/cellulose hydrogel displayed a sharp decrease in the uptake values when pH increased. The cause for the phenomenon could be the reduced solubility and precipitation of Cu^{2+} under alkaline condition [49]. Therefore, the optimum pH value for Cu^{2+} absorption onto GO/cellulose hydrogel was about 5.3. The effect of hydrogel dosage on the adsorption properties was investigated in the range 0.01–0.05 g, and the results are presented graphically in Figures 4,5 and 6. It was found that q_e decreases from 81 to 27.5 $mg^{\cdot}g^{-1}$ with an increase in adsorbent mass from 0.01 to 0.05 g. The reason for this phenomenon is attributed to the unsaturation of adsorption sites through the adsorption process. Another reason may be the particle interactions, such as aggregation, resulting from high adsorbent concentration. Such aggregation would lead to a decrease in the total surface area of the adsorbent [50].

Adsorption Kinetics Studies

The copper(II) adsorption capacities of the GO(20)/cellulose(100) hydrogel were measured as a function of contact time, and the results are shown on Figure 7. The adsorption capacities of Cu^{2+} increased rapidly at short time scale and the adsorption process attains equilibrium within 150 min, indicating that plenty of readily-accessible sites were available for a rapid adsorption [51]. Adsorption kinetic provided important information about the mechanism of Cu^{2+} adsorption onto GO/cellulose hydrogel, which was necessary to describe the adsorbate-adsorbent interactions.

The Lagergren's pseudo-first-order and pseudo-second-order models are the most commonly used models. The linear pseudo-first-order kinetic model (Equation (8)) and pseudo-second-order model (Equation (2)) are expressed by the following equations:

$$\ln (q_e - q_t) = \ln q_e - k_1 t \quad (8)$$

$$t/q = 1/k_2 q_e^2 + t/q_{e(2)}$$

where qt and qe are the amounts adsorbed ($mg¨g^{-1}$) at time t (min) and at adsorption equilibrium, respectively, k_1 (min^{-1}) is the kinetics rate constants for the pseudo-first-order model, and k_2 (g/mg/min) is the kinetics rate constants for the pseudo second-order model. The values of $\ln(q_e - q_t)$ obtained from the kinetics experimental data. The kinetic models are examined by linear plots of $\ln(q_e - q_t)$ against t and (t/q) against t, respectively. The boundary conditions are $q = 0$ at $t = 0$, and $q = q$ at $t = t$. Table 2lists the characteristic parameters and regression coefficients obtained from the first- and second-order kinetic models.

comparing the two kinetics models, the higher correlation coefficients (R^2 in Table 2) were obtained for the pseudo-second order kinetic model, By and the calculated data (q^{cal}_ein Table 2) from the pseudo-second-order kinetic model generally deviate less from the experimental data. These results indicate that the adsorption system is well-represented by the pseudo-second-order kinetic model, and the rate of occupation of adsorption sites is proportional to the square of the number of unoccupied binding sites [52]. Therefore, the adsorption of Cu^{2+} by bioadsorbent is dominated by a chemical adsorption process. The interaction may occur between the COO^- and the Cu^{2+} ions, which means that the adsorption mechanism of GO/cellulose hydrogel is ion exchange [53]. The calculated adsorption capacities at equilibrium (q^{cal}_e) for GO(20)/cellulose(100) hydrogel was 94.34 $mg¨g^{-1}$, which was much higher than that of pristine cellulose hydrogels [54]. The value is much higher than those of acrylic acid-grafted and acrylic acid/sodium humate-grafted bamboo cellulose nanofibers (46.53 and 45.38 mg/g, respectively) [55] and cellulose/chitosan composite microspheres (65.8 mg/g) [56].

Adsorption Isotherm Studies

The adsoption isotherms of the GO(20)/cellulose(100) hydrogel for Cu^{2+} ion are presented in Figure 8. Cu^{2+} ion uptakes of the GO/hydrogel cellulose increased linearly with increasing Cu^{2+} concentration, suggesting that the adsorption capacity was dependent on the amount of metal ions. To further understand the process, the adsorption data were subjected to Langmuir (Equation (9)) and Freundlich (Equation (10)) models for simulation. The Langmuir model is a widely-applied model based on the assumption of monolayer adsorption onto a surface containing a finite number of adsorption sites of uniform strategies of adsorption without transmigration of adsorbate in the plane of the surface [57]. The Freundlich model is derived by assuming an exponential decay energy distribution function inserted in the Langmuir equation with the amount adsorbed being the summation of adsorption on all sites with different bond energies [58].

$$(Ce / q_e) = (1 / Q_{Max} b) + (Ce / Q_{Max}) \quad (9)$$

$$\log q_e = \log K + (1 / n) \log C_e \quad (10)$$

where q_e(mg/g) is the amount of Cu^{2+} ion adsorbed at equilibrium, C_e(mg/L) is the concentration of Cu^{2+} ion, Q_{max}($mg¨g^{-1}$) and b (dm^3mg^{-1}) are the Langmuir equation parameters; k is the Freundlich isotherm constant ($L.mg^{-1}$), and n is the Freundlich factor.

The parameters of the simulation are all listed in Table 3. The correlation coefficients (R^2) of the linearized Langmuir equation are lower than that of the Freundlich equation. The GO/cellulose hydrogel was described better with the Freundlich model than with the Langmuir model, which reveals that the bioadsorbency to Cu^{2+} ions is mainly through parallel π–π stacking interactions and form multilayer adsorption. The presence of such heterogeneous adsorption sites may be the reason for the better applicability of the Freundlich isotherm [59]. Isotherms with $n > 1$

are classified as L-type isotherms reflecting a high affinity between adsorbate and adsorbent and is indicative of chemisorption [60].

Repeated use of Hydrogel and Adsorption of Other Hazardous Metals

The effect of five consecutive adsorption-desorption cycles on the efficiency of the adsorption of Cu^{2+} on GO(20)/cellulose(100) hydrogel was studied, and the results are presented in Figure 9. As shown in Figure 9, no noticeable losses were observed in the adsorption capacity or desorption efficiency of GO/cellulose hydrogel as the number of cycles increased. In 1 M HCL solution, the protons compete with metal ions for carboxyl groups, which are responsible for the easy desorption of metal ions. This, again, confirms that the main adsorption mechanism is ion exchange [1]. During the regeneration process with NaOH solution, COOH groups were converted to COO^- groups which exhibited stronger affinity to Cu^{2+} [60]. The present study further revealed the advantage of GO/cellulose hydrogel which allowed for excellent reusability. The adsorption measurement was also performed on Zn^{2+}, Fe^{3+} and Pb^{2+} ions (Figure 10). The $q_e$value was different for each ion and was in the order of $Fe^{3+} > Zn^{2+} > Pb^{2+}$. The GO/cellulose hydrogel sufficiently adsorbed all of the metals tested, suggesting that the GO/cellulose hydrogel is a general-purpose bioadsorbent.

CONCLUSION

A novel and easy method has been proposed to prepare cellulose / GO hydrogel with good adsorption of heavy metal ions from aqueous solutions. FTIR and XRD measurements indicated the existence of cross linking reaction between the GO and the cellulose matrix. The incorporation of GO increased the compressive strength of the GO/cellulose hydrogel and significantly improved their adsorption capacities for the metal ions. The adsorption capacity of Cu^{2+} increases with an increase in the GO/cellulose ratio, while the adsorption capacities decreased continuously with an increasing dosage of GO/cellulose hydrogel. The adsorption kinetics data could be well described by the pseudo-second-order model, and the adsorption process followed the Freundlich isotherm model. This study provided a highly efficient bioadsorbent for the removal of heavy metals from an aqueous solution.

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Table 1.Water content, compressive modulus, surface area, pore volume, and pore size of GO(*x*)/cellulose(100) hydrogels with *x* = 2.5, 5, 10, 20, and 30, respectively.

Sample	2.5	5	10	20	30
Water content (wt %)	92.7	90.3	94.1	92.5	93.5
Compressive modulus (kPa)	114	193	144	128	115
*S*BET ($m^2.g^{-1}$)	0.19	13.41	40.72	25.11	45.12
Pore volume ($cm^3.g^{-1}$)	0.0023	0.0575	0.1807	0.0048	0.1856
Pore size (nm)	3.11	7.49	7.08	5.15	6.73

Table 2.Comparison between the pseudo-first-order and pseudo-second order kinetic models for Cu^{2+} sorption onto GO(20)/cellulose(100) hydrogel.

C_0(mg.L^{-1})	Pseudo-First-Order Model			Pseudo-Second-Order Model		
	*q*cale (mg.g^{-1})	*k*1 (g.mg-1.min^{-1})	*R*2	*q*cale (mg.g^{-1})	*k*2 (g.mg^{-1}.min^{-1})	*R*2
50	16.44	0.0106	0.876	37.59	0.0023	0.991
200	46.92	0.0187	0.846	94.34	0.0009	0.998

Table 3. The parameters for Langmuir and Freundlich models for Cu^{2+} sorption onto GO(20) / cellulose(100) hydrogel.

T	Langmuir			Freundlich		
(K)	Q_{max}(mg¨g^{-1})	*b* (L¨mg^{-1})	*R*2	*k* (mg1´1/n¨L1/n¨g´1)	*n*	*R*2
293	138.888	0.014	0.9552	18.01	3.19	0.9703
298	384.615	0.001	0.9406	0.92	1.19	0.9982
303	192.308	0.004	0.8098	1.72	3.78	0.9633

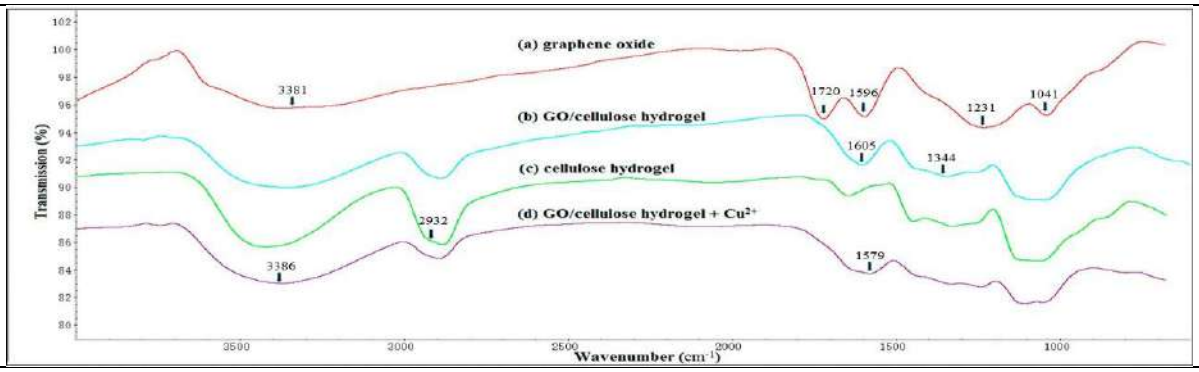

Figure 1. FTIR spectra of GO, GO/cellulose hydrogel, cellulose hydrogel, and Cu(II)-loaded GO/cellulose hydrogel.

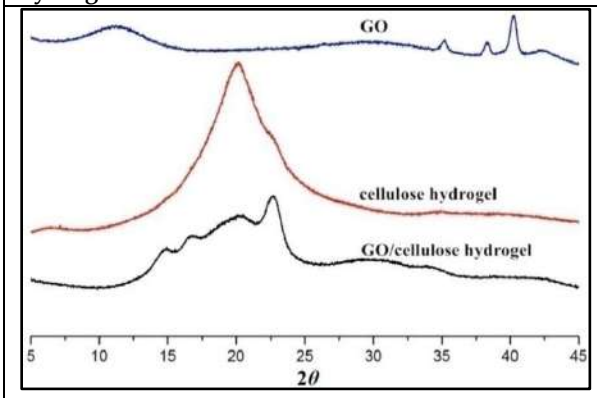

Figure 2. XRD patterns of GO, cellulose hydrogel, and GO(20)/cellulose(100) hydrogel.

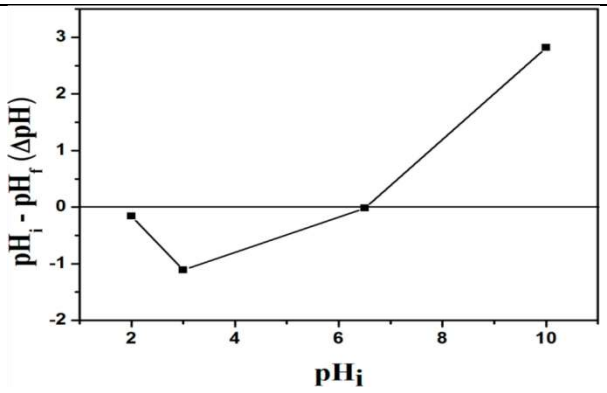

Figure 3. Point of zero charge of GO(20)/cellulose(100) hydrogel.

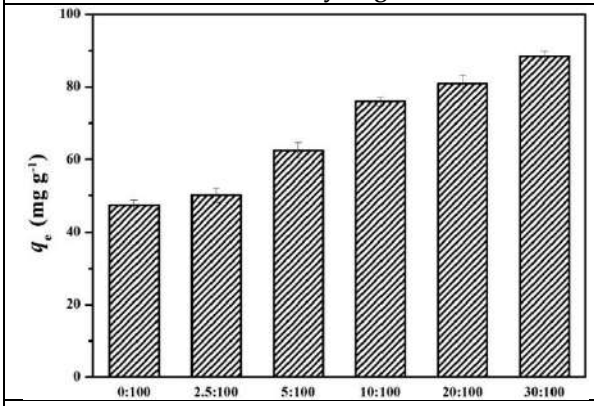

Figure 4.Effects of GO to cellulose ratios on Cu^{2+} ion adsorption on the hydrogel.

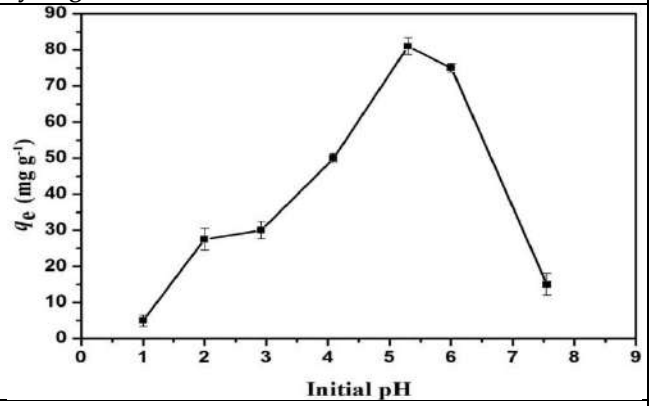

Figure 5.Effect of pH on the adsorption capacity. The error bars represent standard deviations based on three measurements.

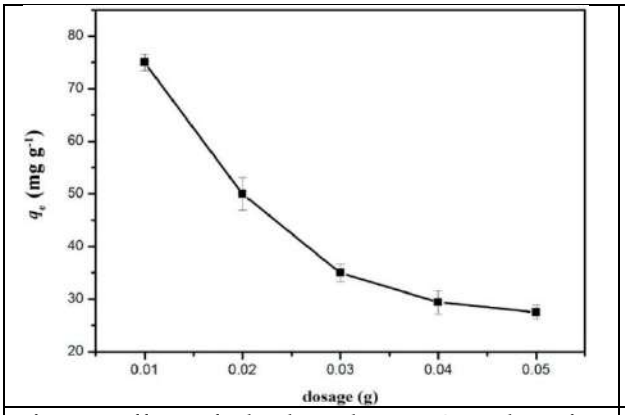

Figure 6.Effects of adsorbent dose on Cu^{2+} adsorption by the GO(20)/cellulose(100) hydrogel.

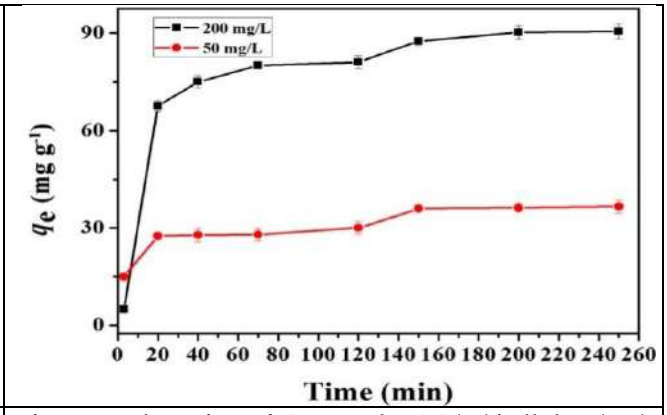

Figure 7.Adsorption of Cu^{2+} on the GO(20)/cellulose(100) hydrogel as a function of contact time.

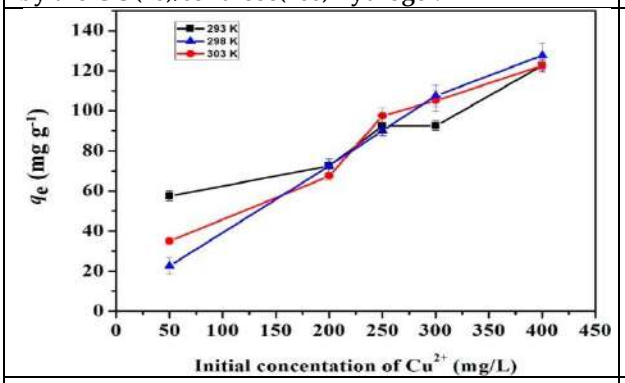

Figure 8.Adsorption of Cu^{2+} on the GO(20)/cellulose(100) hydrogel as a function of Cu^{2+} concentration.

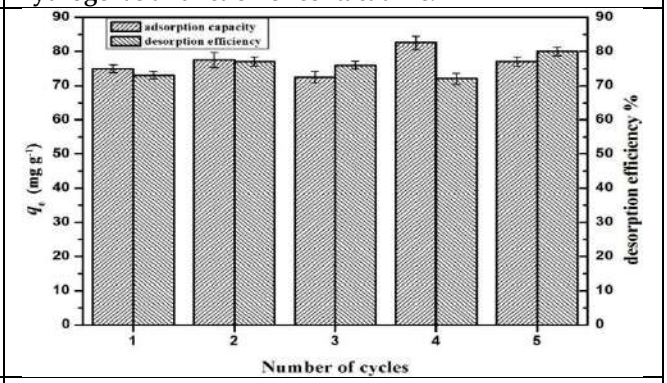

Figure 9.Effect of recycling bioadsorbents on Cu^{2+} adsorption (initial concentration 200 mg¨L^{-1}; initial pH of solution 5.3, temperature, 298 K; contact time, 120 min).

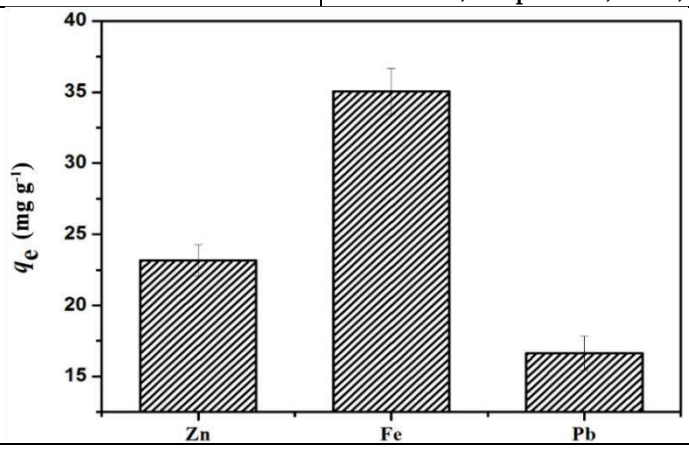

Figure 10.Adsorption amount of various metals on GO(20)/cellulose(100) hydrogels.

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RESEARCH ARTICLE

Studies of Navier- Stokes Equations in New Techniques

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ABSTRACT

An effort has been recently paid to derive and to better understand the Navier–Stokes (N–S) equation, and it is found that, although the N–S equation has been proven to be correct by numerous examples, some concepts and principles behind the equation may not be correct or consistent. In this paper we have introduced Navier stokes equations, Concept of boundary layer, Solution techniques. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure), and 11 (Sustainable cities and Communities).

Keywords: Blasius Flow, Navier stokes equations, prandtl boundary layer equation

INTRODUCTION

Navier Stokes Equations
(For incompressible fluids)

$$\frac{Du}{Dt} = \vec{g} - \frac{1}{\rho}\nabla p + \nabla^2 \vec{u}$$

where ρ = density of fluid
v = kinematic viscosity of fluid
p = static pressure
$\vec{u}$ = velocity field
$\vec{g}$ = body force per unit mass

$$\frac{D}{Dt} = \frac{\partial}{\partial t} + u\frac{\partial}{\partial x} + v\frac{\partial}{\partial y} + w\frac{\partial}{\partial z}$$ substantial derivative

Navier Stokes equations-features

- Elliptic partial differential equations.
- Boundary conditions required on entire boundary.
- Difficult to get analytical solutions for the general case
- Simplifying assumptions and/or approximations required.[1]

Concept of boundary layer-Application [2]

- Wherever fluid flows near a solid surface of another stationary fluid.
- Ex. Fluid flow around submerged bodies in pipes, in jets etc.
- Boundary layer entirely accounts for the effects of fluid viscosity.
- Primarily useful for calculating shear stresses on the surface of the solid body and thus the total drag force on it due to the flowing fluid.
- Ex. Estimation of drag force on an airplane, the body of a swimmer, on a racing car, in wind tunnel testing etc.
- Also useful for estimating other parameters such a s entrance length in pipe flow, momentum transfer due to jet etc.

Concept of boundary layer-Need

Away from solid boundaries effect of fluid viscosity negligible.
Navier stokes equations reduced to Euler equations[3]

$$\frac{D\bar{u}}{Dt} = \vec{g} - \frac{1}{\rho}\nabla p$$

$\vec{u} =$ Velocity fluid

$\vec{g} =$ body force per unit volume

ρ = density of fluid

P = static pressure

$\frac{D}{Dt}$ = substantial derivative

Euler's equation is of first order
Cannot satisfy both boundary conditions near solid surface.

$u_r = 0$ (no penetration condition)

$u_i = 0$ (no slip condition)

where $u_n =$ velocity component normal to solid surface

$u_r =$ velocity component tangential to solid surface

So it's a good approximation near the surface
On the surface of the solid boundary.
u = 0 where u = component of velocity parallel to free stream velocity.
In the free steam:
u =U, where U = free stream velocity.
Boundary layer thickness defined as the thickness over the solid surface over which u varies from 0 to 99U.

Physical significance of the terms:
Continuity equations:[4,5]

$$\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0$$

- The continuity equation expresses the law of mass conservation for an incompressible fluid.

- The LHS is the divergence (in 2-D) of the velocity field which signifiesthe rate of mass production at a given point in the flow field.
- Since n the flow field considered there are no sources of mass production, it is identically equal to zero throughout the field.

y-momentum equation:

$$\frac{\partial p}{\partial y} = 0$$

Expresses the fact that there is no pressure variation along the direction normal to the solid surface.
This means that the pressure at any location x in the boundary layer is same as that in the outer inviscid region.
The variation of pressure in the inviscid region can be calculated by solving the Euler equations for the external flow field and the same can be used inside the boundary layer.
Thus pressure is not an unknown quantity in the boundary layer equations. It is simply imposed on it by the external inviscid flow.[6,7,8]

Illustration: Blasius Flow Governing equations

$$\frac{\partial u}{\partial x} + \frac{\partial v}{\partial y} = 0$$

$$\frac{\partial p}{\partial y} = 0$$

$$\frac{1}{\rho}\frac{dp}{dx} = -U_\infty \frac{dU_\infty}{dx} = 0$$

$$\Rightarrow u\frac{\partial u}{\partial x} + v\frac{\partial u}{\partial y} = v\frac{\partial^2 u}{\partial y^2}$$

Boundary conditions:
At y = 0, u = v = 0

At $y = \infty, u = U_\infty$

Eliminate continuity equation using stream function

$$u = \frac{\partial \psi}{\partial y}, v = \frac{\partial \psi}{kdx}$$

The boundary layer equation transforms to:

$$\frac{\partial \psi}{\partial y}\frac{\partial^2 \psi}{\partial x \partial y} - \frac{\partial \psi}{\partial x}\frac{\partial^2 \psi}{\partial y^2} = v\frac{\partial^2 \psi}{\partial y^2} \text{.....(*)}$$

$$\frac{\partial \psi}{\partial y} = U_\infty \text{ as } y \to \infty$$

$$\frac{\partial \psi}{\partial x} = 0, \frac{\partial \psi}{\partial y} = 0 \text{ at } y = 0$$

In accordance with the law of similarity we define a similarity variable

$\eta = Ayx^2$ so that $\psi = \psi(x, y) = \psi(\eta, x)$

Using boundary condition

as $y \to \infty, u \to U_\infty$

$$\Rightarrow u(x,\infty) = \left.\frac{\partial \psi}{\partial y}\right|_{y\to\infty} = \left.\frac{\partial \psi}{\partial \eta}\right|_{\eta\to\infty} \frac{\partial \eta}{\partial y} = U_\infty$$

$$\Rightarrow Ax^2 \left.\frac{\partial \psi}{\partial \eta}\right|_{\eta\to\infty} = U_\infty$$

RHS is constant, so to make LHS constant ψ must be of the form:

$$\psi = Bx^* f(\eta) \Rightarrow u(x,\infty) = ABf(\infty) = U_\infty$$

Let $AB = U_\infty$

$$\therefore f(\infty) = 1$$

Using second boundary condition:

$$u(x,0) = \left.\frac{\partial \psi}{\partial y}\right|_{x=0} = ABf'(\eta)\big|_{\eta=0} = 0 \Rightarrow f'(0) = 0$$

Using third boundary condition:

$$v(x,0) = -\left.\frac{\partial \psi}{\partial x}\right|_{x=0} = -Bbx^{b-1}(\eta f' - f)\big|_{\eta=0} = 0 \Rightarrow f(0) = 0$$

Substitute ψ in forms of η in the differential equation (.)

Choose the free constants A, B & b such that x & y do not appear in the final equation resulting in:

$$A = \sqrt{\frac{U_\infty}{v}}, B = \sqrt{U_\infty v} \ \& \ b = -\frac{1}{2}$$

Giving:

$$f(\eta) f'(\eta) + 2f''(\eta) = 0$$

With the boundary conditions:

$$f(0) = f'(0) = 0 \ \& \ f'(\infty) = 1$$

$$\eta = y\sqrt{\frac{U_\infty}{vx}} = \frac{y}{x}\mathrm{Re}, \ \psi\sqrt{vU_\infty} f(\eta)$$

$$u = \frac{\partial \psi}{\partial y} = U_\infty f'(\eta), \ v = -\frac{\partial \upsilon}{\partial x} = \frac{1}{2}\sqrt{\frac{vU_\infty}{x}}(\eta f' - f)$$

$$r_w = \mu \left.\frac{\partial u}{\partial y}\right|_{y=0} = \mu U_\infty f'(\eta) \left.\frac{\partial \eta}{\partial y}\right|_{v=\infty} = \mu U_\infty \sqrt{\frac{U_\infty}{vx}} f'(0)$$

$$\mathrm{Re}, = \frac{U_\infty}{v} = \text{ Reynolds number}$$

r_w = wall shear stress

μ = dynamic viscosity

Thus the original variables (x, y, u and φ) are replaced by the two variables $f'(u/U_\infty) \& \eta$ in the similarity technique.

By the Blasius equation, those two variable will uniquely determine the velocity profile at any location.
Values of G(∞) estimated from G curves, as in upper graph.
Calculate improved guess of H(0) by finding the value H(0), at which the line a b in the lower graph crosses the line G(∞)=1.
Using similar triangles

$$\frac{H(0)_2 - H(0)_1}{1 - G(\infty)} = \frac{H(0)_2 - H(0)_1}{G(\infty) - G(\infty)}$$

CONCLUSION

- Boundary layer flows occur ubiquitously in nature, hence important topic of study.
- Prandlt's hypothesis reduces the general Navier Stokes equation to the boundary layer equations which are easier to solve.
- Analytical approach based on laws of similarity.
- As an illustration, Blasius flow (unbounded fluid flow over a flat plate) was solved analytically.

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REVIEW ARTICLE

Potential Therapeutic Efficacy of Catechin : A Comprehensive Review

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ABSTRACT

Catechins, a type of polyphenol present in many plants and a key component of tea leaves, are powerful antioxidants.Due to their various therapeutic effects, the scientific community now recognizes flavonoids as a distinct class of medicinal chemicals. Recently literature studies provide sufficient evidence in hypoglycemic effect of catechin and epicatechin in the management of type 2 DM. Table 1 summarizes the source of catechin and quantity of catechin present in different food , vegetables and beverages. Catechin has also been studied for a variety of pharmacological properties. The goal of this review is to look at the data for catechin's effectiveness and pharmacological effects. The study discovered that catechin has protective benefits on the functioning and integrity of the liver, kidneys, and heart, as well as age-related memory decline. Catechin has antioxidant, antidiabetic , cardioprotective, neuroprotective, immunomodulatory, anticancer, muscle growth, lipid lowering activity. The current review summarises existing knowledge on catechin's health-promoting properties. The same has also been considered in terms of its chemotherapeutic potential.

Keywords: Catechin, antidiabetic, antioxidant, anticancer, immunomodulatory, neuroprotective

INTRODUCTION

In the past few year hypoglycemic activity of catechin have been extensively studied to improve the microvascular complication of type 2 diabetes mellitus. Catechin is a flavonol-like secondary metabolite generated from plants that is frequently found in nature. Table 1.Illustrates key features and mechanism of action of catechin in diabetes. The word catechin is derived from catechu which is obtained from the boiled extracts of Mimosa catechu(Zheng *et al.,* 2008).Catechin contains two benzene rings (A ring, B ring) along with dihydropyran (C ring) onto which the hydroxyl group is attached to carbon 3. The presence of two chiral centres molecule at carbon 2 and 3 is accountable for the generation of diastereoisomers. Two isomers with trans configuration are termed as ‗catechin'; while the other two with cis configuration are known as ‗epicatechin'. These isomers can be distinguished by chiral chromatography (Rinaldo *et al.,* 2010). In the present review, a comprehensive attempt has been made to

provide an insight into the potential role of catechin. The focus of this review is on the pharmacological potentials of diverse experimental animals.

Biological Potential

Antidiabetic

By slowing the process of carbohydrate hydrolysis and absorption, inhibitors of -glucosidase and -amylase lower postprandial glucose levels, making them beneficial in the treatment of type 2 diabetes(Schäfer, *et al.,* 2007).An in vitro study conducted by Zhu, W *et al.,* 2014 revealed the α- glucosidase inhibitory activity of catechin and catechin grafted chitosan at the concentration of 1mg/ml shows 58.86% and 72.45% respectively which suggest that catechin having potential hypoglycemic activity(Zhu, W *et al.,* 2014). Morever W *et al.,* al also revealed the potential α-amylase inhibitory activity of catechin and catechin grafted chitosan at the concentration of 10mg/ml shows 32.35% and 36.47% (Zhu*et al.,* 2014). Similarl Liu, J *et al.,* showed the inhibitory activity of catechin and catechin grafted inulin at the concentration of 1mg/ml were 96.46% and 97.81% respectively(Liu *et al.,* 2014). Mrabti *et al.,* cited the α- glucosidase inhibitory potency of catechin from root of Arbutus unedo L. by high-pressure static extraction using Zippertex technology as 87.55%(Mrabti *et al.,* 2018).Similarly, Mechchate *et al.,* in their recent study demonstrated the synergistic combination of catechin, rutin and epicatechin showed the antihyperglycemic activity in alloxan induced diabetic mice for 28 days. Another study by Shin *et al.,* demonstrated that catechin could significantly promotes adipocyte differentiation (Shin *et al.,* 2009). Meena *et al.,* reported that catechin treatment of 35mg/kg for 60 days in albino rats confirms hypoglycemic effect (Meena *et al.,* 2017).Moreover Meena *et al.,* also reported that catechin loaded eudragit microparticles have potency for preventing obesity which is a major concern in the management of diabetes mellitus (Meena *et al.,* 2017).

In another study Kempegowdaand co-workers found that catechin can potentially inhibit DPP-4 by binding with the α- helix of enzyme evidence from fluorescence spectroscopy (Kempegowda *et al.,* 2018). Further … *et al.,* reported the binding affinity of catechin with DPP-4 showd6.601kcal/mol (Kempegowda *et al.,* 2018). Bhardwaj, *et al.,* revealed that catechin treatment of 50mg/kg / for three weeks by oral route significantly ameliorate diabetes mellitus induced vascular endothelial abnormalities (Bhardwaj, *et al.,* 2014). Another study by Shahid et al explore the antioxidant efficacy of catechin by administrating 40mg/kg b.wt for 7days by oral gavage significantly decrease the enzymatic cellular antioxidants (Shahid *et al.,* 2016).

Anti-Oxidant

Lu, N., et al, investigated the potential of catechin which act as pro- oxidant by antagonize hemoglobin relate damages(Lu, N., *et al.,* 2011).Similarly Zhao and co- workers in their recent study found that catechin have the potential to alleviate chlorpyrifos induced oxidative damege in zebrafish model(Zhao *et al.,* 2021).Experimental evidence showed that administration of catechin 20mg/kg b. wt to male wistar rats for 21 days significantly reduce the activity of antioxidant enzymes(Ahmed *et al.,* 2013). Rizv *et al.,* found that catechin can ameliorates the long term complication of diabetes mellitus(Rizvi *et al.,* 2005).In another study Anithaand co-workers compared the scavenging activity of catechin and epicatechin by DPPH assay and found the IC50 value as 8.83×10^{-6} M and 8.19×10^{-6}M respectively (Anitha *et al.,* 2021). Further, Wang*et al.,* in their study found that how introduction functional group – $N(CH_3)$ in catechin would improve its antioxidant activity (Wang *et al.,* 2021).Experimental evidence showed that catechin obtained from Arceuthobium exert antioxidant effect in vitro(Orhan *et al.,* 2019). Caro *et al.,* determine the antioxidant effect of catechinsunder CYP2E1-dependent oxidative stress(Caro *et al.,* 2019). Another study by Zhao *et al.,* cited the effect of catechin in zebrafish larvae model showed antioxidants effects (Zhao *et al.,* 2021).Green tea extracts had half maximal effective concentration (EC50) values of 2.17 - 2.75 mg/mL for antioxidant activity and 0.22 - 0.30 mg/mL for reducing power, respectively, and 3.31 - 4.54 mg/mL for scavenging ability on hydroxyl radicals and 1.63 - 3.09 mg/mL for chelating ability on ferrous ions (LIN *et al.,* 2010).

Decaffeinated-GTE decreased p47 and p22phox (NADPH oxidase subunits) expression in immunoblotting of aortas, but promoted phosphorylation of eNOS and Akt(Ihm *et al.,* 2012).Through its significant antioxidative effects, green

tea EGCG reduced the progressive increase in blood pressure in spontaneous hypertension rats (SHRs) and prevented most of the increased locomotor activity, in addition to enhancing learning and memory (Wang *et al.,* 2012).The results revealed that catechin have potential antioxidant properties and can be employed in ameliorating the macrovascular complication due to diabetes mellitus.

Neuroprotective

Experimental evidence showed that catechin protected SH-SY5Y cells from NMDA-induced damage and death by modulating NR2B expression, activating PI3K/Akt signalling, and activating the caspase-dependent pathway(Liu, J. *et al.,* 2019). Catechin decreased c-Jun phosphorylation while increasing GSK-3 phosphorylation (Ser9) (Ruan, H *et al.,* 2009). In addition to aboveIn mice, catechin has been shown to protect dopaminergic neurons in the substantia nigra against MPTP toxicity and to recover striatal dopamine depletion (Ruan, H *et al.,* 2009).Similarly Josiah and co-workers reported that In the brains of rotenone-intoxicated rats, quercetin and catechin ameliorated the reduction in complex 1 and Na+K+ATPase activities while attenuating the increased lactate dehydrogenase activity(Josiah *et al.,* 2021).In a recent study conducted by Cai et al revealed neuroprotective effect of green tea against oxidative stress in PC12 cells(Cai *et al.,* 2019).Another study by Teixeira *et al.,* investigate potential effect of catechin at the dose of 10 and 30mg/kg by intraperitoneal injection in male wistar rats for 14 days restore GSH levels and increased dopamine content which indicates its use in parkinsons disease(Teixeira *et al.,* 2013). Ahmed, et al cited the effect of catechin in neurodegeneration using rat model, catechin at the dose of 10 and 20mg/kg ameliorating the oxidative stress and effective in preventing memory loss in Alzheimer,s disease(Ahmed, *et al.,* 2013). Another study by Ban *et al.,* revealed the efficacy of catechin in improving neurotoxicity caused by amyloid β proteins in cultured rat cortical neurons by inhibiting glutamate release , ROS production and caspase-3 activity(Ban,*et al.,* 2006).

Cardioprotective

Endothelial dysfunction is a systemic condition and a major factor in the development of atherosclerosis. It is regarded as a comprehensive indicator of all atherogenic and atheroprotective variables present in a person. Experimental evidence showed thatin kidney transplant recipients, black tea drinking enhanced posthyperemia brachial artery diameter (BAD), flow-mediated vasodilation (FMV), and FMV percent (p 0.05), resulting in improved endothelial function and endothelium-dependent arterial vasodilation (Ardalan *et al.,* 2007). In the prediabetic stage, Ihm *et al.,* discovered that catechin intake stabilised blood pressure and prevented endothelial damage and IR (Ihm *et al.,* 2012).

In different experimental groups, different dose levels and combinations of catechin and doxorubicin were examined in rats, in which catcchin was reported to effectively inhibit dox-induced cardiotoxicity(Kozluca *et al.,* 1996).In another study Enayati et al reportedthat catechin were evaluated for their cardioprotective effects via glycogen synthase kinase 3β (GSK-3β) and glucocorticoid regulated kinase-1 (SGK1) protein kinase inhibition by Molecular Docking(Enayati *et al.,* 2021).In addition to above with a binding energy of 8.8 kcal/mol, catechin showed substantial inhibitory actions against GSK-3 and SGK1 protein kinases (Enayati *et al.,* 2021). Liang *et al.,* discovered that intragastric administration of green tea at doses of 0.2 and 1.0 g/kg/d reduced blood pressure and plasma angiotensin II levels, as well as improving ultrastructures of the left ventricular mitochondrion and myofibrillae in SHR (Liang *et al.,* 2010). In Dahl salt-sensitive rats fed a high salt diet, the GABA (gamma-aminobutyric acid)-rich tea was more efficient in minimizing the development of hypertension (Abe *et al.,* 1995). In rats with remnant kidney surgery, 0.25 percent GTE reduced left ventricular hypertrophy, hypertension, and retained cardiac Na-K-ATPase activity (p 0.01) (Zheng *et al.,* 2004).

Green tea gavage at doses ranging from 0.2 to 2.0 g/kg/day protected mitochondria of the left ventricular myocardium and aortic vascular smooth muscle cells from damage in SHR, as well as a dose-dependent decrease in SBP and plasma nitric oxide, aldosterone, malondialdehyde, and left ventricular hypertrophy index (LHVI) (Liang *et al.,* 2011). Transaortic abdominal aortic constriction (TAC) reduced the number of mitochondrial DNA copies and the activity of respiratory chain complexes I, III, and IV in rats, however these reductions could be reversed with

EGCG therapy(Chen *et al.,* 2009).Green tea prevented and reversed glucose intolerance, as well as elevated systolic blood pressure, left ventricular wet weight, interstitial collagen, and passive diastolic stiffness, in rats on a high carbohydrate diet (Rickman *et al.,* 2010).).Experimental evidence showed that EGCG prevented Ang II-stimulated VSMC hypertrophy at both the transcriptional and posttranslational stages via inhibiting the JNK signalling pathway(Zheng *et al.,* 2004).56 obese, hypertensive patients were randomised to receive a daily dosage of 1 capsule containing either 379 mg of green tea extract (GTE) or a corresponding placebo in a double-blind, placebo-controlled experiment. Both systolic and diastolic blood pressures were considerably lower in the GTE group after 3 months of supplementation compared to the placebo group (p 0.01) (Bogdanski *et al.,* 2012).

Immunomodulatory

Ganeshpurkaret al cited the effect of In a rat model, the effect of catechin on humoral and cellular immunity at doses of 25, 50, and 100mg/kg given orally results in a significant rise in antibody titer in the hemagglutination test, as well as higher levels of immunoglobulin(Ganeshpurkar *et al.,* 2018). Another study by …. *Et al.,* demonstrated that catechin could significantly increase the antibody titer dose dependently(Sunil *et al.,* 2019).In another study Konget al reported, iron- catechin nanoparticlesn undergo intracellular pH-responsive dissociation and release catechin molecules under the low pH of lysosomes after endocytosis(Kong *et al.,* 2022). In addition to the above this method increases osteogenic differentiation while inhibiting adipogenic differentiation in human adipose-derived stem cells by delivering catechin intracellularly(Kong *et al.,* 2022). Simmilarly Marinovic *et al.,* demonstrate that catechins, alone or in combination, have potent immunomodulatory properties(Marinovic *et al.,* 2015). In a dose-dependent manner, the Epigallocatechin Gallate preferentially elevated the production of interleukin-12 (IL-12) and tumour necrosis factor alpha (TNF-) and down regulated the production of IL-10 in macrophages caused by L. pneumophila infection which confirms its immunomodulatory effect (Matsunaga *et al.,* 2001). Sunil *et al.,* evaluate the immunomodulatory effects of heartwood extracts of A. catechu in swiss albino mice which shows the number of antibody-producing cells in the spleen increased after treatment with extracts(Sunil *et al.,* 2019). Another study by da Costa Krewer *et al.,* determine whether guarana supplementation can modulate the levels of proinflamatory cytokines by doing a randomised, placebo-controlled in vivo study was also conducted to see if guaraná had any effect on the blood cytokine levels of 14 healthy volunteers who were supplemented for 14 days. (da Costa Krewer *et al.,* 2014). Similarly, Ganeshpurkar *et al.,* in their study found that Catechin was compared to tumour necrosis factor alpha (TNF-), interleukin (IL)-1, IL-6, inducible nitric oxide synthase (iNOS), and cyclooxygenase 2 (COX-2) in this study(Ganeshpurkar *et al.,* 2018).Experimental evidence showed that following induction of relatively low local and systemic innate tumour necrosis factor (TNF-), interleukin-6 (IL-6) and IL-17, but relatively high levels of early systemic IL-15 responses, the combination of EGCG and vitamin A or E in OWE (Nutritive Immune-enhancing Delivery System, NIDS) synergistically enhanced adaptive B-cell, CD4+ and CD8+ T-cell responses(Patel *et al.,* 2016).Tea polysaccharide from immature leaves extract had a stronger immunostimulating activity than TPS from mature leaves, and its activities were depending on the amount of strictinin in the leaf extract(Monobe *et al.,* 2008).Similarly Kuma and co- workers reported that in DOX-induced immunosuppressive rats, *Albizia procera* enhances immune function (Kumar *et al.,* 2022). EGTE pretreatment reduced antigen-specific IgE production in the spleen by increasing the fraction of CD4+ CD25+ regulatory T cells, suggesting that epigallocatechin gallate fraction of green tea extract may play a role in allergic response regulation.(Kuo *et al.,* 2014).

Anti Cancer

In both in vitro and in vivo trials, varied combinations of EGCG and anticancer drugs elicited similar synergistic anticancer effects, with an average reduction in tumour volume of 70.3 % (Fujiki *et al.,* 2015).Curcumin and catechin were investigated in human colon adenocarcinoma HCT 15, HCT 116, and human laryngeal carcinoma Hep G-2 cell lines for their synergistic anticancer activities (Manikandan *et al.,* 2012). Although, both curcumin or catechin suppressed the growth of above cell lines, curiously, in combination of both these substances maximum level of growth control was seen (Manikandan *et al.,* 2012).In another study, Ezzat *et al.,* found thatcatechin-loaded chitosan-tethered liposomes (chitosomes) that would increase catechin oral bioavailability. (Ezzat *et al.,* 2019). In a recent study by Sicard *et al.,* the galloyl moiety of diet-derived catechins gives specificity of action to galloylated catechins

by placing them into the kinase domain of TGF-R1 to inhibit TGF-mediated signalling, which is necessary for ovarian cancer cell invasion and metastasis(Sicard *et al.,* 2021). Ahmad *et al.,* in their study revealed Chitosan coated PLGA nanoparticles of catechin hydrate significantly improve the bioavailability in lungs and effective to treat lung cancer (Ahmad *et al.,* 2020). Chen et al demonstrated thatcombining Mg(II)-Cat NPs with siRNA is a prospective therapeutic approach for combining chemotherapy with gene therapy to achieve higher therapeutic efficacy, and it has demonstrated proof of principle in a preclinical model (Chen *et al.,* 2016). McMillan et al in their study also revealed that catechin and inositol hexaphosphate in combination effective in reduction of vascular endothelial growth factor and can be employed in treatment of pancreatic cancer (McMillan *et al.,* 2007).Another study by Di Leo *et al.,* demonstrated that catechin could significantly improve the catechin's cytotoxic action is greatly enhanced by the nanohybrid. The nanohybrid decreased the capacity of melanoma cells to grow, migrate, and produce neo-angiogenesis at a concentration of (+)-catechin 50 μg/ml (Di Leo *et al.,* 2017). Kuzuhara et al cited green tea catechin has cancer-preventive properties that are mediated by a chaperone-like property (Kuzuhara *et al.,* 2008). Another study by Zhao *et al.,* revealed that catechins with a galloyl moiety can reduce HIV-1 infection by mediating host cell factors such nitric oxide synthase, nuclear factor-B, and casein kinase II (Zhao *et al.,* 2012).With relative binding affinities of 75 percent and 28 percent, respectively, (-)-epicatechin and (+)-catechin were effective competitors of [3H]-testosterone binding to PC-3 prostate cancer cells over expressing ZIP9 (PC3-ZIP9) (Thomas *et al.,* 2021).Al-Hazzani *et al.,* demonstrated that the cytotoxic and growth-inhibitory effects of CH were investigated, particularly the induction of apoptosis in Si Ha cervical cancer cells (Al-Hazzani *et al.,* 2011). Lung *et al.,* revealed that EoL-1 cells might undergo morphological differentiation into mature eosinophil-like cells when exposed to EGCG at a concentration of 40 M (Lung *et al.,* 2002).

Lipid Lowering Effect

Yoo *et al.,* revealed that by limiting lipid intestine absorption and accumulation in adipocytes, co-consuming catechin-rich green tea extracts with by-products such as flavonols and polysaccharides generated during green tea processing could be prospective natural components on anti-obesity(Yoo *et al.,* 2020). Hui *et al.,* cited the antihyperlipidemic effect of catechin from Morinda citrolia (Hui *et al.,* 2020).In addition to above Jin *et al.,* in their study investigated the lipid lowring and antiobesity activity of black tea extracts on obese rats which shows significantly decreased the total cholesterol, Triglycerides, LDL andleptin in liver(Jin *et al.,* 2013).

CONCLUSION

Irrespective of several studies which confirms hypoglycemic activity of catechin and epicatechin still the detailed molecular mechanism behind reducing the microvascular complication need to explore more. Recent advances focus on molecular level to improve the bioavailability of catechin. Catechin has been shown to have a variety of beneficial, therapeutic, and protective effects on organ systems in numerous pharmacological trials.It would be fascinating to trace the process by which it modifies the biological system because of its antioxidant and anti-cancer properties.Catechin is a phytochemical having numerous pharmacological actions, as evidenced by the aforementioned facts. Catechin, which may be found in plants, vegetables, and fruits, is a "vital phytochemical" that needs to be thoroughly explored in humans in order to create a sufficient safety profile and get therapeutic advantages.From the literature survey catechin showed many pharmacological activity which can be employed to achieve good health and well-being in human. Regardless of several established studies which confirms the hypoglycemic effect of catechin a detailed study on molecular mechanism involved should be need to be study.

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Table 1 Source of catechin:

Biological source of Catechin	Total amount of Catechins	Reference
Fruits		
Black grape	108.3mg/kg	Tsanova-Savova *et al.*, 2005
White grape	58.9mg/kg	Arts *et al.*, 2000
Black grape	203.9 mg/kg	Arts *et al.*, 2000
Blackberry	184.4 mg/kg	Arts *et al.*, 2000
Sweet cherry	117.1 mg/kg	Arts *et al.*, 2000
Apricot	110.1mg/kg	Arts *et al.*, 2000
Strawberry	2-50mg/g	Gadkari *et al.*, 2015 Manach, C *et al.*, 2004
Beverages		
Cider	4mg/g	Gadkari *et al.*, 2015
Red wine	8-30mg/g	Gadkari *et al.*, 2015 Arts, *et al.*, 2000
Algae		
Red algae	217mg/g	Yoshie *et al.*, 2000
Green algae	33.3 mg/g	Yoshie *et al.*, 2000
Eisenia bicyclis	38.6 mg/g	Yoshie *et al.*, 2000

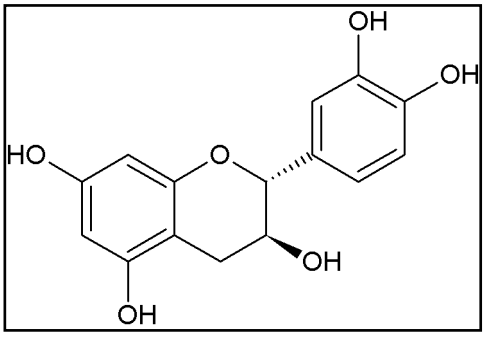

Fig. 1. Catechin

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RESEARCH ARTICLE

Process Parameter Optimization in FDM 3D Printing for Minimizing Surface Roughness

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ABSTRACT

Additive layer manufacturing creates the desired shape automatically by adding material. Layer technology is more frequently referred to as 3D printing. 3D printing, therefore, ensures the best conversion of the CAD model into a valuable product. This analysis aims to find the best input parametric combination to lower surface roughness using the Taguchi method. Taguchi L27 orthogonal array was used to carry out experiments with three input parameters/factors (nozzle temperature-T, layers height-t, and printing speed-v), each with three levels, and surface roughness measurements were done. The nozzle temperature significantly reduces surface roughness, followed by printing speed. Layer thickness has a slighter role on surface roughness. Taguchi method results indicate that the optimal parameter settings should be 220^{0}C of nozzle temperature, 0.125 mm of layer thickness, and 20 mm.s^{-1} of printing speed.

Keywords: FDM, Sustainable Manufacturing, Taguchi Design & Optimization

INTRODUCTION

FDM-Fused Deposition Modelling or FFF-Fused filament fabrication is the extensively used Additive Manufacturing (AM) process for modeling, prototyping, and makingend-use components. The products are shaped by depositing the semi-liquid material in layers [1]. The product's first 3-D CAD model is made using suitable CAD software in this method. Data is then converted into STL-stereolithography format to generate the toolpath. FDM is cheap and reasonably efficient for any shape [2]. Growing practices of this technology are in aerospace, auto industry, machine tooling, medical implants, fashion designing, and architectural models [3].

The choice of FDM filaments/raw materials depends on the mechanical performance and visual quality of the product. The most standard FDM filaments are thermoplastics (PLA-Polylactic acid, ABS-Acrylonitrile butadiene styrene, PETG-Polyethylene terephthalate glycol, Nylon, and TPU-Thermoplastic polyurethane).The combination of FDM & ABS material is trendy for providing strong and rigid (high-temperature resistant and higher toughness), cost-effective, and high-level finished products. ABS parts can be further machined, polished, or electroplated effectively. Sustainability is becoming more important in product design and manufacturing. Manufacturers adopt 3D printing to innovate, create parts fast, and make lighter parts without sacrificing strength. Sustainability is becoming important in additive manufacturing (AM).Manufacturing is expected to be a combination of traditional and 3D printing in the future. It's too greener and cleaner.

Surface roughness measurement is an integral part of quality inspection in making and processing all types of materials.[4]. Surface roughness generation is process intensive, dynamic, and complicated. Effective 3D printing technology to manufacture products with better surface characteristics, enough strength, and minimum dimensional inaccuracy increases. The research exploration for 3D printing has entered a new phase, with more significant attempts to optimize the technique to expand its applications.

Torres *et al.* [5] adopted the Taguchi method to design experiments and express the influence of printing parameters on the tensile strength of PLA samples. Internal density and layer thickness affect the tensile strength. Again, raising the temperature increases tensile strength. Tontowi *et al.* [6] optimized the FDM process parameters (printing temperature, layer thickness, and printing angle) with an integrated Response Surface and the Taguchi methodology. They printed ASTM D638 standard parts with better tensile strength and dimensional accuracy. The results revealed that layer thickness affects tensile strength, while printing angle affects dimensional error. Abdullah *et al.* [7] studied ABS printed parts' topological and mechanical properties, viewing the result of layer thickness and orientation. ANOVA showed a substantial influence of both variables on output.

Manikandan *et al.* [8] evaluated the parameters to assess the result of the FDM input parameters on the strength and surface finish of the ABS-PC component. Taguchi's method showed that the surface roughness and flexural strength were influenced by contour style and raster angle, respectively. Nidagundi *et al.* [9] followed L9 Taguchi Orthogonal Array (OA), and the SN ratio was calculated to enhance fill angle, layer thickness, and orientation. Output parameters were dimensional tolerance, surface roughness, ultimate tensile strength, and build time. Kumar *et al.* [10] analyzed the effect of 5 variables on the surface quality of ABS parts. Taguchi analysis and ANOVA to signify the impact of the process inputs. Also, voids in layers and thin layers reduce surface roughness. An investigation of surface roughness by adjusting input variables such as nozzle temperature, layer thickness, and printing speed is not examined yet in ABS 3D printing. This research aims to find the best input parameter combination to reduce surface roughness using the Taguchi method and investigate various elements of ABS material printing. There are 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure), and 11 (Sustainable cities and Communities).

Experimental Work

Equipment and Material

The necessary process parameters for the experiment were Nozzle Temperature, Layer thickness, and Printing Speed. These process parameters affect the Surface Roughness (Ra, μm) of the product of ABS thermoplastic polymer. A rectilinear infill pattern was used to print the specimen. Rectilinear is one of the primary and fastest printed in fills, which saves filament and doesn't gather material at intersections [11][12]. Printing time, filament

usage, flexibility, strength, and weight depend on infill patterns. The AMS-Hyrel3D printer works with Repetrel. Repetrel is based on the Repetier platform and has embedded Slic3r software, providing an optimized printing background. The printer is excellent for large-scale prints, multiple material prints, and volume production. The filament used was the high temperature resistant and rigid ABS (Diameter- 1.75 mm; Dimensional Accuracy ±0.03mm). To measure the surface roughness parameter Ra (average roughness), a Taylor Hobson roughness checker (Model- Surtronic 25; Resolution 0.01μm; Diamond stylus Tip radius- 5μm) was used.

Experimental Results and Optimization

Taguchi's DOE is suitable for optimizing the input parameters with fewer experimental runs. The experimental design technique can help reduce variation in product and process quality[13].A L27 orthogonal array was selected for performing experiments [14][15]. Taguchi analysis was done using Minitab 19.0 software, and the S/N ratio plots and analysis of variance (ANOVA) effects were obtained and examined. The outputs are converted into signal-to-noise ratio (S/N ratio) for smaller the better quality characteristics to improve the machinability. The main effect plot shows the parameter setting for the lowest surface roughness is a Nozzle Temperature of 220^{o}C, Layer Thickness of 0.325 mm, and Printing Speed of 20 mm. From ANOVA Nozzle Temperature has a more significant impact on surface roughness than other parameters, and it's percent contribution is higher. The residual figure shows a normal distribution for the residuals. It confirms ANOVA's correctness.

Since an experiment takes a lot of measure, expense, and time, it is tactful to suggest a valid but straightforward model to predict the response. Empirical modeling does forecasting, prediction of process parameters, and knowing the behavior of the experiment. So linear regression analysis was done to formulate the predictive mathematical models for the input independent factors and output dependent responses. A confirmation test was run to validate the model. From table found that the model is adequate as the error percentage is less than 10%.
Regression Equation

$$Ra= -109.75+0.5418T+0.69h-0.0771v;\ R^2=96.83\% \quad \text{(Eq-1)}$$

CONCLUSION

The experimental results led to the following conclusions. Optimum printing input parameter combination for obtaining the low surface roughness was T= 220 ^{0}C, h= 0.125 mm, v= 20 mm/s. From the ANOVA, it was observed that surface roughness is significantly affected by the nozzle temperature followed by printing speed. The difference between experimental surface roughness and predicted values through ANOVA is found to be 10%. Therefore, it is concluded that Taguchi's experimental analysis has been conducted in the correct way. Surface roughness is inversely proportional to nozzle temperature, and directly proportional to layer thickness and printing speed.

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Table 1: Printer Specifications

Model	HYDRA 16A-S
Positional Accuracy; micron	60x60x10 micron
Positional Resolution; micron	6x6x1 micron
Positional Repeatability; micron	30x30x5 micron
Bed Size (X, Y, Z); mm	600, 400, 250
Maximum Bed Temperature; ^{o}C	450
Maximum Print Speed; mm/s	60
Maximum Chamber Temperature; ^{o}C	55

Table 2: Input Printing Parameter with Different Levels

Input Parameters	**Symbols**	**Unit**	**Levels**		
Nozzle Temperature	T	^{o}C	220	225	230
Layer Thickness	h	mm	0.125	0.275	0.325
Printing Speed	v	$mm.s^{-1}$	10	15	20
Machining Duration	s		120		

Table 3: Experimental Results

Run	**T**	**h**	**v**	**Ra**	**SNRA1**
1	220	0.125	10	8.292	-18.3736
2	220	0.125	15	8.001	-18.0631
3	220	0.125	20	7.118	-17.0472
4	220	0.275	10	8.616	-18.7057
5	220	0.275	15	8.452	-18.5396

6	220	0.275	20	7.704	-17.7339
7	220	0.325	10	8.696	-18.7860
8	220	0.325	15	8.484	-18.5724
9	220	0.325	20	7.924	-17.9793
10	225	0.125	10	11.841	-21.4679
11	225	0.125	15	11.745	-21.3972
12	225	0.125	20	10.536	-20.4532
13	225	0.275	10	12.161	-21.6995
14	225	0.275	15	11.969	-21.5613
15	225	0.275	20	11.521	-21.23
16	225	0.325	10	12.408	-21.8738
17	225	0.325	15	12.052	-21.6215
18	225	0.325	20	11.617	-21.302
19	230	0.125	10	14.072	-22.9669
20	230	0.125	15	13.732	-22.7549
21	230	0.125	20	13.624	-22.6858
22	230	0.275	10	14.596	-23.2849
23	230	0.275	15	14.257	-23.0807
24	230	0.275	20	14.148	-23.0141
25	230	0.325	10	12.801	-22.145
26	230	0.325	15	12.462	-21.9118
27	230	0.325	20	12.353	-21.8356

Table 4: Signal to Noise Ratio Response Table (Smaller is better)

Level	T	h	v
1	-18.20	-20.58	-21.03
2	-21.40	-20.98	-20.83
3	-22.63	-20.67	-20.36
Delta	4.43	0.40	0.67
Rank	1	3	2

Table 5: Analysis of Variance for S/N Ratios

Source	SS	MS	F	P	C %
T	94.174	47.087	295.59	0.000	93.897
H	0.810	0.405	2.54	0.104	0.811
V	2.123	1.061	6.66	0.006	2.116
Residual Error	3.186	0.159			3.176
Total					100

Table 6: Confirmation Results for the Developed Model

Run	Experimental Ra	Predicted Ra	Error %
2	8.001	8.365	4.354
8	8.484	8.504	0.235
15	11.521	10.792	6.320
27	12.353	13.536	8.739

Figure 1: 3D Printer

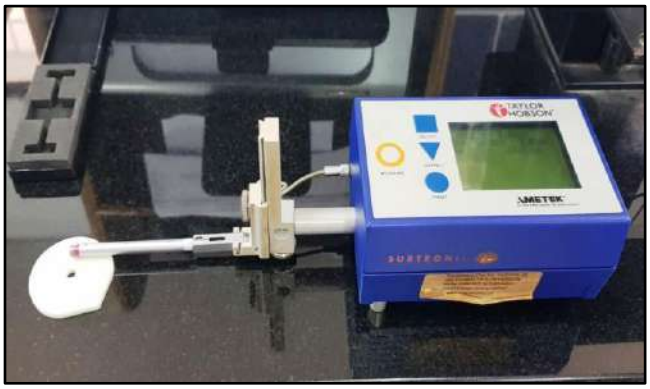

Figure 2: Surface Roughness Checker

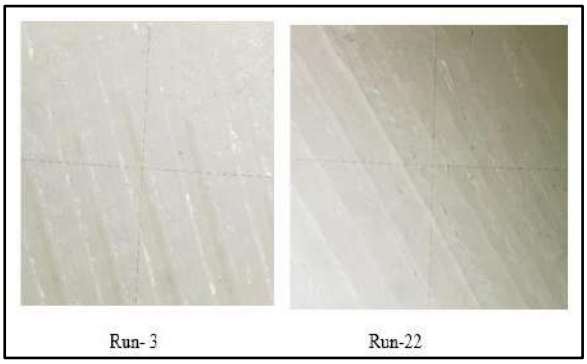

Figure 3: Microscopic Images of Surfaces

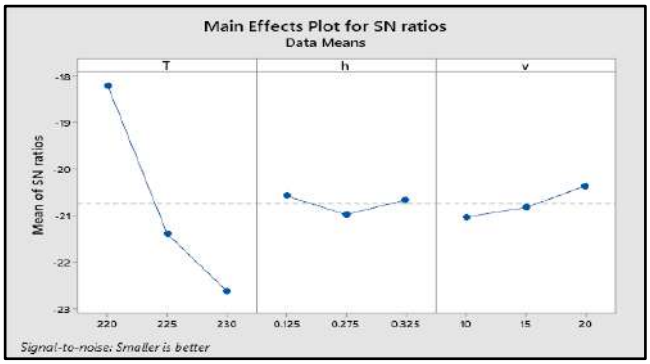

Figure 4: Main Effects Plot

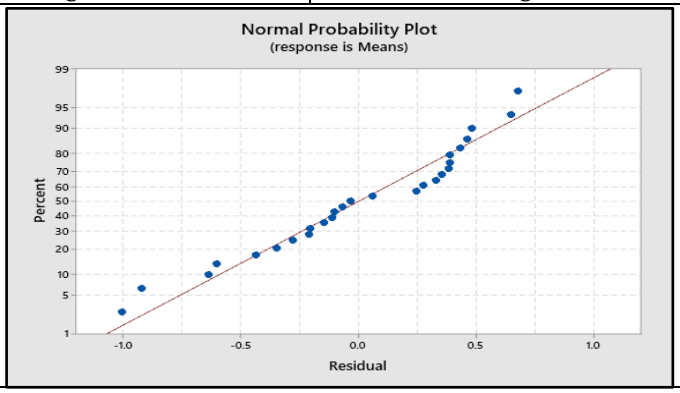

Figure 4: Normal Probability Plot

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RESEARCH ARTICLE

A Characteristic Chest X-Ray Findings in Diagnosis of Covid-19

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ABSTRACT

The global pandemic of corona virus is regarded as one of the most fatal epidemics. The COVID-19outbreak has continuously put an enormous stress on emergency departments, ICU's and hospital systems,after its beginning in the later months of 2019. Wuhan, the city in China, reported the 1st case of COVID-19which was treated as an unusual pneumonia. It was tagged as pandemic by the WHO on 11thMarch 2020[1-4]..COVID-19, is an infectious and highly transmissible disease caused by anovel strain of family Corona viridae, a pathogen i.e, responsible for respiratory illness of the disease. Its replicating 2 previous epidemics, the Severe Acute Respiratory Syndrome (SARS) & the Middle Eastern Respiratory Syndrome (MERS). The disease that's persuaded by SARS-CoV-2 was labeled asCOVID-19 by the International Classification of Diseases (ICD).Different diagnostic methods such as Molecular test of RT-PCR or imaging tests of chest can be used for diagnosis of this disease. Imaging tests plays a major role in assessment of disease severity and act as a tool for planning the management or treatment of the affected individual based on its severity. One such imaging is chest x-ray, Multiple studies on COVID-19 patients showed typically a various patterns of CXR finding in an affected individuals. the most common CXR findings noted in COVID-19 affected individual is ,bilateral, basal & peripheral multi-focal airspace opacities i.e, the Ground-Glass Opacity (GGO) and Consolidation.

Keywords: COVID-19, PCR, SARS, CGO, X-Ray

INTRODUCTION

The Corona virus (COVID-19) diseases first case was reported in year 2019 in late December. From where, it quickly spread to entire world. Rapid global spread of this virus had an extensive social, health &economic backlash. The number of confirmed worldwide cases of COVID-19 in October 2020, outstretched to 46 million,& the mortality rate

surpassed 1,140,000[5,6]. The count of cases expanded due to absence of any specific promising vaccine in sigh or treatment, thus leading to devastation of the financial and health systems of the entire world. This infection usually takes place within 14 days of exposure ,commonly within 4-5 days[7]. The middle-age group &elderly male adults are most commonly affected by this disease, although it can affect any age group. This disease is predominantly transmitted via coming in contact with droplets of secretions from the COVID-19 infected individuals[8]. Contaminated droplets present on objects can also ease transmission of this infection[8]. Diagnosis of this disease can be done via both molecular or imaging test. Usually in both symptomatic or asymptomatic subjects diagnosis is done by molecular testingby identifying the viral RNA in Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) This laboratory testwas adapted and was in massive demand because it shortens the reaction time & simultaneously the reporting time, but it is still challenged by a risk of contamination& substantial amount of false negatives [9,10,11].

Reciprocally in cases of clinically suspected COVID-19patientshaving negative RT-PCR, imaging tests can detect the signs of pneumonia thus enabling rapid decision making on patients management and treatment. The imaging tests were thus recommended for patients those were presented with moderate-to-severe characteristic features of COVID-19 pneumonia irrespective of the RT-PCR tests [11-12]. Chest imaging has been contemplated as an important diagnostic tool for patients with suspected or confirmed COVID-19 disease, when RT-PCR is unavailable, or results are initially negative or are delayed, To determine the levels of disease severity, from completely asymptomatic to critically ill individuals. Different imaging modalities are available for diagnosis of COVID -19 most commonly the chest x-rays and CT Scans, whose sensitivity, specificity and diagnostic features are specified in the recent literature's of COVID-19. However, the choice of imaging modality for COVID-19, is still a matter of debate [13,14].

Chest X-Ray

In the suspected cases of COVID -19, CXRs are the most commonly performed imaging tests [15-16]. CXR care used instead of CT due to its quick & easy decontamination procedures&substantial availability [17-23]. An easy and simple internationally recognized Chest x-ray reporting template developed by The British Society of Thoracic Imaging (BSTI)has been included into an National Health Services England (NHSE) radiology tool for diagnosis of suspected COVID-19 [23, 24]. The certain limitations of RT-PCR testing in diagnosis of COVID-19 like delay in its results, risk of contamination of swabs and large false negative results have made CXR an important tool in diagnosis and control management strategies in COVID-19 patients

X-ray findings in suspected COVID- 19 patients have been divided into 4 categories : [25-30].
Normal CXR- Its common in the early stage of the disease, thus it does not rule out infection.
Typical findings(typically associated with COVID-19) - It includes reticular pattern GGO, consolidations, with rounded, patchy or confluent multi-focal appearance usually distribution noted in bilateral, peripheral, with dominance in lower lung fields [31].
Indeterminate findings - findings seen in cases of COVID-19 pneumonia, it can also have other causes.like consolidations/ GGO with a unilateral, upper lobe or central distribution
Atypical findings - uncommon, or findings not reported in COVID-19 pneumonia such as lung nodules or masses, cavitation, lobar consolidation, milliary pattern, and pleural effusion, those are reported only in 3% of patients . The most common findings for the COVID-19 affected individual include the ,bilateral, basal & peripheral multi-focal airspace opacities i.e, the Ground-Glass Opacity (GGO) and Consolidation, other findings such as Septal thickening, Lymphadenopathy, Bronchiectasis, Cavitation , and Pleural Effusion, are less commonly noted [19-22,32].

Ground Glass Opacities (GGO): Its a an area of higher attenuation in lungs with a maintained vascular and bronchial markings. Its an non specific sign with aetiology including acute alveolar disease, infection and chronic interstitial disease. radiographic appearance of GGO is often fairly diffuse region of hazy lung radiopacity, in which

edges of pulmonary vessels are difficult to appreciate. It has 3 different morphological forms namely Focal GGO, Diffuse GGO and Isolated GGO 33

Consolidations: Its an area of alveolar air spaces filled with fluid, cells, tissue or other material. The most commonly the complete consolidation is seen as a result of pneumonia. This spread through the lobes via the pores of Kohn between alveoli's. the general radiographic features of consolidation on CXR include air space opacification obscuring the pulmonary vessels and air bronchograms (phenomenon of air filled bronchi) [34].

Septal Thickening: The thickening of the interlobular septa can be of different types namely smooth, nodular, irregular, reticular. Reticular pattern with interlobular septal thickening is common finding of CXR in COVID-19 after GGO and consolidation. The radiographic features of septal thickness include **Kerley A lines**- 2-6cm long lines oriented towards hilum & **Kerley B lines -** nearly 2cm **s**hort line oriented perpendicular to pleura [35-37].

Pleural Effussion: An abnormal accumulations of fluid in the pleural cavity, seen in pathological conditions due to loss of pleura's ability to reabsorb fluid. The radiographic features include blunting of costophrenic & cardiophrenic angle, along with presence of fluid within horizontal or oblique fissures of lung [38].

Lymphadenopathy: Its a term that refers to pathology of lymph nodes that may include increase in size, abnormal numbers of nodes or derangement of its internal architecture. Radiographic appearance include increase in size, change in architecture of lymph nodes like cystic or neurotic appearances [39].

DISCUSSION

Various literature's have been published worldwide on the different findings of chest X-ray for diagnosis of COVID 19. diagnosis of the disease is very important not only for the confirmation of presence of disease but it also act as a tool for finding the severity, distribution and most importantly the treatment and management of the disease in the affected individuals. In a study performed by Abdelwahed Abougazia *et al* [40] on COVID-19 patients of Qatar the CXR findings most commonly showed the airspace opacities mostly distributed in lower (87.1%) & peripherallung zones,(69.5%) with most patients having the bilateral lung involvement (74%). Pleural effusions were noted in very few cases(2.4%). In the similar study by David L. Smith *et al* [41] the common CXR findings for COVID-19 included presence of bandlike, confluentand/orpatchy GGO or consolidation involving the mid to lower and peripheral lung zone. Liqa A. Rousan [2]. Found peripheral GGO involving the lower lobes as most common finding. The GGO were progressed into consolidations around 6–11 days (consolidations 30% ,GGO 70%,). consolidations further regressed into GGO in the later phase at 12–17 daysof illness (GGO 80%, consolidations 10%). another study by Misbah Durrani [42] COVID-19 CXRs generally showed consolidation and GGO of pure and mixed opacities involving the bilateral middle peripheral, and lower lung zones. In the study of Asraf Hussain *et al* [17]. According to the COVID-19 CXR classification, of BSTI 6 patients (5.4%) were found to have normal chest X-rays. 79(71.17%) patients had classic picture of COVID-19, while (7.2%) had intermediate findings for the disease. out of total classicCOVID-19 CXR findings i.e of 79 patients, 71 (89.8%) showed bilateral GGO/consolidations, 66 (83.5%) with middle & lower zone involvement. and lastly 72 (91.1%) showed peripheral lung involvement thus the most common X-ray findings seen in this study was GGO or consolidations with bilateral involvement with peripheral, middle, lower zone distribution, which was similar to the results of E. Martínez Chamorro *et al.* [30] Thus consolidation/GGO involving the middle, peripheral and lower lung fields and bilateral distribution were the most common radiographic signs of COVID-19 with respect to the results of various literature's of COVID 1.

CONCLUSION

GGO and consolidations involving bilateral lung with middle, peripheral and lower lobe distribution are the common findings seen in the chest x-rays of COVID affected patients in an intermediate stage of the disease. These

signs cannot be assessed by CXR in the early stage of COVID-19 and thus the specificity of CXR for diagnosis comparatively becomes less in the early diagnosis when compared with CT and RT-PCR tests. CXR can be used along with RT-PCR test for the better diagnosis and access the severity of this disease. Thus is one of the first line imaging modality for COVID-19 diagnosis. Thus early diagnosis, assessment of the disease severity and differential diagnosis of the COVID-19 with help of CXR findings will help in reducing the mortality rate, improving the life expectancy and thus promoting good health and well-being of people around the globe which satisfies the SDG 3 Goals .

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RESEARCH ARTICLE

Artificial Intelligence: an Insight In to Modern Healthcare

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ABSTRACT

Artificial intelligence (AI) is a multidisciplinary field aimed at automating tasks that currently need human intelligence. AI has wide application in various sectors of society with the advanced software and hardware. Biomedicine system including research on various diseases, disease diagnosis, living assistance, and biomedical information processing are highly influenced with system of AI. AI has transformed the aspects of life in the form of smart technology and application equipped smart devices. Also, it automates different tasks, reduces time and cost, and improve work quality. The objective of this study is to retain track of current scientific achievements, comprehend technology availability and provide scope of AI research in field of biomedicine. In recent, the application of AI in biomedicine is an emerging field and it may be expanded to great level on adopting modern technological tools and software in near future.

Keywords: Artificial intelligence; advantage; machine learning; drug discovery; health care

INTRODUCTION

Artificial intelligence (AI) is a discipline of computer science that deals with the creation of intelligent computers that are programmed with unique algorithms or programs. Human intelligence such as cognition, deep learning, adaptation, engagement, and sensory perception are interpreted by machines. These strategies are interdisciplinary in nature and can be used in a variety of sectors, including medicine and health. (Fig. 1) [1].AI keeps track of previous experiences and use a variety of technologies to feel, comprehend, and act in order to solve a variety of problems. It learns and solves problems in a similar way to human brains using both skilled machines and computer

programs. It employs advanced computational methodologies in issue solving, such as natural language processing (NLP), pattern recognition, interpretation, visual checking, and decision making (Fig. 2) [2].

The concept of artificial intelligence was introduced by John McCarthy in 1956. Since then, the use of AI has been expanded in various fields and recently it is used in health care sector for disease diagnostics, personalization of treatment, supportive health services, gene editing and drug development[3-4]. The advancement in computer technology and availability of vast digital data has generated interest of AI towards pharmaceutical sector. AI technologies analyse a large volume of data across different modalities to diagnose disease and guide clinical decisions. So many arising problems in drug discovery and development have been solved by utilizing machine learning and artificial intelligence. This article is aimed to focus on sustainable development of goals such as industry, innovation and infrastructure of pharmaceutical industries and modern health care services. In this article, we comprehensively discussed some of the major advantages, disadvantages and opportunities with the integration of AI in health care system [5].

METHODOLOGY

Systemic literature search has been made through available databases such as researchgate, google scholar, pubmed, sciencedirect, scifinder etc. Approximately 27no. of literatures were investigated to compile and present the relevant data in the current study.

Types of artificial intelligence

AI is a wide-ranging concept and can be classified into a number of ways. Based upon their caliber, AI system is classified as follows [6-8]

Weak intelligence or artificial narrow intelligence (ANI)

This system of intelligence is designed and trained to operate a narrow task such as traffic signaling, driving, online game, facial recognition, virtual personal assistance, and tagging in social media.

Strong AI or artificial general intelligence (AGI)

This is also referred as human level AI which can perform simplification of human intellectual. So, it is capable enough to find the solution when exposed to an unfamiliar task.

Artificial super intelligence (ASI)

This kind of system is smarter and more active than human brains in each and every aspect of science to arts. It can act trillion times smarter than humans.

Arend Hintze, an AI scientist classified AI technology based upon their presence and not yet present and they are as follows

Type 1

This type of AI system is called as reactive machineswhich do not use the past experiences. It can't store data in its memory and hence may not be useful in every situation. It is designed and developed for narrow purpose only.

Type 2

This type of AI systems is called as limited memory systems. This system has the ability to store the information and that helps in solving present and future problems. The memory is not permanently stored in the device. This kind of technology is used in autonomous vehicles.

Type 3
This type of AI system is called as theory of mind. This technology is based on human thinking, desire and intentions that directly impact on decisions.

Type 4
This type of AI system is called as self-awareness. AI system has sense of self and consciousness. It understands the condition and uses the ideas present in other's brain. This is a non-existing AI.

Advantages of artificial intelligence technology
AI technology is a combination of mathematics, computer science and other sciences. The complexity of computer programming helps the machines to recognize and reproduce the cognitive abilities of human beings. AI is complex in nature and to use but it has multiple advantages.

Error reduction
In an experiment the probability of getting manual/experimental/technical error is unpredictable. However, AI helps to reduce these errors with maximum accuracy and precision [9].

Difficult exploration
AI helps to explore the mines and fuel present in deep earth crust and oceans which is beyond the limitation of human being. AI technology based robots can perform this hard and laborious workwithout exhaust[9].

Daily application
AI has wide applications in our daily life. GPS system installed in devices helps to locate the actual location, helps to minimize typographical errors in mobile or computers, identifies and tags the person on social media (face book and twitter) picture post, manages large volume of data in financial or banking sectors and also detect the swindles[9].

Digital assistants
Human resources can be minimized by using AI based digital assistants as like Avatar. Human judgments are associated with emotions so the efficiency of human thinking reduces with mood swing. But these AI bases robots are free from all these kinds of emotional thoughts and are able to think logically and take correct decisions[10].

Repetitive jobs
Simultaneous handling of multiple tasks is a tedious process and that results in error in the studies. But these robots can perform multiple tasks in short span of time with no error. Also, the working speed of these machines is faster than human. These machines are capable enough to handle hazardous tasks and trouble shoot the difficulties if arise[10].

Medical applications
In recent advanced years, AI helps the physicians to assess and analyze the health of patients without any trouble. It gives information regarding prescribing the modern medicines towards different diseases and their possible side effects or adverse effects. Surgeons are also benefited with the application of AI which gives knowledge of simulators such as brain simulation, heart simulation, GIT simulation for artificial surgery[10].

No breaks
Human being needs few hours of rest to energize themselves as they get tired or bored on doing the same activities. But the robots are programmed to perform continuously for long duration without any rest. The machines do not get tired or confused on doing lot of work constantly to give errorless output[11].

Increase technological growth rate

AI technology facilitates the transition towards a world of more advanced technical advancements. AI system has the ability to generate millions of computer modeling programs such as QSAR and QSPR that can assist in the discovery of novel chemical compounds and entities[11].

No risk of harm

Human operated tasks have some risk to their lives. But the machines have no such issues; if they get broken then also it is possible to mantle them[12].

Act as aids

AI bases machines are used to serve physically challenged children or elders. They are used in security alert system in fire alarm, bank robbery and in other difficult climatic conditions[13].

Limitless functions

Robots have no work limits. They operate efficiently and accurately than humans. So, that human get free time to make relax[13].

Disadvantages of artificial intelligence technology

High cost

AI robots are equipped with high sophisticated machineries and software which need to be maintained and updated in regular intervals. The reinstallation and up gradation of old machine parts are highly cost consuming. Also, design and development of these machines and software are time consuming[14].

No replicating humans

Robots are designed to think like human but they have no emotions. They do work as the programme has been set in them. But sometimes it creates problems. If the machine faces an unfamiliar issue, then it will be not able to fix it by itself. Thus, the machine gets broken down and generated false result[14].

No improvement with experience

AI technology based machines cannot be improved as like human beings. The machines are incapable to distinguish between the persons who work hard or not. Also, machines lack empathy, concern, a sense of belonging, and a sense of community[15].

No original creativity

Robots do not have any sense of emotion and feelings. They are incapable to think and judge. So, they do not have their creativity action. The partial characters of human being may be replicated in robots but not all natural abilities[16].

Unemployment

The vast use of machineries in every sector reduces the employment of human beings. Human will be more dependent on machines and become lazier and lose their creativity[16].

Applications of AI in drug discovery

Human brain is not so much efficient to analyse and understand vast number of publications, patents and genomic data science. So, pharmaceutical manufacturers use deep learning software (NVIDIA, DGX-1) and NLP to interpret the result from all these data for advanced scientific research.AI based supercomputers are incorporated with sufficient data of natural, synthetic or semisynthetic compounds and it analyzes the information to establish the relation between the compounds to propose the new drug candidate. The whole process takes about 15 years to transfer a drug discovery idea from initial commencement to a marketed product. The design and synthesis of a new

drug candidate costs an average of $ 2.6 billion and takes over a period of 15 years and also, it is difficult to identify or screen successful drug candidate from bunch of potentially pharmacological active chemical entities (Figure 3). Benevolent AI is used to screen few molecules out of thousands and those drug candidates have maximum drug likeness properties. Next generation AI is needed to determine *in silico* medicines so that many problems can be easily solved. Another deep learning technology known as generative adversarial networks (GANs) was developed by Google which has ability to design drug molecules. GAN technique is based on interaction between two deep neural networks. One neural network evaluates the other and generate more suitable drug candidate. Next generation AI is reinforcement learning based on *in silico* approach of drug discovery. In recent AI technologies, new algorithms are used to tackle the earlier raised difficulties and to recognize the difference in normal and diseased profiles within complex data[17-18].

AI and machine learning

In recent years, scientists are utilizing the support of machine learning technology to analyse bulk of scientific data e.g. judgment correlation system (JACS) has been developed to conduct research on amyotrophic lateral sclerosis (ALS). This JACS made possible to retrieve information from trillions of sentences and paragraphs of various abstracts and research and review articles. JACS has established direct link between data and regulation process as known facts which are useful to design possible number of hypothesis and the final hypothesis may be applied for designing and synthesizing new chemical entity. The advanced technologies give systematic insights to diseases and help the scientists to invent or discover promising drug candidate. It helps in drug design, selection of best chemical compound with maximum efficacy and safety and selection of patients to clinical trials. Pharmaceutical industries are using these advanced technologies for screening of large number of molecules by using algorithm of *in silico* approach in which the system generates new chemical structures by combining the properties of existing drugs. The deep learning software of Aspuru-Guzik can study about 2,50,000 drug like molecules by using CUDA parallel computing platform, NVIDIA Tesla K80 GPU accelerators and TITAN X GPUs with cuDNN on the Theano and Tensor Flow deep learning frameworks. But ultimately the results must be validated by human being. AI and machine technologies help in diagnostics, identifying new drug targets, developing efficacious drugs. This technology finds solution for repurposing of drugs and accelerates the process of drug development[19-20].

AI in health care system

In healthcare, AI system is useful to organize patient dosage forms,route of administration or treatment plans in a better manner and to guide physicians to make good decision.

Maintaining of medical records

The maintenance of record of large number of patients is a difficult task. AI technology has made easier to store the information of patient. Google Deep Mind may be used to mine the patient record in short span of time[21].

Treatment plan designing

In treatment of critical patients having multiple diseases or chronic pathological conditions, AI assist to design systematic treatment plan form the patient reports, clinical expertise, past data and suggest suitable treatment plan to the physicians. For example, IBM Watson launched a program for aiding the oncologists for treatment of critical cancer patients[21].

Helping in repetitive jobs

Recently, medical diagnostics devices such as CT-scan, X-ray, ECG and Echo are equipped with sophisticated AI technology to interpret the diseases. An AI based medical sieve (developed by IBM) helps in cognitive assistance to interpret radiological images. Also, broad spectrum diseases of whole body can be diagnosed with the assistance of deep learning process[22].

Attainment of in person and online consultation

AI has developed software and systems so that the patient consultation to doctor can be possible on virtual mode. British subscription has launched Babylon, an online medical consultation which assists patients in treatment based on patient history and medical knowledge. The patient has to submit the symptoms of disease so that it compares with its stored information in the database and suggest suitable course of action to the patient. This application reminds the patient to take medicine and so, it is useful to older patients who have tendency to forget and it reduces the waiting time for doctors[22].

Health support and medication assistance

AI technology provides health support and medication assistance to the patients. Molly, a virtual nurse is designed to assist people for monitoring their condition and treatment. It gives support to chronic patients till their visit to doctor. Similarly, Ai Cure helps to manage patient's critical conditions and who participate in clinical trials[23].

Accuracy of medicine

AI shows good impact on genomics and genetic development. Deep Genomics, an AI system is useful for observing patterns in the genetic information and medical records to identify the mutations and linkages to diseases. This system informs doctors about the events happening with in a cell when DNA is altered by genetic variation. Another AI technology, Human Longevity is useful to identify the exact location of cancer and vascular diseases in their early stage[24].

Drug creation

The design and development of drug takes more than a decade and consumes billions of rupees. Atom wise, an AI technology is useful to find out the therapies from the database of molecular structure. It hurled a virtual search program for safe and effective therapy for Ebola virus with the existing drugs. The technology identified two drugs which caused Ebola infection. This analysis was completed within one day compared to months to years with manual analysis. A Bophirima company of Boston developed a big data for the management of patients. It reserves data to find the reasons why some patients survive diseases. They used patient's biological data and AI technology to find out the difference between healthy and disease friendly atmospheric conditions. It helps in discovery and design of drugs, healthcare and problem-solving applications[25].

Healthcare system analyzing

In healthcare system, if all the treatment related data, patient name, physician name, and hospital name are computerized then retrieval of data will be easy.IBM Watson cloud technology provides AI technology software to do this kind of data management. If any mishap occurs, it recognizes immediately and takes the correct action so that patient hospitalization may be avoided[25].

Diagnostic and imaging sector

AI technology has wide application in diagnosis of different diseases. Mainly, it focuses on mental health, cancer, and coronary diseases. Prost A sure Index is used for differentiation of benign and malignant prostate cancer. PAPNET was developed to screen the cervical cancer. EEG images can be analyzed by neural networks which is useful in diagnosis of epilepsy and sleep disorders. Some ANN models are developed to analyze electro myographic (EMG), doppler ultrasound and hemodynamic patterns[26].

Prognosis

Prediction of appropriate treatment plans is very important in healthcare system. The perfect identification of high-risk patients in healthcare system is very important to improve their survival. ANNs have the ability to exploit the relation between variables to analyze complex data of cancer. Neural networks forecast the survival in breast and colorectal cancer patients. Also, they are useful in checking the outputs of lung and prostate cancer[27].

CONCLUSION

Artificial intelligence in the pharmaceutical and health-care industries is a rapidly growing field with huge promise. In recent future, saturation in AI technology may happen with this current race of technological and computational growth. If this happens, human physicians will be replaced with AI based robots however this will not be absolute. To achieve singularity in health care, AI will require a significant component of artificial empathy (AE). All AI-enabled health services or devices will always be guided by the core principles of humanity and patient-centered care.

CONFLICT OF INTEREST

Authors have no competing interest.

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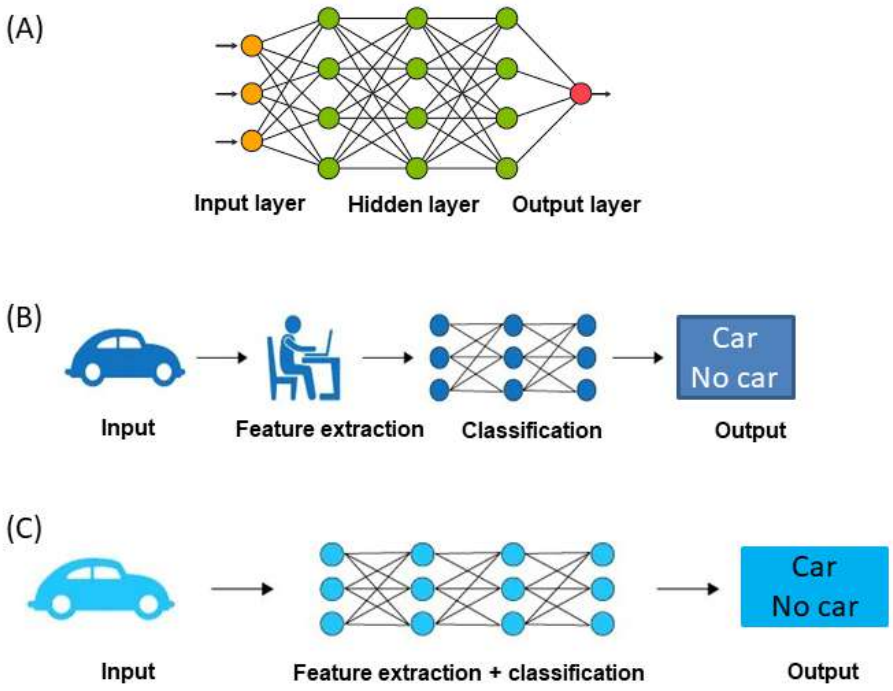

Fig.1.Different stages of computer programming

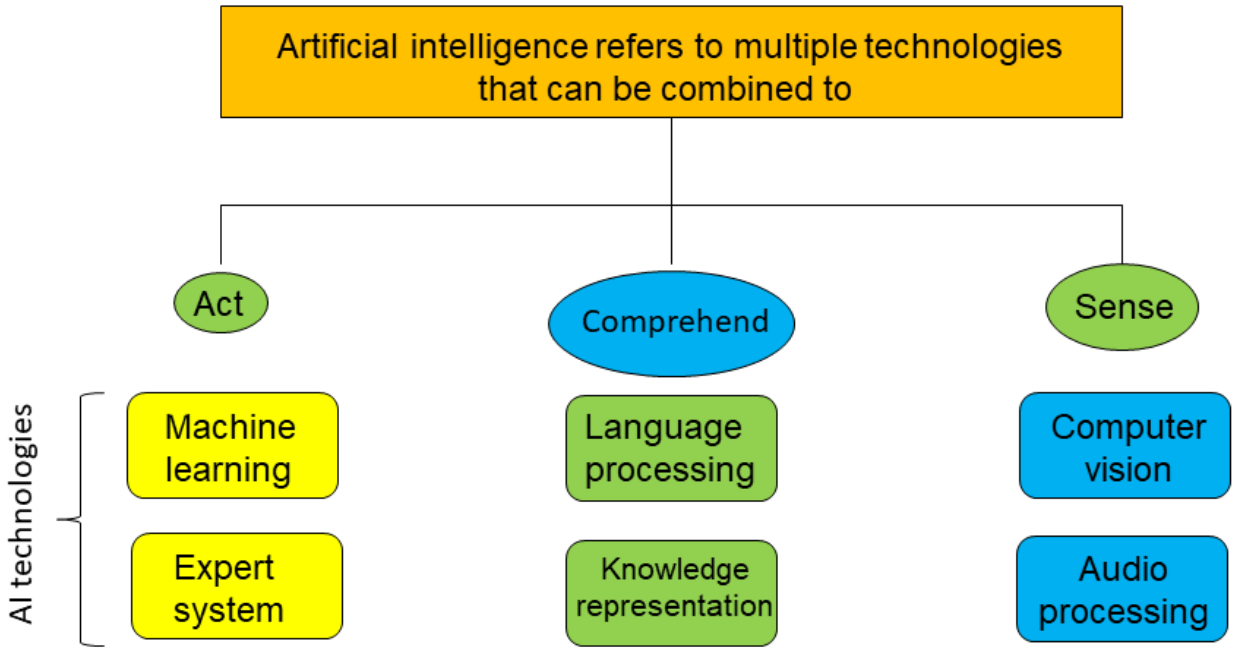

Fig.2.Representation of artificial intelligence

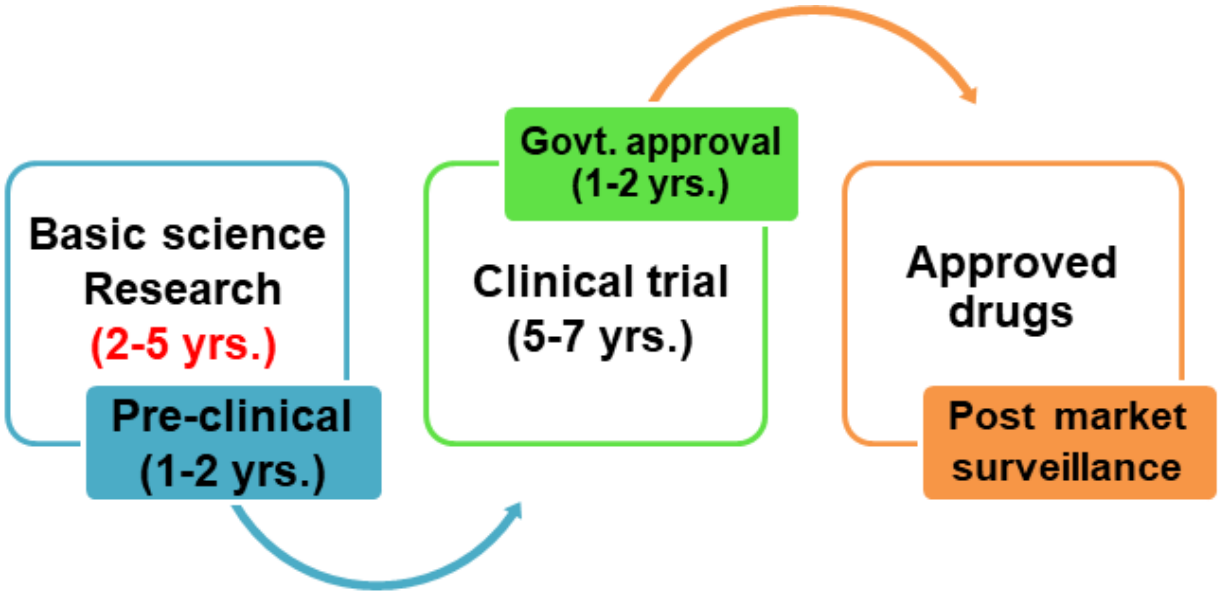

Fig.3.Process of drug development

RESEARCH ARTICLE

Studies on Inter Polymer Complexation of Chitosan Carboxymethyl Derivative of Polysaccharide for Colon Targeted Drug Delivery

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ABSTRACT

Colon-targeted drug delivery has been the focus of increasing the availability of drug therapy for local and systemic. Colon-specific drug delivery is currently a popular therapy option for significant local diseases such as ulcerative colitis, inflammatory bowel disease, colon cancer, and other infections. Before compressing the granules, tapped bulk density (TBD), loose bulk density (LBD), compressibility index, angle of repose and drug content were all assessed. The angle of repose was determined using the funnel method. The cylinder method was used to determine tapped density, bulk density and Carr's index. Compatibility studies were carried out to determine drug and polymers interaction. UV-spectroscopic and FT-IR investigations were used to determine the compatibility of drug and polymer. Post compression parameters were evaluated by using approved methods. In addition, stability studies and in vitro drug release studies were conducted. When compared to other formulations, in vitro dissolution studies revealed that the formulation of mesa amine matrix tablets with polysaccharides had good release behavior in the colon (99.83%) and controlled release in the stomach and intestine. Chitosan and carboxymethyl tamarind kernel polysaccharide (CMTKP) were discovered to be effective carriers for mesalamine administration to the colon in the form of matrix tablets in this work.

Keywords: Mesalamine, matrix, chitosan, colon drug delivery system, carboxymethyl tamarind kernel polysaccharide

INTRODUCTION

Controlling the delivery of drug substances inside the body has been a prominent challenge in pharmaceutical sciences in recent decades. The growing recognition of the essential requirement to localize drugs in particular body regions such as the colon is a major motivation for the advancement of controlled release delivery systems [1, 2]. The colon is located at the end of the alimentary canal and is hard to access since orally administered colonic delivery systems have a lot of complications [3, 4]. Colon-targeted drug delivery is most desirable and preferable for the administration of the drug for the systemic and local effect for better drug delivery and effectiveness which results in good health and well being of patients. It is ideal for local treatment of intestinal disorders such as Crohn's disease, ulcerative colitis, and amoebiasis [5]. Drug absorption and degradation in the upper GI tract are the big concerns with delivering drugs to the colon. So to better treat colon diseases, research interest has sparked in the area of colonic delivery. The colon drug delivery system (CDDS) can protect the drug release and absorption from the stomach as well as the small intestine. Peptides and protein drugs are well absorbed in the colon region. In addition, drug molecules that are poorly absorbed may have higher bioavailability in this site. In addition, the colon has a longer retention time and is more vulnerable to drugs absorption enhancers. [6, 7]. Thus, CDDS could be a significant starting point for colonic absorption thereby prolonging the targeting of dosage forms [8, 9]. To obtain a low drug release rate or elongation in release durations, the easiest strategy to deliver medications to the colon is to use greater layers of standard enteric coatings or incredibly slow releasing matrix [10, 11]. Mesalamine (5-aminosalicylic acid), an anti-inflammatory drug, is used to treat ulcerative colitis and Crohn's disease via the oral and rectal routes [12]. In the present study, a mesalamine oral colon targeted tablet was formulated by using natural polymers like chitosan, tamarind kernel powder and evaluated for its *in vitro* drug release.

MATERIALS AND METHODS

Reagents and Chemicals

Mesalamine was achieved as a gift sample from Cosomo Pharmaceutical, Goa, India. Tamarind keernel powder, chitosan, insulin, amylose, starch were purchased from Ganesh Polymers Pvt. Ltd, Mumbai, Shrividya Enterprises, Mumbai, Molychem, Mumbai, Loba chemical, Mumbai, Research Lab. Islampur, India respectively. S. D. Lab. Kolhapur, India, provided pectin, microcrystalline cellulose, magnesium stearate, and talc.

Preformulation Study

Drug And Polymers Compatibility Studies

Prior to the development of dosage forms, the pre-formulation study of mesalamine and mesalamine-polymer (1:1) was performed by using UV (UV-1800 Shimadzu, Japan) and FT-IR spectroscopy (FT-IR-410 Jasco Japan) [13,14].

Pre-Compression Parameters

The tapped bulk density (TBD), loose bulk density (LBD), angle of repose and compressibility (Carr's) index of the granules were evaluated. The angle of repose was evaluated using the funnel method. The cylinder method was used to calculate bulk density and tapped density. Carr's index (CI) was determined by using the following equation [15].

$$\text{Carr's index} = (\text{TBD}-\text{LBD})\times 100/\text{TBD}.$$

Method of Preparation of Tablet

Mesalamine (400 mg), chitosan (15-30 mg), carboxymethyl tamarind kernel powder (CMTKP, 15-30 mg), microcrystalline cellulose (15-30 mg), magnesium stearate (15-30 mg), starch paste (3 mg), and talc (1 mg) were mixed properly to prepare granules by wet granulation method. The drug and polymer were mixed with proper portion followed by the addition of other excipients. The granules were sieved (sieve no. 10) before being dried in a

hot air oven. After that, it was mixed with magnesium stearate and talc before being put through a tablet punching machine (Karnavati, Mini-II MT, 12 stations) to form tablets [16, 17, 18].

Post-Compression Parameters

Shape, colour, uniformity, thickness, hardness, weight variation, friability, drug content uniformity, *in* vitro dissolution tests, and stability tests (CHM10S Remi Instruments) were all performed on the produced tablets. [15]. A Monsanto hardness tester was used to determine the hardness of the tablets. A friabilator was used to test the friability of tablets (Roche friabilator). A Vernier caliper (Mitutoyo, Japan) was used to measure the thickness of the tablets. The official procedure (USP) was used to conduct the weight variation test [19, 20]. The drug content was measured using a spectrophotometer (UV-1800 Shimadzu, Japan) at 230 nm. Finally, stability and *in vitro* drug release experiments were performed.

Shape and Color of Tablets

The shape of uncoated tablets was studied with a lens and the color was assessed by exposing the tablets to light [21].

Uniformity of Thickness

A micrometer (Mitutoyo, Japan) was used to measure the thickness of each tablet, allowing for precise measurements and providing information on variation between tablets [22].

Hardness Test

To withstand mechanical shocks during manufacture, packaging, and transportation, tablets must have a specified level of strength or hardness as well as resistance to friability. The tablet hardness was determined using a Monsanto hardness tester. The mean and standard deviation values were calculated after three tablets were randomly selected from each formulation, and the results were reported in Kg/cm^2 [19].

Friability Test

Friability test was performed by subjecting the tablets to mechanical shock or attrition; the surfaces are impaired and/or exhibit traces of coating or breakage by using a friabilator (Roche friabilator). Initially, 10 tablets were weighed and placed in the friabilator ($W_{initial}$). The friabilator was run for 4 minutes at 25 rpm or up to 100 revolutions. The tablets were weighed once more (W_{final}) and the percentage of friability was computed [19].

$$F = (W_{initial}\text{-}W_{final} \times 100) / W_{initial}$$

Weight Variation Test

Each formulation tablets were chosen at random and weighed independently to verify for weight variation as specified by USP [24].

Drug Content Uniformity

Five numbers of tablets were randomly selected and weighed appropriately, with the average weight each tablet recorded. One by one, the tablets were ground into a fine powder. In a 50 mL volumetric flask, accurately weighed tablet powder equivalent to 400 mg of mesalamine was deposited, and 0.1 N HCl was poured up to the mark. The solution was filtered after a few minutes, and the first few ml of the filtrate were discarded. From this 5 ml of filtrate was taken and then diluted up to the mark with 0.1 N HCl in a 50 ml volumetric flask. The solution was filtered after a few minutes and the first few ml of the filtrate were discarded. In addition, 5 mL of the filtrate was poured into a 50 mL volumetric flask, diluted with 0.1 N HCl to the appropriate concentration, and spectrophotometrically examined at 230 nm (UV-1800 Shimadzu, Japan) [25].

Drug Release Studies

In vitro Dissolution Studies Using Goat Cecal Content

USP dissolution was used to conduct drug release tests in the presence of goat cecal. Experiments were conducted in a 250 mL beaker filled with water and kept in the dissolution test apparatus' jars. Initial experiments were conducted

in 150 mL of 0.1N HCl (pH 1.2) for 2 hours. After that, 50 ml of 0.2M trisodium phosphate was added to the dissolution media, the pH was changed to 6.8, and the experiment was continued for another three hours. Then after, 4 and 8 g of goat cecal content were added to 1000 ml of buffer (pH 6.8), resulting in a final cecal dilution of 2 and 4 percent, respectively. Dissolution in the cecal content media was continued for a total of 24 hours [27].

Stability Study of Optimized batch

Drug stability refers to a formulation's ability to stay within its physical, chemical, therapeutic, and toxicological characteristics while stored in a certain container. Stability testing shows how the quality of a drug or drug product changes over time as a result of environmental factors such as temperature, humidity, and light, allowing for the estimation of ideal storage settings, re-test periods, and shelf life. The ICH specifies the research period and storage conditions for long-term testing (25°C ± 2°C; 60% RH ± 5% for 12 months, and expedited testing at 40°C ± 2°C; 75 % ± RH 5% for 6 months). Stability studies for the selected formulations were done in the current study at 40°C± 2°C; 75 % RH ± 5 % for a specific timeframe up to 30 days.

Data Analysis

To explore the mechanism of release and release rate kinetics of the dosage form, the data were fitted into zero-order, first-order, Higuchi matrix, Peppas, and Hixson Crowell models with PCP-DISSO-V2 software [28]. The r-value was used to select the best-fit model.

Zero-Order Kinetics

If the area remains constant and no equilibrium conditions are achieved, the following equation can be used to depict drug dissolution from pharmaceutical formulations that do not disaggregate and release the drug gradually:

$$Q_t = Q_o + K_o t$$

Q_t= amount of the drug dissolved in time t, Q_o = initial quantity of drug in the solution, and K_o= release constant (zero-order).

First-Order Kinetics

The release rate data were fitted to the following equation to explore first-order release rate kinetics:

$$\text{Log } Q_t = \log Q_o + K_1 t/2.303$$

Q_t = amount of drug released in time t, Q_o = initial quantity of drug in the solution and K_1 = release constant (first-order).

Higuchi Model

Higuchi developed several theoretical models to investigate the release of water-soluble and low-soluble drugs buried in semisolids and/or solid matrices. For drug particles dispersed in a uniform matrix acting as diffusion media, mathematical equations were discovered, and the formula is

$$Q_t = K_H \cdot t^{1/2}$$

Q_t = drug amount released in time t, K_H = Higuchi dissolution constant.

Krosmeyer and Peppas Release Model

To explore this model, the following equation is utilised to fit the release rate data:

$$M_t/M_\infty = K \cdot t^n$$

Mt/M_∞ = fraction of drug release, K = release constant, t = release time and n = diffusional coefficient for the drug release.

Formulation Design

A total of 9 distinct formulations of mesalamine colon targeting tablets have been developed based on a compatibility investigation of API (mesalamine) and excipients (Table 1).

RESULT AND DISCUSSION

Preformulation Study

The solution of mesalamine in 0.1N HCl exhibited UV absorption maxima at 229 nm (Figure 1) and the same has been reported in the literature. The identity of mesalamine, chitosan, and CMTKP were established by comparing IR peaks for corresponding functional groups (Figure 2) with the standard reported in the literature. Thus, it has been proved that meselamine and excipients were free from adulteration and used for formulation.

UV Compatibility Study

The compatibility study of the substances was carried out by using a UV spectrophotometer at the initial, second, and fourth weeks. The scanning values were found in the range of 230 nm. This result remains constant throughout testing. Therefore it was enough to deliberate that the drug was compatible with given excipients (Table 2).

IR Compatibility Study

IR spectrum of drug and physical mixture of drug with excipients showed characteristic peaks of the corresponding functional group. It indicated that the drug and excipients had no major interaction. Therefore it was enough to deliberate that the drug was compatible with given excipients (Figure 3).

Pre-Compression Study

The bulk densities and tapped densities of all batches of mesalamine matrix coated tablet blend ready for compression were found to be in the range of0.453- 0.470 gm/ml and 0.568-0.575 gm/ml respectively. This value of bulk densityindicated a good packing character of the final blend. The value of the Hausner ratio was less than 1.6 which indicated good flow properties. The compressibility index for all these formulation blends was found to be below 25% indicating fair to good flow properties. The angle of repose gives a qualitative assessment of the internal cohesive and frictional effect when external loadings are small, such as in powder mixing or tablet die filling. All of these formulation blends had an angle of repose of between 23.1 ± 0.17°-25.3 ± 0.17°, suggesting that the angle of repose was within acceptable limits (Table 3).

Post-Compression Evaluation Of tablets

For mesalamine matrix-coated tablets, post-compression factors such as thickness, hardness, friability, weight fluctuation, drug content and stability were investigated. The results showed that all the formulations comply with the pharmacopoeial standards (Table 4 and 5). Various trial batches of mesalamine with different concentrations of polysaccharide polymer were formulated to decide the composition of the mesalamine tablet. The matrix-coated tablet was formulated to achieve the desired controlled drug release after 24 h. It was observed that the polysaccharide polymer of mesalamine from the F-5 batch was found to be a cumulative release of 99.83% at the end of 24 h (Figure 4). These results were due to the optimum concentration of polysaccharides above this concentration changes were observed in drug release before and after 24 h. Thus the results of the study showed that the increase or decrease in chitosan and CMTKP concentration caused drug release before and after 24 h. Thus the composition of batch F-5 was selected for further work for the optimization.

Study of the Regression Coefficient (r^2) of Different Kinetic Models

The *in-vitro* drug release data of the final optimized batch F-5 was fitted into different kinetic models to determine the mechanism of drug release. The correlation coefficient (r^2) was used to evaluate the model that best suited the release data (Table 6). After comparing the regression coefficient (r^2) values of different kinetic models, the regression coefficient value of the Korsmeyer-Peppas model was found to be best fitted for theseformulations.

Factorial Design with Surface Plot & Optimization of Process Variables

To evaluate the selected response, an interactive statistical second-order complete model equation was developed with Y as the predicted response, b0 as the arithmetic mean response of 9 runs, and b1 as the estimated coefficient for the factor X1. The principal impacts represent the average outcome of changing one factor from a low to a high value one at a time (X1 and X2). When two factors are changed at the same time, the interaction (X1X2) shows how % drug release and time of formulation release change, and the exponential terms (and) reflect curvature. From the experiment's results, the coefficients for linear effects (b1 and b2), interaction (b12), and quadratic effects (b11 and b12) were calculated (Design expert 8.0.7.1). The 9th batch experiments 2nd h drug release (%) (Y1), 5th h drug release (%) (Y2), and 24thh drug release (%) (Y3) were utilized to construct predictor equations for mesalamine, with independent variables such as chitosan concentration (X1) and CMTKP concentration (X2) (Table 7). Multiple regression analysis and the analysis of variance test (ANOVA) results were summarised.

Equation in Terms of Actual Form

2rd h drug release **(%)** = 2.226667 + 1.126667 X A[1] – 0.24 X A[2] + 1 X B[1] -0.22556 X B[2] -0.28667 X A[1]B[1] +0.32 X A[2]B[1] + 0.325556 X A[1]B[2] -0.17444 X A[2]B[2]

Equation in Terms of Actual Form

5th h drug release **(%)** =4.151481 + 1.627407 XA[1] – 0.26037 X A[2] + 1.498519 X B[1]-.40148 X B[2] -0.78407 X A[1]B[1] + 0.253704 XA[2]B[1]+0.485926 X A[1]B[2]+A[2]B[2]

Equation in Terms of Actual Form

Time of release= 95.37296+3.717037×A[1]+ 0.68037× A[2] +3.354815 × B[1] + 0.262593 × B[2] 3.50481× A[1]B[1] -0.84481 × A[2]B[1] -0.09926 × A[1]B[2] –3.067407 × A[2]B[2]

The 2nd, 5th, and 24th h drug release time showed r^2 values of 0.9922, 0.9636, and 0 .9893 respectively. Moreover, for all batches, there was a reduced disparity between predicted and actual values, indicating good agreement for the use of the quadratic model for optimization. According to the surface response curve, both polymer concentrations have a significant impact on the formulation's % drug release. Drug release decreases when the concentration of chitosan increases, but drug release decreases as the concentration of CMTKP increases. The surface response curve reveals that both polymer concentrations have a considerable impact on the formulation's percent drug release. As the concentration of chitosan increases, the time of the release of the formulation increases whereas an increase in the concentration of CMTKP shows an increase in release period. ANOVA indicated the contribution of factor X1 (concentration of chitosan) is higher than factor X2 (concentration of CMTKP) for optimizing the 2nd h drug release (%) and the contribution of factor X2 (concentration of CMTKP) is higher than factor X1 (concentration of chitosan) for optimizing the 24th h drug release (%) and release period. As a result, the best batch was identified as batch no. F-5 which had a medium level of chitosan concentration (X1, 0) and a maximum level of CMTKP concentration (X2+1) (Figure 5).

CONCLUSION

The inter polymer complexation of Chitosan-CMTKP can be used to formulate matrix coated tablets of mesalamine, an anti-inflammatory agent. The polymer and excipients included in the formulation were found to be compatible with the drug (mesalamine) using infrared spectral analysis. For all formulations, post compression evaluation such as hardness and friability suggested that the tablets had good mechanical resistance. Pharmacopeial Standards were found to be met in terms of percentage weight variation and drug content uniformity 99.83 % of the drug was released at the end of the 24-hour in-vitro release experiments.

DECLARATIONS

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Conflict of Interest

All the authors declare that there is no-confliction of interest among themselves.

Author's Contribution

Satish Kanar, Amulyaratna Behera, Yashwant Giri and Sachin Patil have equal contribution for the paper.

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Ethics Statement

As the work is concerned with *in-vitro* evaluation hence no requirement /issue related to ethical committee.

Informed Consent

As the work is concerned with *in-vitro* evaluation hence no requirement/issue related to ethical committee.

Data Availability

This is an original research work carried out by the authors, the data presented this paper are obtained from the experimental evaluation results.

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Table 1. Formulation of mesalamine colon targeted tablets

Ingredient	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
Mesalamine (mg)	400	400	400	400	400	400	400	400	400
Chitosan (mg)	100	100	100	150	150	150	200	200	200
CMTKP (mg)	100	150	200	100	150	200	100	150	200

MCC (mg)	235	175	135	185	135	85	135	85	35
Mg. stearate (mg)	5	5	5	5	5	5	5	5	5
Talc (mg)	10	10	10	10	10	10	10	10	10
Starch paste (mg)	50	50	50	50	50	50	50	50	50

Table 2. UV compatibility study of mesalamine and excipients

Sl. no.	Name	λ_{max} (nm)		
		Initial	after 2 weeks	after 4 weeks
1	Mesalamine + Chitosan	230	230	230
2	Mesalamine + CMTKP	230	230	230
3	Mixture	230	230	230

Table 3.Precompression studies

Batch no.	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose	Compressibility index (%)	Hausner ratio
F-1	0.395±0.11	0.450±0.17	23.96±0.16	11.63±0.18	1.13±0.14
F-2	0.395±0.18	0.469±0.11	23.49±0.12	15.77±0.13	1.18±0.09
F-3	0.407±0.13	0.474±0.16	24.44±0.17	14.18±0.23	1.16±0.21
F-4	0.388±0.11	0.465±0.13	23.70±0.06	16.66±0.14	1.20±0.07
F-5	0.386±0.07	0.458±0.11	22.83±0.19	15.83±0.11	1.18±0.04
F-6	0.398±0.21	0.465±0.17	23.38±0.11	14.30±0.15	1.16±0.13
F-7	0.386±0.13	0.452±0.19	23.19±0.14	14.50±0.09	1.17±0.08
F-8	0.381±0.17	0.452±0.09	23.38±0.21	15.64±0.11	1.18±0.11
F-9	0.394±0.09	0.456±0.17	23.70±0.14	13.63±0.16	1.15±0.14

Table 4. Post-compression study of mesalamine tablet

Batch no.	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Weight variation (mg)	Drug content (% w/w)
F-1	4.0± 0.02	9.6±0.07	0.55±0.02	885.2±0.21	100.57±0.11
F-2	3.9 ±0.03	9.4±0.09	0.52±0.05	883.0±0.54	99.56±0.27
F-3	4.1± 0.02	9.8±0.14	0.60±0.05	899.6±0.96	99.89±0.51
F-4	4.0 ±0.02	9.7±0.18	0.66±0.06	891.5±1.13	99.91±0.21
F-5	4.1± 0.02	9.9±0.11	0.47±0.04	897.3±0.78	99.83±0.18
F-6	4.0±0.008	9.8±0.13	0.77±0.06	881.1±0.38	98.96±0.34
F-7	4.1±0.03	9.4±0.21	0.83±0.07	880.9±1.13	99.76±0.26
F-8	4.0±0.009	9.7±0.11	0.86±0.03	900.2±0.97	98.86±0.41
F-9	4.1±0.009	9.5±0.07	0.74±0.04	893.3±0.87	99.91±0.76

Table 5. Stability study of optimized batch

Sl. no.	Parameter	Batch no. 5
1	Appearance	No change
2	Hardness	9.9±0.012

3	Drug content	101.56±0.09

Table 6.Correlation coefficient (r^2) values of different release kinetic models for mesalamine tablet (F-5)

Sl. no.	Release kinetic models	Correlation coefficient (r^2)
1	Zero order plot	0.993
2	First order release	0.865
3	Higuchi model	0.939
4	Korsmeyer-peppas model	0.997

Table 7. Actual and predicted response for studied parameters of meselamine tablet

Batch No.	2nd h drug release (%)		5th h drug release (%)		24th h drug release (%)	
	Actual	Predicted	Actual	Predicted	Actual	Predicted
F-1	4.23	4.0666	6.56	6.4933	99.11	98.94
F-2	3.56	3.4533	5.91	5.8633	99.41	99.2533
F-3	2.63	2.54	5.11	4.98	99.56	99.0766
F-4	3.24	3.3066	5.76	5.6433	98.23	98.5633
F-5	1.65	1.5866	3.73	3.5533	99.73	99.383
F-6	1.14	1.0666	2.96	2.4766	91.12	90.2133
F-7	2.34	2.3066	4.89	4.8133	98.83	98.68
F-8	0.97	0.9633	1.96	1.8333	89.23	88.27
F-9	0.86	0.75	1.65	1.7066	86.79	85.9766

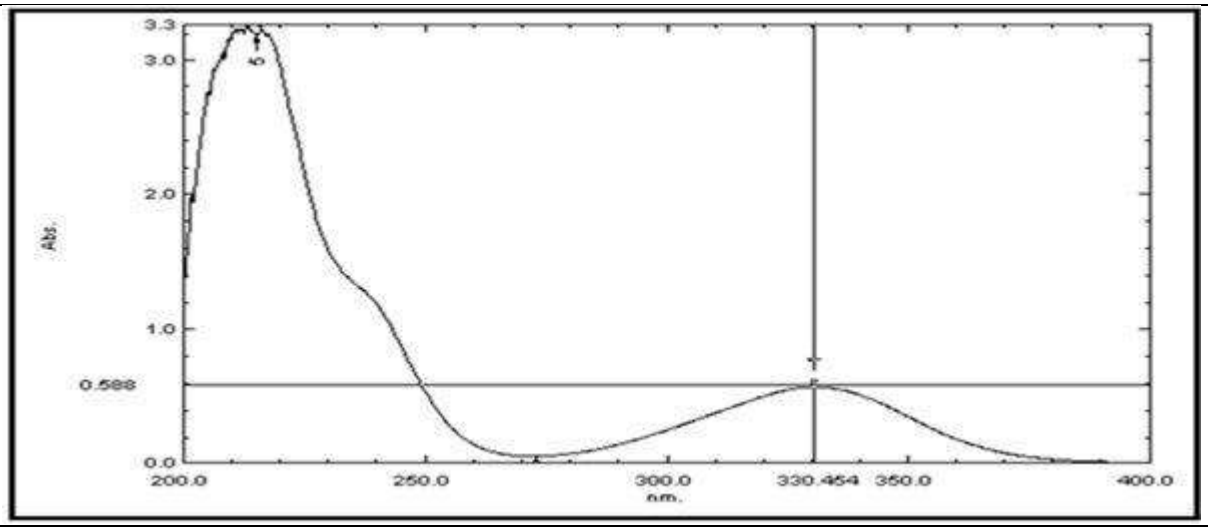

Figure 1. UV Spectrum of Mesalamine

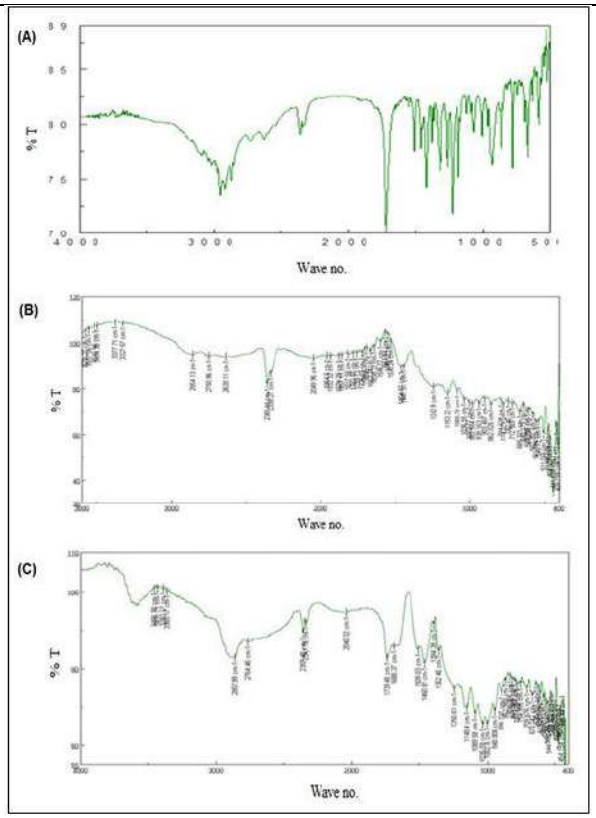

Figure 2.A-C. FT-IR spectrum of Mesalamine, chitosan and carboxymethyl tamarind kernel powder.

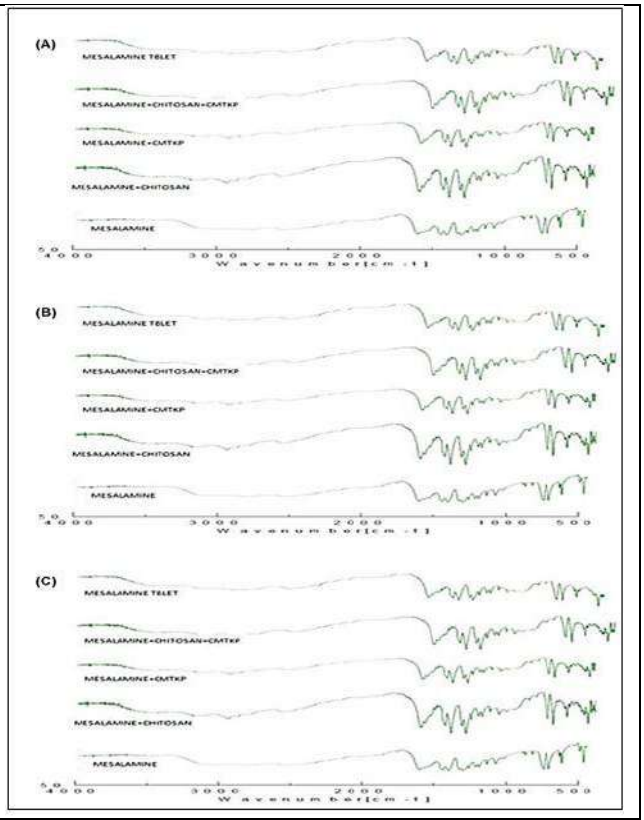

Figure 3.FT-IR compatibility study of Mesalamine, chitosan and carboxymethyl tamarind kernel powder.

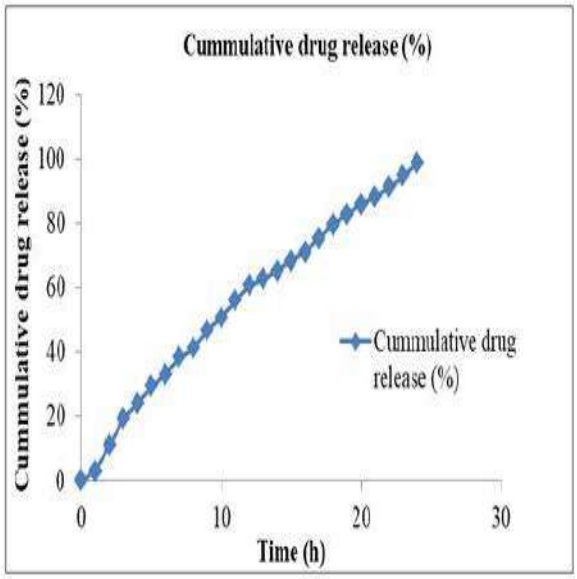

Figure 4. Drug release study after 24h

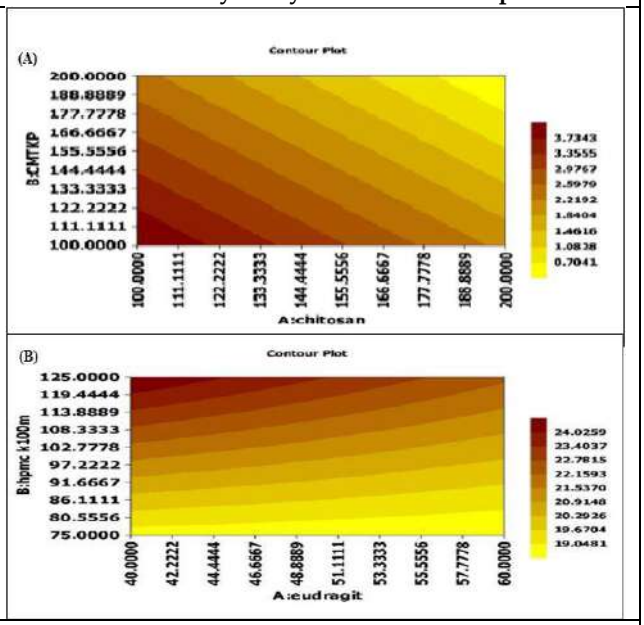

Figure 5. Contour plot of 2nd and 24 h drug release.

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REVIEW ARTICLE

A Short Review on Infectious Disorders: Transmitted through Various Pathway

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ABSTRACT

Infection a short term but having a large capacity to became deadly disease conclusion. It may cause through various way and by several infectious micro-organisms present in human surrounding environment. Infection can caused by invasion of various microbes in to human body through various pathway. These organisms may virus, bacteria, fungus and Parasite. Microbes invade the host cell in various circumstances like if people came in to contact with some infectious organism present over anywhere. Pathogenic Microbes can invade and multiply itself and live inside host cells and started to spread infection inside the body. People may feel some physical changes during the infection spreading phase. People should be aware about these infection types and causing agents also prevention properties. Strategy for gathering knowledge about infectious agents, different pathway of infection and its prevention is presented through this short review.

Keywords: Pathogenic Microbes, Infection, infectious agents

INTRODUCTION

The state or a condition produced by more than one pathogenic microbes on a host body is called infection. It caused by various micro-organisms present over everywhere in this surroundings. Microbes are generally survives in and on human bodies which are generally harmless. An infection can caused by some harmful agents, that may produced toxins which can caused several infectious disorder. These infectious disorder may arises through transmission of infectious agents produced by harmful microbes, also known as transmissible or communicable diseases. Pathogenic

organisms can invade the host body by several ways such as through air, water, soil, food, contact with infectious body fluids. Microbes can enter through broken skin, eye, nasal cavity, oral cavity or through some medical devices such as used needles, catheters etc. Infection generally occurs when germs enter the body, increase in number, and cause a reaction of the body. There are several types of infections occur in human being such as, waterborne diseases, air borne diseases, nosocomial infections, zoonotic or vector-borne disorder, Sexual transmitted infections which may caused by bacteria, virus, fungus, Parasites etc. Clinical sign and symptoms of infectious disorder, such as various tissue injury, inflammation on skin, cough, fever, itchy dermis. These physical changes occurs after invasion of pathogenic organisms in to the host body and they started replication and cell destruction that stimulate severe cell damage which leads systemic sickness.

Prospective Study of Infectious Disorders

Types of Infections

Microbes can cause different types of infections such as: Primary & secondary infection, Reinfection, Focal infection, Nosocomial infection, Opportunistic infection, Iatrogenic infection, Endogenous infection, Exogenous infection, Inapperant or sub-clinical infection, Atypical infection, Latent infection, Local and Systemic infection [1].

Primary infection: This is a type of infection which occur during first time of expose with any pathogenic organism. During this condition body has no innate defense against causative unknown organism such as antibodies .

Secondary infection: One type of infection that occurs when primary infection has made a person more susceptible to disorder.

Reinfection: This type of infection also called recurring infection. Reinfection defined as a reappearance of infection within at least 6 months after any infection.

Focal infection: In present medical consensus, this is a localized infection, often asymptomatic, that causes diseases elsewhere in the host, but focal infection are completely infrequent and limited to clear uncommon disorders.

Nosocomial infection: This is also called hospital associated or hospital acquired infection occur during the process of treatment in any health care section. In this case patient admitted for any treatment have to stay long time in hospital, at that time many causative organism make sick the admitted patient by different source of infection.

Opportunistic infection: This type of infection occurs frequently and get more worsen in people with weakened immune systems than in people with healthy immune systems example HIV.

Iatrogenic infection: It is an infection otherwise called drug induced disorder. In this condition sometimes patient may affected with some adverse reaction by medical treatment. It is usually results from a negligence made in treatment or diagnosis.

Endogenous infection: This is a type of chronic infection caused by an overgrowth of organism that are normally affected genital tract.

Inapperant or Sub Clinical Infection

Atypical infection: Researchers considered that bacteria as being atypical if they are hard to detect through standard bacterial methods. The infection is caused by different bacteria than the more common ones that cause pneumonia.

Latent infection: A type of hidden, inactive or dormant infection. Generally it means that residence in the body of a specific infectious agent without any manifest symptoms.

Local infection: This is generally a localized infection which occurs in a specific region, which affects a specific organ or area of a body part.

Systemic infection: It means an infection affecting the entire body, rather than a single organ or body part such as hypertension, Serositis, SLE etc.

Harmful and Disease Causing Organisms

Micro-organisms found in our environment not only harmful but also useful for human health. Infection occurs when harmful causative agents enter in to host body and replicate inside the living cells. In response to an infection, WBCs started activating and produced antibodies against the foreign invasive agent and leads to appear several

symptoms previously discussed as fever, cold, cough, vomiting etc. There are several categories of harmful micro-organism are present in our surroundings. These agents of infection can be divided in to different groups on the basis of their size, biochemical properties in which they interact with the host body. such as: Virus, Bacteria, Fungus, Parasite etc.

Virus: A submicroscopic small collection of genetic code surrounded with protein layer , may be DNA or RNA. It cannot replicate alone so it takes components of host cells by infecting host body. Sometimes in the process of replication it may damage host body parts. Viruses can not destroy by antibiotics because it does not contain components like bacteria. So only antivirals and vaccines can reduce the cell severity [2].

Bacteria: It is a single celled organism present over everywhere in our environment. It can survive in every whether condition. There are different types of bacteria present in the environment. Some of them are healthy and useful bacteria but some of them are highly toxic and may cause various types of infections [3].
Fungus: Most of the fungus saprophytic and may not cause any disease but some are phytopathogenic organism which can cause infections [4].
Parasites: Parasites are the organisms which spread infections by intestinal helminths and protozoan parasite act like vector of infections. They usually live off other organisms, hosts to survive. This types of infections usually found in contaminated food, water or bug bites [5].

Pathway of Infection

Transmission pathways are divided in to main six route.

1. **Aerosol transmission:** It is a very easy spreadable disorder. Infectious agents may spread through air by coughing, sneezing droplets (fig. 1) [6]. SARS-CoV-2 is now a days found a highly infectious disorder which is spread through air by inhalation of carrying droplets and aerosol particle spread by infected patients.
2. **Oral Ingestion transmission:** 80% of ingestion infection caused due to Unhygienic hands, food and drinking water which contamination occurring through human sewage (fig. 2). Under developed areas are high in risk due to unhygienic habit [8]. Flies are a causative source of transmission through oral ingestion by in taking contaminated food.
3. **Vector-borne transmission:** Infectious disorder transmitted through insect vector called vector borne disorder (fig. 3). Dengue, Malaria are the most well know deadly wide spread vector borne disorder. These infection generally transmitted through insect bite [9]. Insects like mosquitoes used to bite the infected person with Dengue, malaria and then same insect bite again to normal healthy person and they spread the infection in to the blood.
4. **Fomite transmission:** This is a type of infection widely spread over environment. Infected person is here act like career or play a critical role as a spreader of infection (fig. 4) [10].
5. **Zoonotic transmission:** Infection transmitted from animal to human in various way is called zoonotic disorder. It can be transmitted from vertebrate animal (fig. 5) [11].
6. **Sexual transmission:** This is a infection generally found in adult and new born baby. These infections generally occur due to sexual contact with infectious male and female. Example: Gonorrhea, Syphilis, Trichomoniasis, Chlamydia, Genital herps etc [13].

Prevention

Precautions should be taken by human being to avoid infectious disorder caused by several infectious agents. Infection causing agents such as bacteria, virus, parasites and fungus can survive everywhere and multiply infections as it is. Strong precaution technique should be regulate by human being to prevent water, air and hospital borne disorder.
Those prevention criteria are:
1. Ensure water is free from silt and visibly clean.
2. Drinking water should be purely filtered through water purifier and ensure store water is free from germ.

3. Regularly wash hands with soap before preparing and eating any food.
4. Always take a shower after returning to home.
5. Ensure food and vegetable thoroughly cleaned before cooking.
6. Avoid street food and drinking water.
7. Take vaccination for improve immunity against infectious disease like: Hepatitis, Polio, Typhoid.
8. Use disposable plates and glass whenever eat outside.
9. Use sterilized masks when travel outside.
10. Try to avoid public toilet.
11. Being a medical profession always were PPE to avoid contact with any infectious agent.
12. Isolate by own to avoid contamination by you to healthy person after getting any infection.
13. Avoid unprotected and unhygienic sexual habit.
14. Use mosquito net and mosquito protection gel for avoiding vector transmission.
15. Biomedical waste should be dispose properly.
16. Avoid half cooked or raw non veg diet.
17. Maintain clean and hygienic washroom for regular use.

CONCLUSION

Infectious disorder may transmitted through various pathway and some of them are deadly and non curable. All micro organisms are not healthy for human, some of them are highly toxic and harmful. They transmitted very easily and treatment is very complication to eradicate completely. Overall above study giving idea about types of infection transmission pathway and precautions of various infectious agents causing transmitted disorder. Good Health is very much important for sustainability of healthy global and this is possible if we know how to control or prevent the infection causing pathways which is a helping element to maintain good health and well-being and this awareness satisfies the goal of SDG no. 3.

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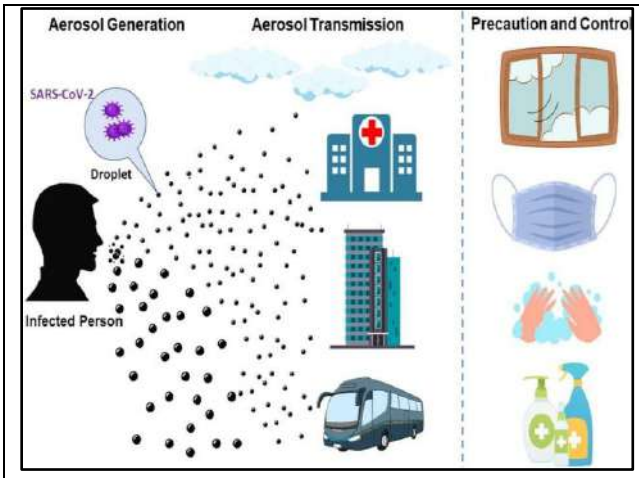

Fig. 1: Aerosol Transmission (Source: Tang *et al.*, 2020) [7]

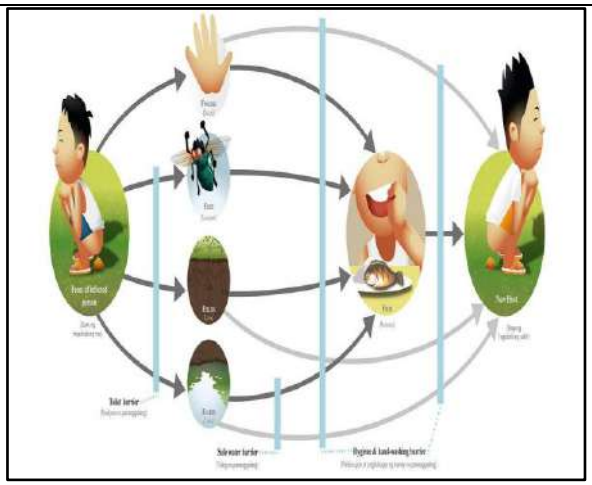

Fig. 2: Oral Ingestion transmission (Source: Wikipedia)

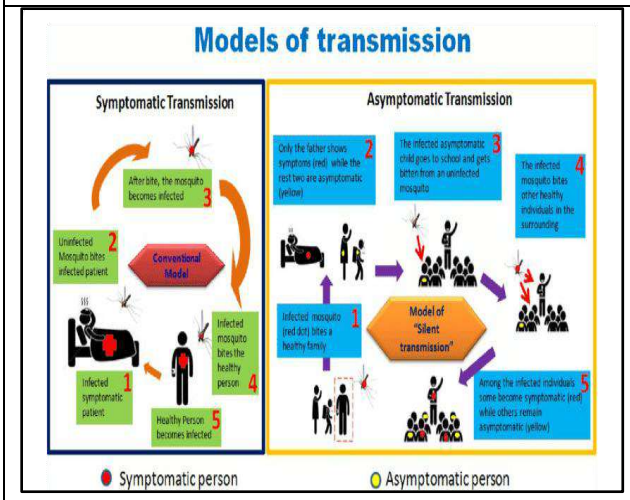

Fig. 3: Vector-borne transmission (Source: Singh *et al.*, 2016)

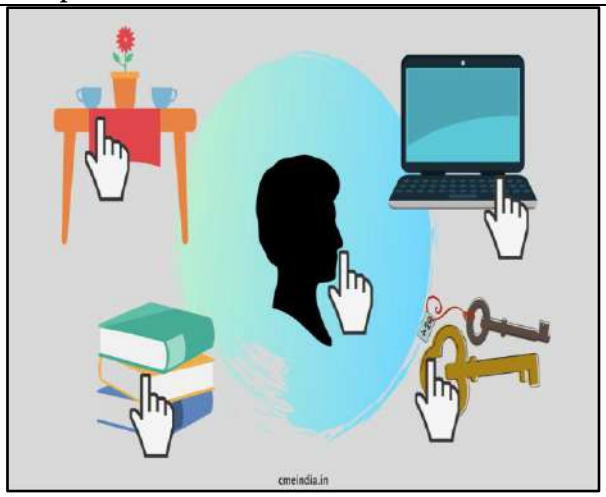

Fig. 4: Fomite transmission (Source: cmeindia.in)

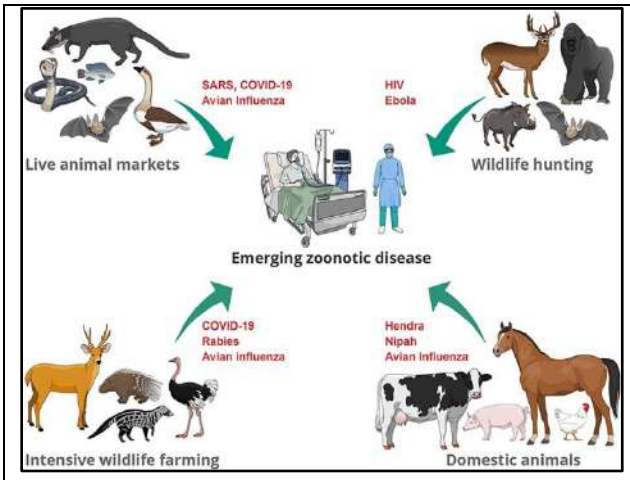

Fig. 5: Zoonotic transmission (Source: Magouras *et al.,* 2020) [12]

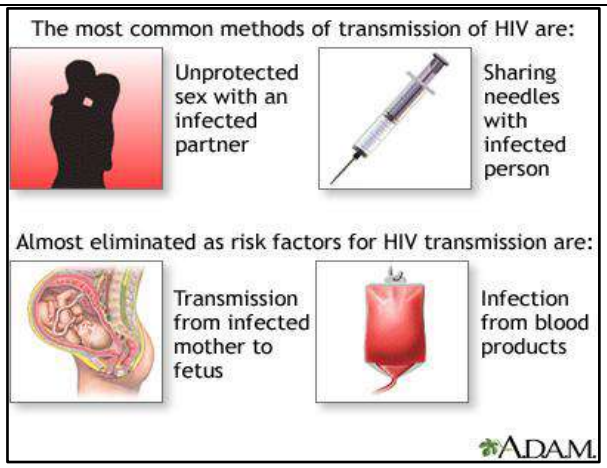

Fig. 6: Sexual transmission (Source: stlukes-stl.com)

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RESEARCH ARTICLE

Kepler Exoplanet Search Results using Machine Learning Classification Model

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ABSTRACT

The Kepler exoplanet mission is specially organised for searching of the Milky Way galaxy to discover many earth-size and tiny planets near or in the habitable zone. Exoplanet means orbiting of planet around the other stars beyond our solar system. The dataset contains 9564 samples and 50 columns which is collected from Kaggle website. The dataset, target variable is KOI-disposition which contains confirmed, false positive and candidate. Out of 9564 samples we found 5000 samples are false positive, each confirmed and candidate are 2282. In the Milky Way galaxy many stars and planets are there, but we have considered some of them. We have used machine learning algorithms like decision tree, random forest, KNN classification and Naive Bayes classification on stars and planets for searching of exoplanets beyond our stellar atmosphere.

Keywords: Kepler Exoplanets; Solar System; Decision Tree; Random Forest; KNN; Naive Bayes Classifier.

INTRODUCTION

The Kepler space observatory is a NASA build satellite that was launched in 2009. The telescope is dedicated to searching for exoplanets in star systems beside our own, with the ultimate goal of possibly finding other habitable planets besides our own [1]. *Kepler* alone has confirmed 2345 planets out of 4765 announced candidates [3] from its original four year mission, accounting for more than half of all planets known today [1], [2], [3], [4], [5], [6], [9].The mission results provided data on a wide range of planet and planetary systems orbiting both single and multiple stars of differing sizes, temperatures and ages.

The original mission ended in 2013 due to some technical failures, but the telescope has still been functional since 2014 on a "K2" extended mission [11], [13].The telescope is still alive and continuously collects new data on its extended mission.The main objective of our project is searching of exoplanets using Kepler data like koi_slogg , koi_impact , koi_depth , koi_period , koi_duration , koi_impact and koi_score to get the target variable i.e. koi_disposition which contain false positive , confirmed and candidate.Till the effects of these biases are correctly determined and the full range of orbital periods are considered, estimations of parent distributions come with large uncertainties. There are 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure), and 11 (Sustainable cities and Communities).

Implementation of the Model

Model implementation is a most important part for a machine learning project. Machine learning is a subset of computer science, whereby a computer algorithm learns from prior experience [10]. In this part we have to choose the columns for feature selection then remove all other unnecessary columns after that we have put machine learning algorithms to get results that which is most accurate for this dataset. This research had been done using several Machine Learning algorithms, namely, Decision Tree [7], [10], [14], and Random Forest [7], [10], [12], [14],K-Nearest Neighbours (KNN) [7], and Naive Bayes Classifier.

Decision Tree Algorithms

Decision tree (DST) [7], [8] is a tree structure, which works on the principle of conditions. It is a supervised model, which is used for both classifications as well as regression. DST has terminal nodes, branches, and internal nodes. Terminal nodes i.e. leaves are representing the target variable; branches are representing the possible values of the attributes i.e. conclusion of the test dataset and each "test" attributes are represented by internal nodes. It is a robust and effective model for predictive analysis. Decision tree means it is a decision support tool that uses a tree like model or chart to determine a course of action or represents a possible decision, outcomes or reaction.

Random Forest Algorithms

Random forest (RF) [7], [8], is a supervised machine learning model based on ensemble learning. Ensemble learning is a more powerful prediction model. The combination of same model several times or different types of model is called as an ensemble learning model. RF model combining multiple model of the same type i.e. multiple decision trees, which results a forest of trees. Therefore, it is named as "Random Forest". The random forest is a model made up of many decision trees.

K-Nearest Neighbors (KNN) Algorithm

K-Nearest Neighbors (KNN) [7] is one of the simplest algorithms used in Machine Learning for regression and classification problem. KNN algorithms use data and classify new data points based on similarity measures.

Naive Bayes Classifier

Here we used Naïve Bayes classifiers which are collection of classification algorithms based on Bayes' Theorem. It is not a single algorithm but a family of algorithms where all of them are share a common principle.

METHODOLOGY

Dataset collection is a vital thing for a project which we have collected from the kaggle website that contains 9564 samples and 50 feature columns. In this dataset we have gone through many algorithms to finding the exoplanet

which is our aim to. For the experimental purpose we have used googlecolab for running the program. Many people done this dataset using regression model but we thought for classification because of exoplanet are in categorical format.

Pre-processing

Early of pre-processing, basic dissemination of data analysis was done to find a high level understanding of the data. First of all we have looked for the proportion of the number of sample and found out that the dataset consist of equal no. of samples for each class.

Visualization

After analysed the sample we go for visualization, first visualization is based on all target variable which magnitude is lower in bright position. Then for confirmed planet only it is based on magnitude. The third graph shows us the stellar surface gravity of the Kepler planet means the base 10 logarithmic of the acceleration due to gravity at the surface of the star. The 4th figure shows the 'latitude' and 'longitude' of the objects, so this plot shows their position in the sky. The telescope pointed the same patch of sky for the entire mission and the distribution looks the way it does due to that reason. The 5th figure indicate that the orbital period is the time given astronomical object takes to complete one orbit around the other object. Most confirmed planets have lower orbital periods. This proves that the closer the planet is to its original star. The 6th plot is based on duration of star for orbiting around another star. Durations are on the order of hours, with more detection at smaller hours, again showing the detection bias towards smaller orbits. Duration is measured from first contact between the planet and star until last contact. The 7th graph indicates that the stellar effective temperature in Kelvin and also shows the photo spheric temperature of the star. The last graph i.e. 8th graph gives that stellar radius of star (solar radii) and planetary radii(earth radii). The radius of the planet is the multiplication of the star radius ratio and the stellar radius and the photographic radius of the star.

RESULT ANALYSIS

Instead looking at the visualization we simply consider on the model implementation that is much better for our project to find out the most appropriate consideration. After implementing all the model, we got the most accuracy in Decision tree model which percentage is 100. We have done model visualization to show the accuracy. The accuracy for decision tree model is 100% and for entropy is 81.06%. The random forest algorithms combine the output of multiple decision trees to generate the final output. The accuracy for random forest is 82.97%. The accuracy for KNN classification model is 66.38%. The accuracy for Naïve Bayes model is 44.29%

CONCLUSION

This paper accompanied an experiment on a dataset that contained information about Kepler objects of interests. The dataset holds features observed from the Kepler satellite. Using this dataset , basic exploration of data analysis help us to visualization the data and get a proper understanding of the data. The selection of the machine learning models were carried out depending on the binary classification with the selected model will perform comparable to other experiments with similar conditions. The models were perfectly run with cross-validation to help the best meta-parameters for each model. The Kepler journey was found out how many stars hosted planets and specially to estimate the frequency of earth like planets.

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Table 1. Decision Tree Algorithms

Decision tree Classifier	Decision Tree Classifier using Entropy
Accuracy: 1.0 Confusion matrix: [[1797 0 0] [0 1839 0] [0 0 4015]]	Accuracy: 0.81 Confusion matrix: [[798 553 446] [397 1394 48] [5 0 4010]]

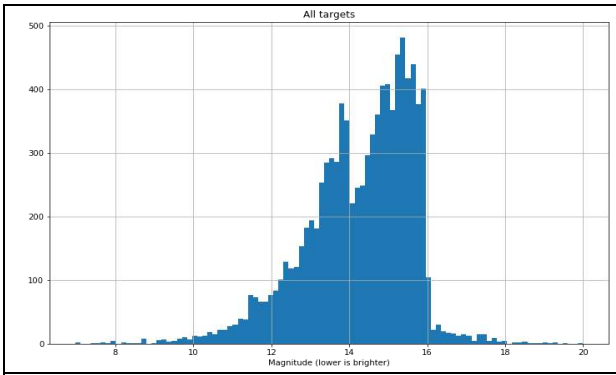

Figure-1: Magnitude wise all targets variable

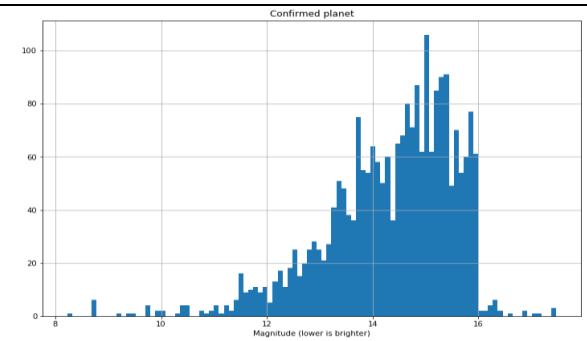

Figure-2: Available of confirmed Exoplanet

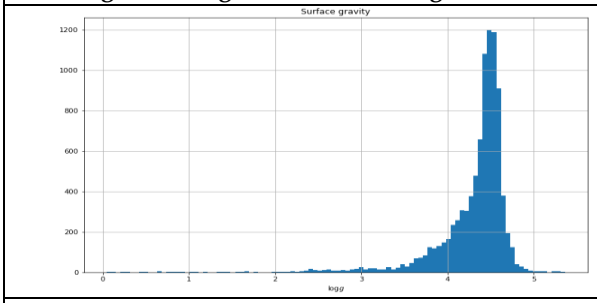

Figure-3: Stellar surface gravity of the Keplerexoplanet

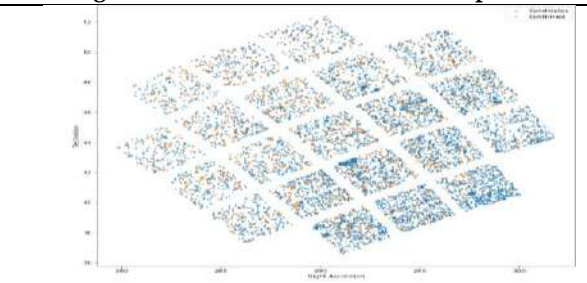

Figure-4: Position of planets in the sky

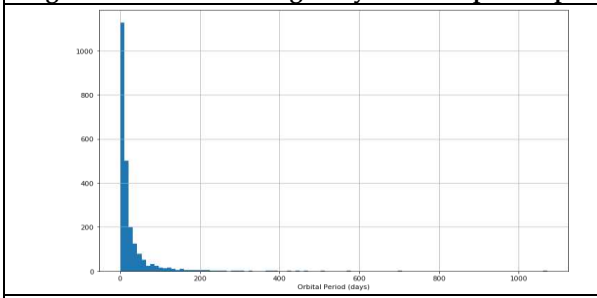

Figure-5: Orbital period in the interval of the consecutive planetary transits

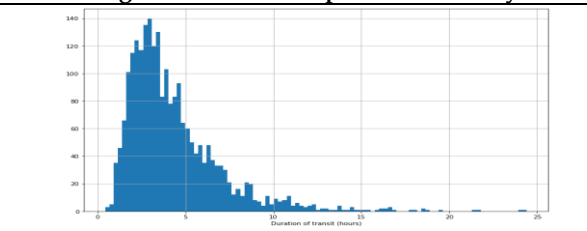

Figure-6: Observation on Duration of Transits

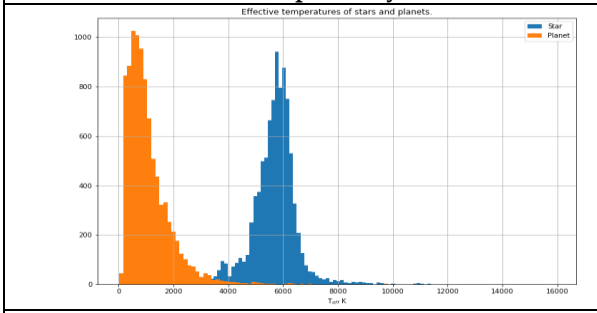

Figure-7: Stellar Effective and Photospheric Temperature of the star

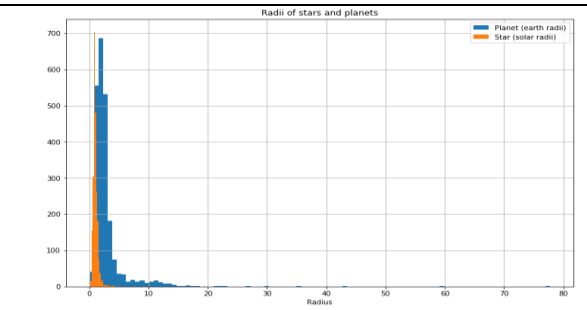

Figure-8: Radius of Star and Planets (Earth)

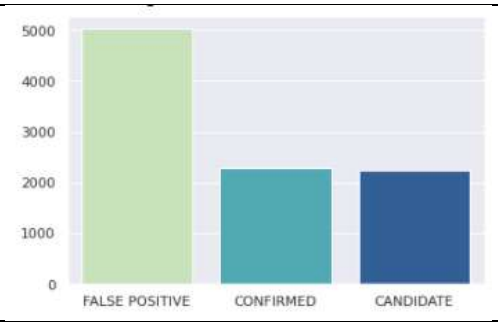

Figure 9: Comparisons of False Positive, Confirmed and Candidate

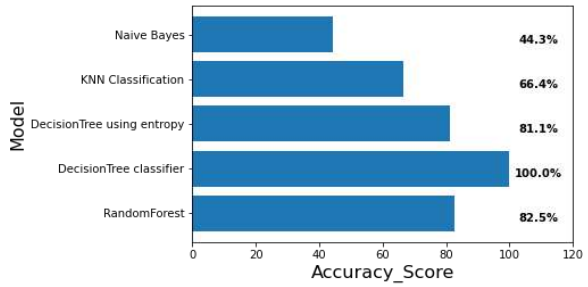

Figure 10: Accuracy of the models

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REVIEW ARTICLE

A Descriptive Review of *Catharanthus roseus*: Pharmacological and Phytochemical Panoroma

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ABSTRACT

Catharanthus roseus is a medicinal herbal plant distributed in various tropical and subtropical regimes of the world and is endemic to Madagascar. As *C.roseus* is a potent medicinal herb it possesses discrete pharmacological actions such as antimicrobial, antifungal, antioxidant, anthelminthic, ant-sterility, anti-diarrhoeal, antidiabetic, antihypertensive and wound healing effect etc. which is used in the treatment of many lethal diseases (SDG3). Due to the presence of two major alkaloidal constituents like Vincristine, Vinblastine, the plant contributes to the anticancer activity and vindoline alkaloid also contributes to some of its effect. In this paper, we provide a brief review to summarize different isolation, identification techniques like Thin Layer Chromatography (TLC), column chromatography, Infrared spectroscopy, UV and HPLC analysis to separate and identify various phytoconstituents produced by the plant and to evaluate pharmacological effect of the plant against various diseases in a concise way.

Keywords: *Catharanthus roseus*, Anticancer drugs, Antimicrobial activity, Vincristine, Vinblastine

INTRODUCTION

Catharanthus roseus is a medicinal perennial herbal plant under the family Apocynaceaeinnate and indigenous to Madagascar. In the year 1950 Vinca alkaloids were discovered by two Canadian scientists Robert Noble and Charles Beer. The plant also possesses various synonyms such as *Vinca rosea*, *Ammocallis rosea* and Lochnerarosea. Species like *Vinca difformis*, *V.erecta*, *V.herbacea*, *V. major*, *V. minor*, *V. pubescent* and *V. soneri* comes under the genus *Vinca* [1, 2, 3].

A rich source of pharmaceutically important terpenoid indole alkaloids is found in *C. roseus* (L.)G. Don.The major monomeric alkaloids as well as biosynthetic precursors for the dimeric alkaloids are vindoline and catharanthine which abundantly present in various leaves and stems of the plant [2, 3, 4]**.** Vincristine and Vinblastine are the2nd most used anticancer drugs to treat leukemia and Hodgkin's diseases. Mainly leaves and stems of the plant possess anticancer activity while roots have antihypertensive activity. The major alkaloid is vincamine and its semi-synthetic derivative i.e., ethyl-apovincaminate or vinpocetine which is widely used as a medicinal agent to treat vasodilation, blood thinning, hypoglycemic and memory-enhancing activity. The various extracts of Vinca have demonstrated significant anticancer activity against innumerable cell types[4, 5]**.**

Anti leukemic alkaloids isolated from *C. roseus*

Vincristine

Vincristine also known asLeurocristine and is marketed under brand name On covin and Vincasar Pfs. Vincristine is administrated by intravenous route with adult dose of 1.4 mg/m^2 (maximum dose of 2 mg) and children dose of 1.5–2.0 mg/m^2 (maximum dose of 2.0–2.5 mg)[11]**.** It irreversibly binds to microtubular proteins which results from their reversible binding to tubulin(The subunit protein of microtubules) and spindle proteins in S- phase of the cell cycle (cell cycle specific) and interferes with the formation of the mitotic spindle, thereby arresting tumour cell division in anaphase of Mitosis [12]. Vincristine is absorbed through G.I tract with rapid distribution from blood to tissue and is metabolised by the enzyme Cytochrome P450 3A in liver. Vincristine possesses numerous side effects likeperipheral neuropathy, bone marrow suppression, constipation, toxicity of nervous system, nausea and vomiting, neurotoxicity, sensory impairment and parasthesis and is used mostly in case of several types of cancer like acute leukemia, rhabdomyosarcoma, neuroblastoma, Wilm's tumor, Hodgkin's disease and other lymphomas [19, 23].

Vinblastine

It is commonly known as vincaleuloblastine and marketed under brand name Velban. The mechanism of action remains same as that of Vinblastine. The drug is absorbed through G.I tract with rapid distribution from blood to tissue, normal distribution from the plasma to tissues, primarily to the lungs, liver, spleen, and kidneys and metabolized primarily in liver [11, 16, 19]. The drug is having numerous side effect like nausea and vomiting, constipation, white blood cell toxicity, dyspnea, chest pain, wheezing, fever, myelo suppression, neutropenia and used to treat various medical condition of testicular carcinoma, Hodgkin Lymphoma and Non-Hodgkin lymphoma, curing of breast cancer and germ cell tumors [22].

Clinical Pharmacology of Vinca Alkaloid

Vinca alkaloids are extracted naturally from the plant *C. roseus* and its different constituents possess different varieties of activities. These are used to treat various medical conditions like diabetes, high blood pressure, different types of cancer of cells and are also used as disinfectants.

Anti-diarrheal activity

The alcoholic (ethanol) extract of the plant leaf is used for medicinal treatment of testicular carcinoma, Hodgkin Lymphoma, Non-Hodgkin lymphoma, breast cancer and germ cell tumors. In an experiment, castor oil is used as an experimental diarrohea inducing agent and the leaf extract was tested in the wistar rats [1]. The ethanolic extracts *C. roseus* showed the dose dependent inhibition of the castor oil induced diarrohea at the doses of 200 and 500 mg/kg which confirms its anti-diarrheal effect [2, 17].

Wound healing property

The various extracts from different parts of *C. roseus* has been studied for the antimicrobial property and is found very useful in many cases of bacteria, fungi and virus also. [17]. The methanol extract of the *C. roseus* flower has been tested on animal modeli.e, on rats for treating wound. As the rate of wound contraction increasesthe epithelialization period decreases and significant increase found in dry weight in the granulation tissues as compared to the control animal was found from the experiments which confirms thewound healing property [18].

Hypoglycemic activity

The alcoholic (ethanol) extracts of the leaves and flowers of *C. roseus* exhibit a dose dependent lowering of blood sugar concentration in the wistar rats in comparison to the standard drug used i.e., Glibenclamide. The Hypoglycemic effect has been confirmed due to the increase of glucose utilization by the liver [1, 18].

Antihypertensive and hypolipidemic activity

The hypotensive and hypolipidemic activity of the leaf extracts of *C. roseus* were studied in the adrenaline induced hypertensive rats [1]. The leaf extract was found to have indicative effect on normalize the cardiovascular parameter with regard to hypotensive and hypolipidemic effect [6, 18].

Antioxidant activity

C. roseus contains suggestive amounts of volatile and phenolic compounds among these compounds caffeoylquinic acids and flavone glycosides possess antioxidant activity. The flowerpetals and seeds of *C. roseus*mainly signify antioxidant properties. These compounds exhibit anti-allergic, anti-inflammatory, antimicrobial, anti-thrombotic, cardio protective and vasodilator effects other than the antioxidant activity [1, 2].In a reported study, the ethanol extract of the roots of Vinca varieties exhibited significant scavenging effect in the entire assay in a concentration dependent manner but the species *C. roseus* was found to possess more antioxidant activity than that of *C. Alba*[17].

Anthelminthic activity

Traditionally *C. roseus* is used as an potent anthelminthic agent. For the evaluation of anthelminthic property *C. roseus* Pherithemaposthuma is used as an experimental model and the activity is evaluated using Piperazine citrate or Albendazole as the standard drug. The alcoholic (ethanol) extract of the plant in concentration of 250 mg/ml was found to show the significant anthelminthic activity with death time of 46.33 min whereas the standard drug show the anthelminthic activity at 50 mg/ml with the death time of 40.67 min. The above investigation supported the ethnomedical claims of *C. roseus* as an anthelminthic plant [2,6].

Anti cancer activity

The two major anticancer alkaloid i.e.Vincristine and Vinblastine are derived from stem and leaf of *C.roseus*. These alkaloids showndecrease the growth of some human tumors. To treat neoplasm Vinblastine is used and is the best choice for Hodgkin's disease and choriocarcinoma [1]. To treat leukemia in children, Vincristine and other alkaloid is used. Using in vitro condition different percentage of the methanolic crude extracts of *C. roseus* was found to show the significant anticancer activity against different cell types and the best activity was found against the multidrug resistant tumor types [6, 17].

Memory enhancement activity

Vinpocetine which is a constituent of *C. roseus* has been disclosed to have a variety of actions and it is more beneficial in case of Alzheimer's disease (AD) which is a CNS disorder. A well-defined cross section analysis in AD patients found no benefit in controlling the disease but when statistic alanalysis studies of vinpocetine was carried out in early stage dementia patients the evidence found was insignificant to support its clinical use evidence at that time [1]. At doses up to 60mg vinpocetine has been well tolerated in clinical trials of dementia and stroke and no adverse events were reported which shows that *C. roseus* not a first choice drug for AD but it found some use in the management of the disease [2].

Neuroprotective activity

To establish the neuroprotective effect of *C. roseus* leaf extract an experiment was carried out against standard streptozotocin induced hyperglycaemia in the rat brain [1].It was found that the treatment with *C. roseus* significantly decreased malondialdehyde (MDA), xanthine oxidase (XO) and Sorbitol dehydrogenase production and increased glutathione levels when compared to the standard streptozotocin induced diabetic untreated rats. So it was confirmed that *C. roseus* leaf extract is an effective neuroprotective agent [17].

Antifertility efficacy

The ant fertility Properties of *C. roseus* extract was confirmed by the oral Administration of the leaf extract which leads to significantly decline the widespread of testicular necrosis, hyalinization of tubules and Sertoli Cell Syndrome as well as reduction of Glycogen and fructose levels in reproductive tissues. When injected along with estradiol into the female albino mice, the petroleum ether extract of *C. roseus* leaves was found to be inhibiting the estrogen induced gain in the uterine weight. Thus it confirmed highly effective in suppressing Pregnancy [1].

TOXICITY

All vinca alkaloids are very similar in structure and nature also but their toxicological profile varies from each other. Majority of vinca alkaloids produce peripheral neurotoxicity but which leads to various central nervous system effects such as mental confusion, depression, hallucinations, impairment of vision and laryngeal paralysis [3]. In case of increased drug exposure severe Myelo suppression and hepatic deficiency has been reported and Vincristine rarely causes hematologic toxicity [14]. In some individuals gastrointestinal toxicities may be reported with the regular usage of vinca alkaloids which includes constipation, ileus and abdominal pain. Mucositis occurs more frequently in case of Vinblastine than Vinorelbine and is most common in case of Vincristine. Nausea, vomiting, tissue damage and diarrhea were also reported. Acute cardiac ischemia, chest pains without ischemia, fever, acute pulmonary effects, Raynaud phenomenon have also been reported with the use of vinca alkaloids [3].

Vinca alkaloids are contraindicated during pregnancy or during breast-feeding as they as it may cause birth abnormalities. Patients should notify their physician in prior about any prescription drugs taken concurrently and also suffering with any other medical conditions such as herpes zoster virus infection, gout, kidney stones, chickenpox, infections, liver disease, nerve or muscle disease .However, thedrug concentration and treatment duration and exposure are of main importance for determining drug accumulation and cytotoxicity [14].

ANTI MICROBIAL ACTIVITY

Antimicrobial screening test microorganisms

The antimicrobial activities of different plant extracts were evaluated by Agar well diffusion technique against common pathogenic microorganisms which includes Gram positive bacteria- *Staphylococcus aureus*, Gram negative- *Escherichia coli* and anti-fungal activity were evaluated against fungal strains like *Asper gillusniger* and *Aspergillus flavus*. The bacterial cultures were grown and maintained on Agar nutrient broth medium at 37^{o}C for 24h while the fungal culture were maintained on Potato Dextrose Agar slants and incubated at 27^{o}C for 48h [2].

Antibacterial Assay

Freshly prepared microbial culture of 0.1ml was spread on the nutrient agar plate with the help of a glass spreader. A well of 6 mm diameter was punched into the agar medium with sterile cork borer and filled with 50µg of ethanol, acetone, chloroform and petroleum ether extracts by using micropipette in each well in aseptic condition. The petriplates were then kept in a refrigerator to allow prediffusion of extract for30 minutes and then further incubated in an incubator at37^{o}C for 24 hr. By measuring the zone of inhibition (ZOI) and minimum inhibitory concentration (MIC) the antibacterial activity was evaluated [17].

Antifungal Assay

The antifungal activity of the various leaf extracts was determined using agar well diffusion method. Small amount of diluted fungal suspension were poured over the agar media to uniformly spread on the surface. Later when the surface was little dried then wells of 8mm were punched in the agar with stainless steel borer and filled with 300µl of plant extracts. Control wells containing only solvents were also run parallel in the same plate. The plates were incubated at 28°C for72 hours and by measuring the diameter of the zone of inhibition at the interval of every 24hrs the antifungal activity was evaluated [20, 30].

QUALITATIVE PHYTOCHEMICAL SCREENING

Phytochemicals are divided in two groups based on their functions in plant metabolism and they are primary and secondary metabolites. Primary metabolite consists of sugar, amino acids, proteins whereas Secondary metabolites includes alkaloids, Flavonoids and tannins. The phytochemical screening in different solvent which gives the crude plant extracts revealed the presence of various secondary metabolites[20, 24].

CONCLUSION

For majority of the world's population medicinal and herbal plant products is used as the most exclusive source of life saving drugs from ancient times and continue to be an important therapeutic aid for various fatal diseases. Today, there is a increase vast interest in traditional medicine and an increasing demand for the production of more drugs from plant sources because green medicine is safe, reliable, cost effective then costly synthetic drug which may produced various adverse effects.

Due to the production of very small quantities of alkaloids inside the plant, various attempts have been made over the past years to increase their production through various biotechnological applications by use of different varieties of methods. The primary indication of Vinca alkaloids are Chemotherapy of Cancer due to the four major vinca alkaloids i.e. Vinblastine, Vinorelbine, Vincristine and Vindesine. Vinflunine is a new synthetic vinca alkaloid which has been in use recently for the treatment of second-line transitional cell carcinoma of the urothelium and other malignancies. Overall, vinca alkaloids are the second line anti-cancer drugs.

The pharmacological activity helps in the detection of various secondary metabolites of the plant present either individually or in combination. This discovery represents great advancement in infection therapies to treat various microorganisms. To understanding the health benefits (SDG3) from potential plant sources, it is important to measure the antioxidant activity using various radical scavenging and oxidation systems. Various studies provide support to the plant's traditional and alternative use against various diseases (SDG3) and infections. Further, the active biomolecules present in the extract which are active against various microbes needs to be identified and characterized. Hence, this study holds importance in using *C. roseus* plant as a potent anticancer agents and an alternative source for treating various fatal diseases.

CONFLICT OF INTEREST

Authors report no conflict of interest.

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Table 1: Ethnomedicinal uses of *C. roseus* in different countries

COUNTRY	PARTS BEING USED	USES	REFERENCES
India	Juice of leaves	To treat bee sting/ wasp sting.	[3],[6]
Philippines	Leaf decoction	Treatment of diabetic	[3],[6]
	Young leaves decoction	Treatment of stomache	[3],[6]
	Decoction of root	Treatment of intestinal parasitism	[3],[6]
	Leaf Infusion	Treatment of menorrhagia	[3],[6]
	Crude leaf and root extracts	Treatment of anticancer activity	[3],[6]
	Root	Treatment of dysentery	[3],[6]
Madagascar	Leaves	vomitive	[3],[6]
	Roots	Used as purgative, vermifuge, hemostatic and toothache.	[3],[6]
Mauritius	Leaves juice	Treat indigestion and dyspepsia	[3],[6]
West Indies and Nigeria	Leaves	Treatment of Diabetes	[3],[6]
Cuba and Jamaica	Extract of flower	Washing eye in infants	[3],[6]
Bahamas	Flower decoction	To treat asthma, tuberculosis and flatulence	[3],[6]
Hawaii	Boiled plant extract	To stop bleeding	[3],[6]
Malaysia	The plant	To treat diabetes, hypertension, insomnia and cancer	[3],[6]
America	Plant Gargle	Treatment of sore throat, chest ailments and laryngitis	[3],[6]
African country	Leaves	Treatment of menorrhagia and rheumatism	[3],[6]

Table 2: Medicinal Uses of Phytoconstituents from *C. roseus*.

CONSTITUENTS	SIDE EFFECT	USES	REFERENCES
Vinorelbine	Damage white blood cell, Bleeding, Anemia, Constipation, Diarrohea, Nausea, Numbness or Tingling sensation in the hands and feet and fatigue	Breast Cancer, Bone Tumor Cells, Osteosarcoma.	[1], [3]
Vindesine	Constipation, Damage white blood cell, Dyspnea, Chest Pain, wheezing and fever	Acute Lymphocytic Leukemia, Chronic Myeloid Leukemia, Malignant Melanoma, Pediatric Solid Tumors and Metastatic Renal, Breast, Esophageal And Colorectal Carcinomas.	[6]
Vinflunine	Myelosuppression and constipation	Lungs and breast cancer, anti tumor, anti angiogenesis	[14]

Table 3: Presence of various phytochemical constituents

Sl. No.	Phytochemicals	Crude Methanolic	Crude ethanol	Soxhelt Methanol extract	Soxhlet Ethanol Extract
1.	Alkaloid	+	+	+	+
2.	Flavonoids	+	+	+	+
3.	Steroid	-	-	-	-
4.	Glycoside	-	-	-	-
5.	Terpenoid	-	+	-	-
6.	Tannis	+	+	-	-
7.	Quinine	-	-	-	-
8.	Coumarin	-	-	-	-
9.	Starch	-	-	-	-
10.	Phenol	-	-	-	-
11.	Saponins	-	+	-	+

Figure 1: Vinca major

Figure 2: Vinca minor

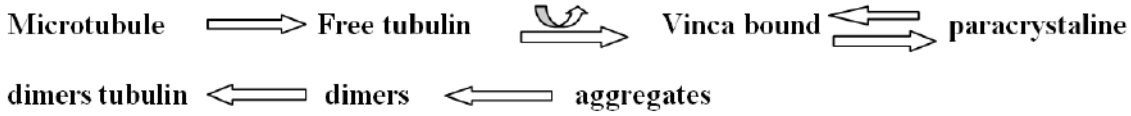

Figure 3:Tubulin binding site of vinca alkaloids

REVIEW ARTICLE

Review on Phytochemistry and Pharmacology of *Neolamarckia cadamba*: A Sacred Indian Medicinal Plant

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ABSTRACT

Neolamarckia cadamba (Rubiaceae) is an under explored medicinal and ornamental plant with religious significance in India. It has been used to cure a variety of disorders since ancient times, including leprosy, anemia, stomatitis, fever, skin problems, uterine difficulties, diarrhoea, and other infections. Further, scientific investigations have documented diuretic, antipyretic, anti-inflammatory, analgesic, antimalarial, laxative and hepatoprotective activities. All these significant remedies may attribute to the different parts (leaf, stem bark, fruit, and root) of this species as they contain large number of diversified potential bioactive secondary metabolites. These metabolites may be used as alternative for synthetic drugs. Since more than a century, researchers have been studying this species, but only a few chemicals have been identified as potential therapeutic drug candidates. This review aims to discuss updated comprehensive information on phytochemistry and pharmacological activities of *N. cadamba*, as well as provide insight into the investigation of medicinal properties at the molecular level, with a focus on its fruit, in order to open new avenuesin pharmacological research on food.

Keywords: *N. cadamba*, ursolic acid, cadambine, antioxidant, antimicrobial

INTRODUCTION

India has a rich culture of medicinal plants, which includes about more than 2000 species and has a vast geographical area with high potential abilities for Ayurvedic, Unani, Siddha traditional medicines but only very few have been studied chemically and pharmacologically for their potential medicinal value [1]. Human beings are using plants for the treatment of diverse ailments for thousands of years [2]. According to the World Health Organization, most populations still rely on traditional medicines for their psychological and physical health requirements since they

cannot afford the products of Western pharmaceutical industries together with their side effects and lack of healthcare facilities [3-5]. Rural areas of many developing countries still depend on traditional medicine for their primary health care needs and have found a place in day-to-day life. These medicines are relatively safer and cheaper than synthetic or modern medicine [6-8]. People living in rural areas from their personal experience know that these traditional remedies are valuable source of natural products to maintain human health but they may not understand the science behind these medicines but knew that some medicinal plants are highly effective only when used at therapeutic doses. Herbal medicines are in great demand in both developed and developing countries as a source of primary health care owing to their attributes having wide biological and medicinal activities, high safety margins and lesser costs[9].

Neolamarckia cadamba (Roxb.) Bosser. (Rubiaceae) is commonly known as cadamba in Ayurveda system of medicine. It is a medium to large size deciduous tree (height, 20-40 m and girth, 2-2.5 m) and has rounded crown and cylindrical branches. It is distributedon the slopes of evergreen forest in all over India. Also, it is scattered in forest of Thailand and Indo-China as well as in Malaysian archipelago and Papua New Guinea. In India, many communities and tribal use its leaf, flower and bark towards treatment of various ailments such as inflammation, sour throat, cough, and fever. Also, it is regarded as sacred medicinal plant in India's well-known ancient medical treatises such as Charaka Samhita and Sushruta Samhita [10]. This review has compiled information on phytochemistry and pharmacology of *N. cadamba* to investigate its therapeutic potential, identify knowledge breaches and assess future research opportunities. Also, this will directly/indirectly impact on sustainable development goals to achieve good health and well-being.

MATERIALS AND METHODS

The ethnomedicinal and scientific reports on *N. cadamba* were collected from published and unpublished articles available on scientific databases e.g., Science Direct, Scopus, Pubmed, Google scholar and Web of Science. The scientific name of plant is validated on the database of The World Flora Online.

PHYTOCHEMISTRY OF *N. cadamba*

Indole alkaloid

Seven no. of indole alkaloids such as cadamine (1), neolamarckine A (2), neolamarckine B (3), neolamarckine C, neolamarckine D, 3β-isodihydrocadambine (4) and neolarmarckine E were isolated from the leaves of *N. cadamba*. The bark of this species reported three no. of indole alkaloids such as angustine (5), harmane (6) and naulafine(7) [11]. Dihydro cadambine (8), an indole alkaloid was isolated from the leaves of *N. cadamba*. The monoterpenoid indole alkaloids such as aminocadambines A (9) and B (10) were isolated from the leaves and bark of *N. cadamba*[12-13].Yuan reported two other monoterpenoid indole alkaloids such as Neocadambine C and Neocadambine D in the bark of *N. cadamba* [13].The leaves contain indole alkaloids such as anthocephaline (11), strictosamide (12), vincosamide and cadambine. Cadambine and iso-cadambine are glycoalkaloids and nonglycosidic isomeric indole alkaloids found in the leaves.Cadambine has also been found in the heartwood [14].The methanol extract of leaves reported three monoterpenoid gluco-indole alkaloids such as 3-isodihydrocadambine, cadambine and 3"-dihydrocadambine[15]. Three glycosidic monoterpenoid indole alkaloids such as cadambine, dihydrocadambine and isodihydrocadambine were reported in *N. cadamba*[16]. Five related indole glucosides such as cadambine, 3"-dihydrocadambine, 3-dihydrocadambine, isohydrocadambines and 3 - isodihydrocadambine were identifiedin the wood and leaves of *N. cadamba*[14] (Figure 1).

Phenolic and flavonoids

Chlorogenic acid (13), catechin (14), epicatechin, rutin (15), and kaempferol 3-O-glucoside (16) were isolated from leaves of *N. cadamba*[17]. Another two flavonoids such as 6-hydroxycoumarin-(4′′→8)-(-)-epicatechin and 6-hydroxycoumarin-(4′′→8)-(-)-epicatechin-(4→6′′)-(−)-epicatechin were isolated form *N. cadamba* [18]. The heartwood

of this species reported the presence of dihydrotectochrysin, dihydrowogonin (17), pinocembrin (18), chrysin (19), naringenin (20), kaempferol, aromadendrin (21), quercetin, taxifolin (22), and 7-hydroxy-5, 2′, 4′-trimethoxyflavanone. Narigenin, apigenin, β-sitosterol, sakuranetin, prunetin, genkwanin were isolated from the stem of *N. cadamba*.The sapwood of *N. cadamba* was identified with 7-O-(β-D-glucopyranosyl)-5-O-methylnaringenin, genistein, prunetin, afzelin (23), kaempferitrin (24)and naringenin. Tectochrysin (25), padmakastein and its derivatives genistein, leucocyanidin, 4′-glucoside of genkwanin, puddumetin, flavanone, sakuranetin (5, 4′-dihydroxy-7-methoxy flavone) and its 5-glucoside, puddumin B, naringenin-4′-methylether-7-O-β-D-galactoside,and taxifolin were isolated from stem bark of *N. cadamba*.The root bark identified the presence of prunetinoside (26)and glucogenkwanin in*N. cadamba*. Naringenin-5-O-*α*-L-rhamnopyranoside,4′-O-methylliquiritigenin-7-O-*α*-L-rhamnopyranoside and naringenin-4′-methylether-7-xyloside were isolated from the seed of *N. cadamba*. Quercetin-3-rhamnoglucoside and kaempferol were isolated from the leaves of *N. cadamba*[19] (Figure 2).

Steroids

β-sitosterol a steroidal compound was isolated form the leaves, stem and sapwood of *N. cadamba*[17]. β-sitosterol glucoside was isolated from sapwood of *N. cadamba*.The stem bark isolated β-sitosterol behenate, and β-sitosterol glucoside in *N. cadamba*. Stigmasterol was isolated from the root bark of *N. cadamba* whereas β-sitosterol-3-O-D-galactopyranoside was isolated from the seed of *N. cadamba*[19].

Terpenoids

Ursolic acid (27) was isolated from the sapwood and root bark of *N. cadamba*[19]. The essential oil from flowers contains linalool, geraniol, gerenyl acetate, *α*-selinene, and *α*-phellandrene as major compounds. Two triterpene glycosides (triterpene glycoside A and B) were isolated from the bark of *N. cadamba*. Two novel triterpenoid saponins such as phelasin A and phelasin B were isolated from the bark of *N. cadamba*[14](Figure 3).

Miscellaneous

The heartwood identified the presence of 2′-hydroxy 2,4,4′,6′- tetramethoxychalconeand 2′, 4′-dihydroxy-2,4,6′- trimethoxychalcone in*N. cadamba*. Oleic, palmitic, stearic acids, n-pentacosane, triacontane, and noctacosanol were isolated from sapwood of *N. cadamba*.Chrysophanol (28), emodin-8-β-D glucosides, physcion (29), orientalone (30), amygdalin, prunasetin, and leucocyanidin were isolated from stem bark of *N. cadamba*[19]. Chlorogenic acid (CGA) an important biosynthetic intermediate in lignin biosynthesis is the ester of caffeic and quinic acid and its presence in *N. cadamba* is reported [14] (Figure 3).

PHARMACOLOGICAL ACTIVITIES OF *N. cadamba*

Antioxidant activity

Chandel reported free radical scavenging activities of *N. cadamba* [17-18]. Among all the extracts, ethyl acetate extract of leaves of *N. cadamba* showed potential DPPH, ABTS, hydroxyl and superoxide radical scavenging activities. These activities may be due to the hydrogen atom transfer and single electron transfer potential of bioactive phenolic and flavonoids such as chlorogenic acid, rutin, kaempferol, and β-sitosterol present in it. Oxidative stress in *in vivo* model causes lipid peroxidation and increases the level of malondialdehyde (MDA) and decreases reduced glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) level in tissues. On treatment of methanol extract of bark of *N. cadamba* on *Ehrlich ascites* carcinoma treated mice exhibited significant lowering in MDA and elevated the level of SOD, CAT and GSH to the normal level [20].

Anticancer activity

The compounds such as 6-hydroxycoumarin-(4′⟶ 8)-(-)-epicatechin and 6-hydroxycoumarin-(4′′ ⟶ 8)-(-)-epicatechin-(4⟶ 6′′′)-(-)-epicatechin of *N. cadamba* showed antiproliferative activity against COLO-205 cells by inhibiting over expression of COX-2.Thus, these compounds may partly embrace as anticancer agents for treatment of colon cancer and further detailed studies are needed for establishment of their activities [18]. Anticancer activity of methanol extract of *N. cadamba* was studied in *Ehrlich ascites* carcinoma (EAC) treated mice. The extract at dose of 400 mg/kg significantly decreased the viable count, tumor volume and increased non-viable cell count. Also, the median

survival time period was significantly increased in extract (400 mg/kg) treated groups.These results may conclude that the extract possesses cytotoxic effect on tumor cells or indirectly it causes inhibition in vascular permeability and activates macrophages [20]. Various extracts (hexane, chloroform, ethanol, aqueous, ethanol-water) of leaves of *N. cadamba* were evaluated for cytotoxic activity against cancer cell lines such as CNS (SF-295), ovary (IGR-OV-1), lung (A-549) and prostate (PC-3) by using SRB assay. The chloroform extract of leaves was found to possess significant inhibitory action on all cell lines whereas hexane, aqueous and ethanol-water extracts were found to be ineffective against cancer cell lines. This activity may be attributed to the presence of indole alkaloids in it [21].

Antipyretic activity

Usman[22]demonstrated antipyretic action of chloroform, ethanol and aqueous extract of leaves of *N. cadamba* in yeast induced hyperpyrexia. This activity is attributed to the presence of various alkaloids in leaves of this species[22].

Antimicrobial activity

The ethanolic extract of stem, leaf and fruits were evaluated for antibacterial activity against *Bacillus subtilis*, *Bacillus licheniformis*, *Micrococcus luteus* and *Pseudomonas putida*. However, antifungal activity was performed against *Aspergillus niger*, *Aspergillus orchrace*, *Trichoderma*, *Rhizopus orchayae*. Among all these extracts only leaf extract showed maximum zone of inhibition than other extracts which concluded the potential antibacterial and antifungal activity of *N. cadamba*. This activity may be correlated to the presence of alkaloids, glycoside, saponins, terpenes, flavanoids, and phenolics in it [23].

Anthelmintic activity

Aqueous and ethanolic extract of bark of *N. cadamba* possess anthelmintic activity towards Indian earthworms *Pheritima posthuma*. On administration of extracts, paralysis and death of worms has occurred within 4 h followed by change in body colour. This activity may ascribe to the presence of saponins, steroids, and glycoside content in the extract [22].

Anti-inflammatory activity

As reported, methanol extract of stem bark of *N. cadamba* exhibit potential anti-inflammatory activity. In *in vitro* study, the extract significantly inhibited heat induced haemolysis by stabilizing HRBC membrane, inhibited production of nitric oxide radicals and also inhibited inflammation in murine macrophage RAW 264.7 cells indicating the anti-inflammatory action of compounds present in it. In *in vivo* carrageenan-induced rats, the extract showed significant decrease in paw inflammation within 5 h of administration which is attributed to diminishing ability of bioactive compounds of this species[24].

Analgesic activity

The ethyl acetate, methanol and aqueous extract of bark of *N. cadamba*possess analgesic activity as evidenced on acetic acid-induced writhing animal models. This activity may attribute to the presence of bioactive alkaloids [6].

Abortifacient activity

In folklore literature, *N. cadamba* is reported to have abortifacient potential. The methanol extract of bark of *N. cadamba* is scientifically validated for evaluation of this activity. The level of LH, progesterone, FSH and estradiol were considered as indicator for failing of pregnancy. The extract possesses glycoside, alkaloid, saponin, tannin, flavonoids, steroids which are responsible to elicit abortifacient activity [25].

CONCLUSION

In Ayurveda, *N. cadamba* is regarded as a scared medicinal plant since it possesses various biological activities. So, many pharmacological investigations were performed still its toxicity, safety and efficacy remain unclear. Few no. of bioactive compounds of this species are well known and remaining compounds have no information on toxicity

profile and biological activities. Further, molecular mechanism of different bioactive compounds of this species has not been established. So, toxicity profiling and pharmacological activities of extract and isolated compounds are warranted. Reverse pharmacological approaches need to be adopted for discovery of potent and safe drug for treatment of various diseases. This review will provide complete and up-to-date information on *N. cadamba*, paving the way for the development of innovative therapies to treat a variety of illnesses.

CONFLICT OF INTEREST

The authors declared that they have no conflict of interest.

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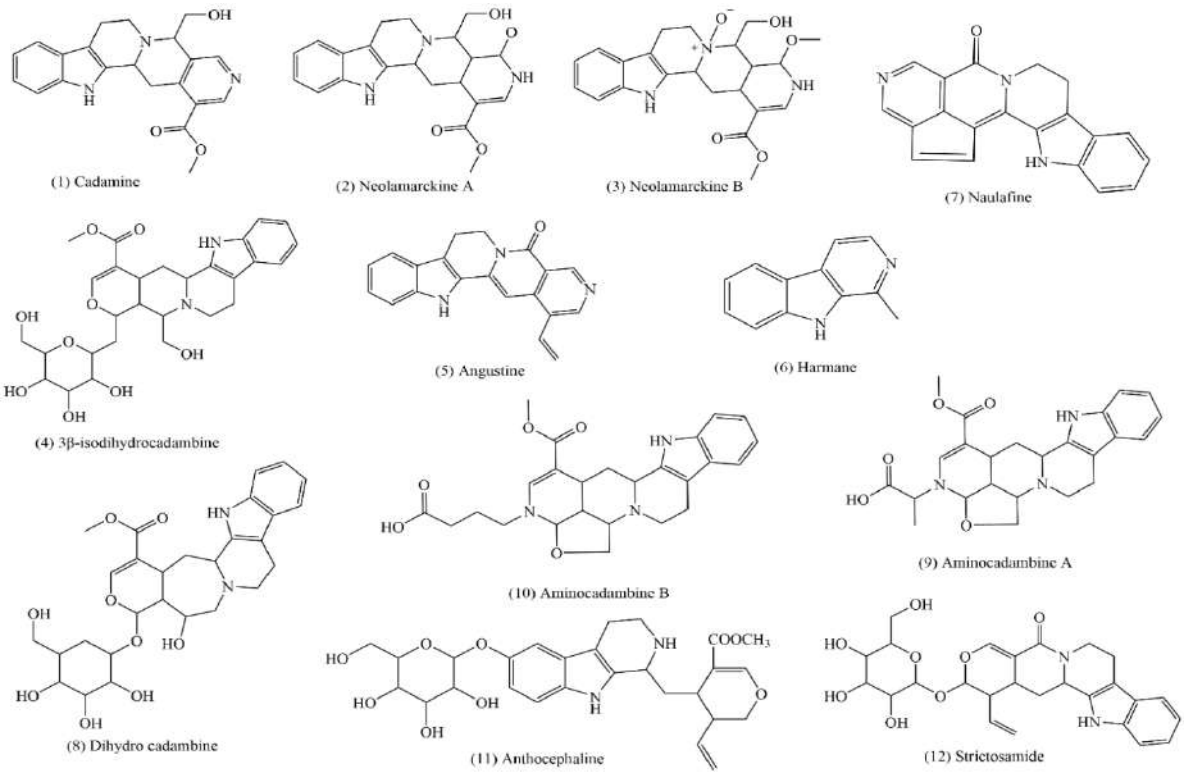

Fig. 1. Structure of compounds from 1-12

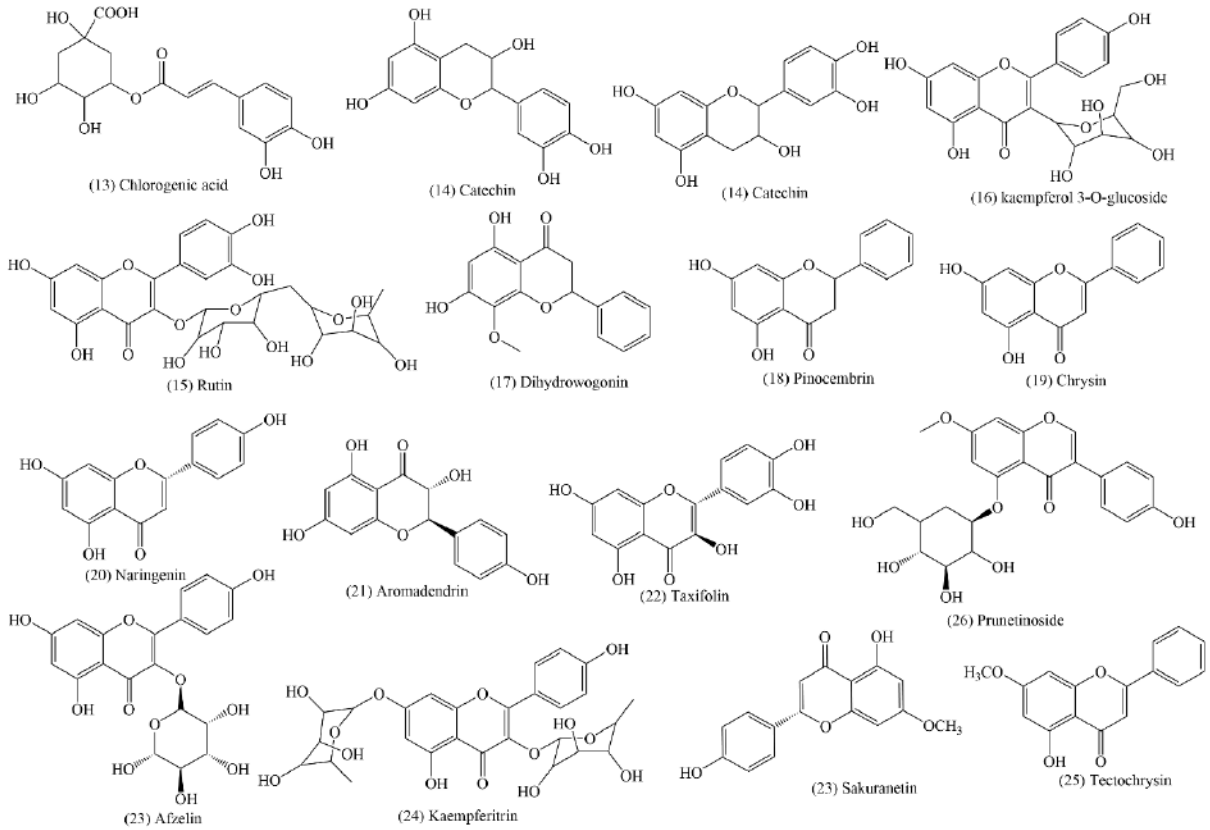

Fig. 2. Structure of compounds from 13-26

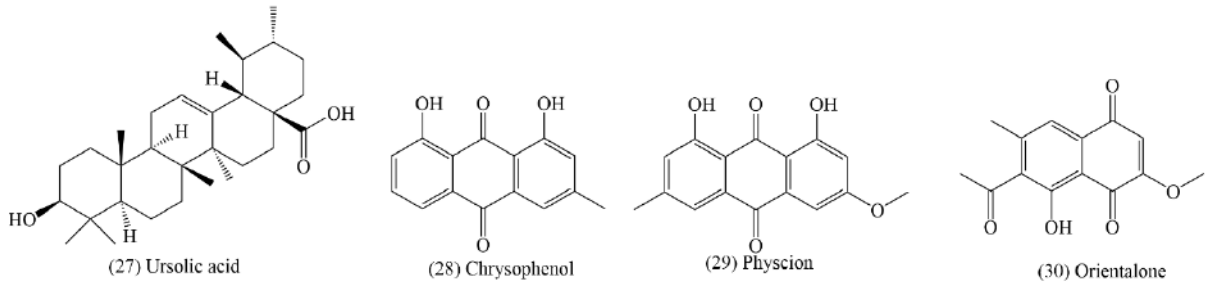

Fig. 3. Structure of compounds from 27-30

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RESEARCH ARTICLE

Computer-Aided Investigation of Phytochemical Gallic Acid Against Pterin-4a-Carbinolamine Dehydratase (PDB ID:2V6S) of Toxoplasma Gondii Causing Toxoplasmosis

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ABSTRACT

Phytochemical Gallic acid is a natural phenolic compound found in various fruits, roots and leaves of medicinal plants. It is reported to have multiple health-promoting effects. It has been previously reported that the phytocompound has potential to control various microorganisms. In this present study, pterin-4a-carbinolamine dehydratase (PDB ID:2V6S) of *Toxoplasma gondii* was retrieved from PDB site and used as target protein. Phytochemical Gallic acid structure was also retrieved from Pubchem. Autodockvina software was used to study the interaction between pterin-4a-carbinolamine dehydrataseand gallic acid. We concluded that, the above-said phytochemical is effective against the protein pterin-4a-carbinolamine dehydratase. It can be used for drug designing.

Keywords: Phytochemicals, Autodock, Pubchem,Gallic acid, *Toxoplasma gondii*

INTRODUCTION

Toxoplasmosis is a zoonotic infection caused by the protozoan parasite, *Toxoplasma gondii*. *Toxoplasma gondii*. This is a facultative heterogeneous parasite belongs to the phylum: Apicomplexa, class: Conoidasida, subclass: Coccidiasina, order: Eucoccidiorida, family: Sarcocystidae, genus: *Toxoplasma*, and species: *gondii* (Rahman *et al.* 2018).Ingestion of undercooked infected meat containing *T. gondii* cysts; ingestion of the oocyst from faecally contaminated hands, food, or water; organ transplantation or blood transfusion; transplacental transmission; and accidental inoculation of tachyzoites are all possible ways to become infected with *T. gondii*. (Mose *et al.,* 2020). Toxoplasmosis symptoms vary based on parasite characteristics such as strain virulence and inoculum size, as well as host factors such as genetic background and immunological condition (Weiss and Dubey, 2009).*T.gondii* infects a huge percentage of the world's population, yet it only produces clinically severe disease in a small percentage of cases. In humans, asymptomatic

infection with *T. gondii* can lead to a latent infection with tissue cysts. However, some people are at a higher risk of developing severe or life-threatening toxoplasmosis. *T. gondii* can cause encephalitis, chorioretinitis, congenital infection, neonatal death, and postnatally acquired toxoplasmosis in immunocompetent humans. These individuals include foetuses, infants, and immunologically compromised patients (Mose *et al.,* 2020). Gallic acid (Fig. 1) is a phenolic compound that can be found in a variety of fruits and medicinal plants. It is said to contain a number of health-promoting properties. Gallic acid has a number of health benefits, including antioxidant, anti-inflammatory, and anti-cancer qualities. This chemical has been shown to be effective in the treatment of gastrointestinal, cognitive, metabolic, and cardiovascular diseases(Kahkeshani *et al.,* 2019).

In this present study, molecular docking was performed by using Autodock Vina. Docking is a method which predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex. Knowledge of the preferred orientation in turn may be used to predict the strength of association or binding affinity between two molecules. Docking is frequently used to predict the binding orientation of small molecule (ligand) drug candidates to their protein targets in order to in turn predict the affinity and activity of the small molecule (Chakrabarty *et al.,* 2020). Here the study has been carried to determine the activity of Gallic Acid by blocking the pathway of pterin-4a-carbinolamine dehydratase (PDB ID:2V6S) of *T. gondii* (Figure 2).

METHODOLOGY

Software Used

AutoDockVina (Trott and Olson, 2010) was used for analysis. AutoDockVina is an open-source program for doing molecular docking. It was designed and implemented by Dr. Oleg Trott in the Molecular Graphics Lab at the Scripps Research Institute.

Phytochemical Used

Gallic acid is abundant in many plants, either in free form or as part of the tannin molecule. Pomegranate roots, Tea, red wine, fruits, beverages, and a variety of medicinal herbs all contain it. Gallic acid can bind to glutamate-gated chloride channels in Caenorhabditiselegans' nervous system and cause hyperpolarization of cell membranes and muscular activation when it comes into contact with protozoa. The worm is eventually paralysed and dies as a result of these events(Kahkeshani *et al.,* 2019).The sdffiles for the phytochemical berberine was downloaded from the website PUBCHEM.

Enzyme Used

Various metabolic cycles have been seen in the protozoal life cycle for its survival. These metabolic cycles are regulated by different enzymes. The protein database code of the pterin-4a-carbinolamine dehydratase (PDB ID:2V6S) was identified from the website RCSB.

Molecular Docking

Molecular docking method has been used to identify the phytochemical from the plant extract, gallic acid, which act as a ligand and form a strong covalent bond with the protozoal protein to successfully inhibit the microbe. Docking was performed in AutoDockVina (http://vina.scripps.edu/), which predicts interactions between small molecules and proteins. The active site of the enzyme was identified via ―receptor cavity‖ protocol found under "receptor-ligand interaction" menu of Biovia Discovery studio. Results were viewed and analyzed with PyMOL version 2.3.2.

RESULTS AND DISCUSSION

From the Autodock molecular docking studies, a good ΔG Kcal/mol value was obtained for the compound berberine. The obtained docking results (Figure 3) confirmed the capability of the selected compounds in terms of effective

molecular interaction with the investigated protein, selected compound berberine was determined to have stronger affinities in binding with the active site of aspartic proteinase. The docking results of the compounds with highest binding energy were found to be -5.8 kcal/mol (Table-1). Gallic acid has anti-inflammatory, anti-mutagenic, anti-cancer, and antioxidant properties. Antifungal, antiviral, antiprotozoal, and antibacterial activities have also been discovered. Gallic acid has been discovered to have cytotoxicity against cancer cells while causing no harm to healthy cells. In cases of internal bleeding, gallic acid is utilised as a distant astringent. It has been shown to be effective in the treatment of uterine, pulmonary, and nephritic haemorrhages. Purpura has benefited from it. It's used to treat diabetes and albuminuria. It's a known inhibitor of matrix metalloproteinases. Gallic acid is a pharmacologically important molecule because of all of these characteristics (Borde *et al.,* 2011). This lesser value of ΔG indicates the successful approach of phytochemical gallic acid as a drug against emerging protozoal pathogen *T. gondii*.

CONCLUSION

From the above study it has been concluded that using Autodockvina software, molecular docking operation result indicated that the phytochemical, gallic acid has an effective interaction with the vital enzyme, pterin-4a-carbinolamine dehydratase enzyme of the T. gondii. It was found that gallic acid can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. This study helps in providing information on controlling infectious pathogens and promoting good health and wellbeing of the community which follows the Sustainable Devlopment Goals 3.

ACKNOWLEDGEMENT

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Table 1: Results of Molecular docking of phytochemicals with Protozoal protein.

Mode	Affinity (Kcal/mol)	Distance from rmsdl.b.	Best mode rmsdu.b.
1	-5.8	0.000	0.000
2	-5.4	26.159	26.927
3	-5.4	26.155	26.850
4	-5.4	25.733	26.579
5	-5.4	25.722	26.624

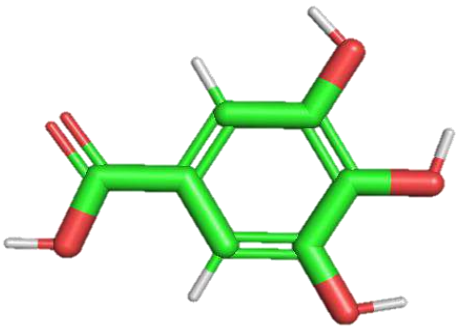

Figure 1: Chemical Structure of Gallic Acid

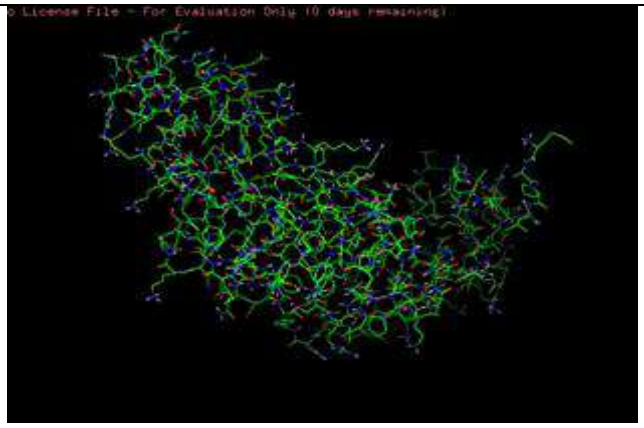

Figure 2:3D view of pterin-4a-carbinolamine dehydratase (PDB ID: 2V6S) of *T. gondii*

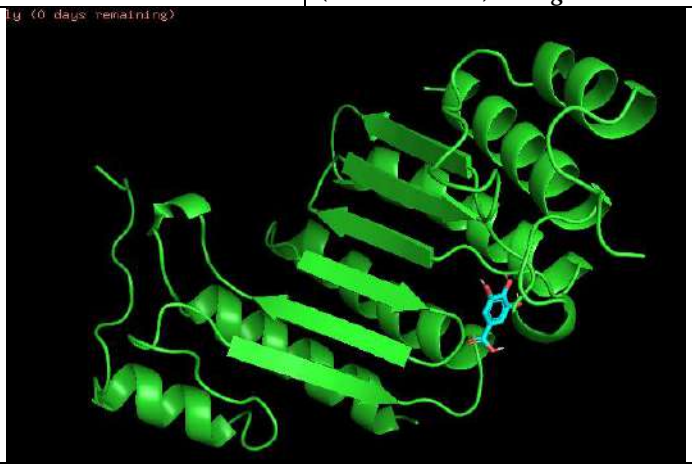

Figure 3: Docking results obtained with AutoDock Vina using PyMOL indicating interaction

REVIEW ARTICLE

Risk factors, Diagnostic Parameters, and Cellular Identification of Ovarian Malignancy: A Brief Review

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ABSTRACT

Women are most likely to develop ovarian carcinoma, the leading source of transience and morbidity for cancers that affect women. As the seventh greatest deadly malignancy among women, it is composed of heterogeneous groups of neoplasms. Studies have identified numerous endogenous and exogenous factors associated with ovarian cancer development. The International Federation released a report of Obstetrics and Gynaecology (FIGO) on this development has led to a revision of the staging system to provide prognostic information and recommendations regarding the treatment of ovarian cancer. Various cancer drugs have been developed over the past several years that are less toxic and more effective, so there is an increasing need for exact and consistent cancer diagnostics and prognoses. In managing ovarian cancer, biomarkers have helped separate benign from malignant mass in the pelvis and monitor response to treatment. Over the past four decades, CA125 has been the primary marker for ovarian cancer. This study is intended to present an updated global view of epithelial ovarian carcinoma, the most common form.

Keywords: Ovarian carcinoma, Osteopontin, Polycystic ovarian syndrome, Endometrioid adenocarcinoma

INTRODUCTION

The most common cause of gynecological cancer mortality is ovarian cancer (OC)because most cases are already advanced at the time of diagnosis. OC also affects good health and well-being. There has not been any improvement in the prognosis of women with OC in the last few decades. Surgery and chemotherapy based on platinum are recommended for these cancers as an initial treatment. In breast cancers that express estrogen receptors, hormonal therapy is the first indeed targeted treatment proven successful. There have been numerous therapies approved since then that adapt to the biology of tumours [1]. In 2019, including 21,530 new cases of OC and 13,980 deaths related to OC, OC was estimated to be the leading cause of cancer death in women with gynaecological malignancies [2]. The majority (75%) of all ovarian tumours and 90-95% of all ovarian malignancies that are found in women are epithelial ovarian cancers (EOCs) [3] of variable origin [4]. On average, patients survive five years after being diagnosed with OC, depending on the extent of the disease at diagnosis[5]. Many theories exist regarding the cause of ovarian carcinoma among women. The "incessant ovulation" hypothesis states that every ovulation creates a wound, causing the epithelial to proliferate more rapidly. Increasing DNA damage may increase the chance of mutations leading to cancer[6, 7].Ovarian carcinomas can be categorized according to their histology into three major categories based on where cancer begins: Ovarian epithelial tumours, sex cord-stromal cell tumours and an ovarian germ cell tumour[8].

Causes

Many review papers discuss the origin and development of ovarian carcinoma[9], its types and subtypes[10, 11], its diagnosis[12, 13], and its prognosis[14], as well as its treatment [15, 16, 17]. In ovarian carcinoma patients, many factors contribute to the poor prognosis, including peritoneal metastasis, malignant transformation, and recurrent disease. Despite the lack of early symptoms, difficulties getting rid of disease either entirely through chemotherapy and surgery, resistance in patients, Survival rates for five years are 45% [18]. This illness is treated with all available treatments, including counting, immune checkpoint inhibitors, antibody therapies, vaccines, combinatorial immunotherapies, and adoptive cell therapies[15]. Ovarian cancer is poorly understood, and its cellular origin and pathogenesis are not well understood. Several theories of origin have been posited based on morphological and genetic studies, especially for high-grade serous tumours that have no apparent progression pattern [19, 20]. In addition, most cancers seem to arise from other gynaecological tissues and affect the ovaries as a secondary site.

Histology

The World Health Organization (WHO) defines it as possible for ovarian epithelial tumours to be benign, have low malignant potential, or be malignant [21]. Borderline or low malignant potential (LMP) tumours do not show stromal invasion characterized by atypical epithelium linings, cellular proliferation, and pleomorphism. There are atypic changes, hyperactive mitotic activity, and stromal invasion in the malignant epithelium. Although ovarian tumours exhibit differential histopathological characteristics, all tumours exhibit similar characteristics [22]. Various dualistic models have assigned EOC to two categories, namely, type I and type II[23, 24]. Serous, mucinous, and clear cell carcinomas are considered Type I tumours. There is also endometrioid carcinoma in this category. TP53 mutations and advanced disease stages correlate with high-grade, clinically aggressive tumours of type II. They are genetically highly unstable and exhibit high levels of clinical aggressiveness. The epithelium of the fimbria on the fallopian tube or the epithelium of the ovary surface may be responsible for type II tumours [25-28].Figure 1 shows the different sorts and subtypes of EOCs.

Tumor of Type I

Serous Carcinoma of Low Grade

There has been an adaptation to nomenclature for grading serous carcinomas in the UK [29]. Adenoma-carcinoma sequences are thought to arise in a stepping-down manner in the case of serous carcinomas, from benign serous cystadenomas through borderline serous tumours to invasive serous carcinomas. Tumours of this type may not be necrotic or multinucleated, exhibit mild atypia, and have a maximum of 12 mitoses per 10 high-power fields [30].

TP53 mutations are not associated with low-grade serous carcinoma, but it is related to mutations of KRAS or BRAF, which are mutually exclusive, in two-thirds of its cases [31].

Mucinous Carcinoma

It is often fatal to children and adults of all ages [32, 33]. Most mucinous carcinomas of the ovary are of the intestinal type. Several of these cancers contain paneth cells, neuroendocrine cells, and goblet cells. Mutations in KRAS are frequently found in ovarian mucous carcinoma, and these characteristics are similar to those of low-grade serous carcinoma. Contrary to serous carcinomas of low grade, ovarian mucous carcinomas are not characterized by BRAF mutations [34].

Clear Cell Carcinoma

This type of carcinoma arises typically from the endometrium and is diagnosed relatively early (stage I or II). However, stage I cancer has a fairly good prognosis, even when the prognosis is poor. The low proliferation index of these tumours makes them resistant to ovarian carcinoma treatment and transitional chemotherapeutics [19].

Endometrioid Adenocarcinoma

Despite their low staging (stage I), endometrioid adenocarcinomas could be high-grade tumours. In most cases, this cancer is caused by the implantation of endometrial tissue, or it is preceded by borderline adenofibromas [35, 36]. Adenocarcinomas of the ovary exhibit similar molecular events to those of the uterus, including mutations of PTEN, KRAS, PIK3CA, and catenin, as well as instabilityof microsatellite [37].

Tumor of Type II

Serous Carcinoma of High Grade

As the tumour emerges at an advanced stage, it is considered a high-grade tumour. Compared to patients with high-grade tumours, chemotherapy patients have a significantly better survival rate with low-grade neoplasms[38]. Atypical nuclear atypia is moderate to marked in high-grade serous carcinomas with necrosis and multinucleated cells, with 12 or more mitoses per 10 high power areas. Tumours that develop early may be linked to TP53 mutations or p53 dysfunction [39-41].

Symptoms

A woman with ovarian cancer may experience no symptoms in its early stages. While ovarian cancer can present with symptoms at any stage, they usually appear in the later stages when growths pressure the bladder, uterus, and rectum. It is most commonly characterized by bloating, pain in the pelvis or abdomen, feeling full soon after eating, and experiencing increased urination frequency. In addition to these symptoms, others include nausea, indigestion, excessive fatigue, constipation, abdominal swelling, cramps during sex, and menstrual changes, such as irregular bleeding [42].

Risk Factors for Ovarian Cancer

Ovarian cancer is a complication in many cases; however, family antiquity of ovarian and breast cancer is one of the most decisive risk factors that epidemiological studies have proven [8, 23, 43]. There is also a possibility that age and other environmental factors are responsible for the disease. Different reproductive factors, including (multiple) parity, oral contraceptive use, hysterectomy, tubal ligation, and breastfeeding, are associated with a decrease in ovarian cancer risk [44-47]. According to evidence from the BRCA gene family, on average, 30% of women in their 70s are at risk for ovarian cancer because of germlineBRCA gene mutations (BRCA1 and BRCA2) [48].

Age

Among women, ovarian carcinoma is most common between 50 and 60. The inheritance of this deadly disease by the time you turn 40 is rare in this disease [49, 50].

Age at Menarche And Menopause

Ovarian cancer is more likely to develop if menopause occurs at a young age or a late age [51].Women's ovulatory cycles have increased primarily as a result. Post-menopausal gonadotropin hormones may reduce the risk in the final phase of menopause, but not before it [52], even though the gonadotropin hypothesis is justified.

Breastfeeding

Lactation has been hypothesized to lower the hazard of ovarian carcinoma in the months leading up to childbirth; agonists suppress the anterior pituitary gland's gonadotropin production, which triggers ovulation [53].

Hormonal and Reproductive Risk Factors

A clear association between OC and hormonal or reproductive factors has been demonstrated in epidemiological studies. Two predominant hypotheses can explain the data. In accordance with the ovulatory cycle hypothesis, after each ovulation, an increased amount of cellular divisions is associated with the repair of epithelial cells, causing a greater number of spontaneous mutations. [54, 55]. In line with this hypothesis, increased lifetime ovulations are correlated with higher risk [56-59]. Gonadotropic hormones, such as follicle-stimulating hormone and luteinizing hormone, are an important contributor to the increase of fertility [60]. Both approaches can interpret epidemiological data regarding exposure to reproductive hormones and its endogenous correlations and the effects of exogenous hormone sources. Riman *et al.* [61] provide a more detailed analysis.

Obesity

Aromatizing androgens into estrogen in adipose tissue is the primary method of moving estrogen in post-menopausal women. Researchers have been looking into potential links between obesity and ovarian cancer because of obesity's persuasive role in hormone linked cancers [62]. The body mass index (BMI) is an important measure. A meta-analysis of 28 population studies published in 2007 found that Ovarian cancer is more likely to develop in obese and overweight women with a BMI of 30 kg/m2 and 25–29.9 kg/m2, respectively than Pooled relative risks (RRs) of 1.2 and 1.3, for women with an average BMI of 18.5–24.9 kg/m2. According to an analysis of 12 prospective cohort studies conducted in 2008, premenopausal obese women had a higher risk than women with a normal BMI (RR =1.72; 95 percent confidence interval [CI]: 1.02–2.89), though this amplifiedmenace was not as obvious in post-menopausal women. [56] Furthermore, the ovarian cancer association consortium, analysing case-control studies, found favourable associations between BMI and ovarian cancer were stronger in premenopausal women. However, increased BMI appears to mitigate the risk of ovarian cancer. Furthermore, the ovarian cancer association consortium, analysing case-control studies, found favourable associations between BMI and ovarian cancer were stronger in premenopausal women. The risk of ovarian cancer was mitigated by increased BMI [63]. Weight control is the best defence against cancer of the ovaries, chronic illnesses and other types of cancer.

Diet and Nutrition

Despite numerous systemic epidemiological studies, there is considerable dispute over whether diet affects ovarian cancer risk [50]. Notable exceptions include vegetables, for which there is some evidence suggesting higher consumption is associated with lower risk [64]. Vitamin D is derived partly from dietary sources and partly from UV-B exposure to the skin. In the liver, the 25-hydroxyvitamin D [25(OH)D] is transformed into 1,25-dihydroxyvitamin D (1,25(OH)2D3) in the kidney. Vitamin D controls cell proliferation and differentiation, bone metabolism, and immune response [65]. The 1,25(OH)2D3 is suspected of reducing ovarian cancer cell proliferation through induction of apoptosis[66].Epidemiological evidence, however, suggests inconsistent vitamin D intake, which, in turn, affects the risk of ovarian cancer [67].

Cigarette Smoking

Smoking wasn't a risk factor, according to early research. The risk of mucinous ovarian cancer may be increased by smoking in a manner of dose-response, However, not for other subtypes [68].

Pelvic Inflammatory Disease (PID)

The most common causes of PID aretubo-ovarian abscesses, endometritis and salpingo-oophoritis. Only a few epidemiological studies have examined the association betweenEOC and PID [69, 70]. Researchers from Canada found a higher incidence of EOC among women who have one episode of PID compared to women who have no episodes (OR 95% CI 1.0–2.1) [70] and that PID was more strongly associated with EOC risk,a young age, nulliparity, infertility, or recurrent PID episodes could explain its occurrence.

Polycystic Ovarian Syndrome

Menstrual abnormalities and obesity, infertility, and hirsutism are manifestations of polycystic ovarian syndrome (PCOS). However, combined PCOS and obesity are associated with an augmented danger of uterine endometrial cancer [71]; the link between PCOS and EOC risk is less studied. Women with PCOS were more likely to have EOC (OR 2.5; 95%CI 1.1–5.9), and these associations were stronger in those who had never used oral contraceptives [72].

Global Scenario

Globally, women die from ovarian cancer at a rate eight times higher than any other form. Approximately 239,000 cases and 152,000 deaths were reported in the Globocan study in 2012. By 2035, the Globocan study predicts that cases will upsurge by 55% to 371,000, while the number of deaths will rise by 67% to 254,000 [19]. The prevalence of ovarian cancer is high among women under 50 in developing countries (five-year prevalence). When looking at the most common gynaecological cancers, the burden depends on the country's state of development but differs depending on the type of cancer. There is a greater prevalence of cervical cancer in less developed parts of the world due to poor sexual health, lack of screening, and vaccination. Uterine cancer has been overgrowing in developed parts of the world in recent years due to its strong association with body mass index. In other words, the priority for preventing gynaecological and women's cancers varies across countries.

Stages of Ovarian Cancer

How serious cancer is and what treatment is best depends on the cancer stage. When talking about survival statistics, doctors cite cancer's stage as well. Most ovarian melanoma patients are spotted in progressive stages (stages III and IV), stage I tumours are relatively rare, but they have a high survival rate [73]. From the stage I (1) to stage IV (4), there are four stages of ovarian cancer. Generally, the lower the number, the more limited the spread of cancer is. Stage IV means that cancer has spread more widely.

How is the stage determined?

A system called the staining of ovarian cancer is done using the FIGO (International Federation of Gynaecology and Obstetrics) and the AJCC (American Joint Committee on Cancer) TNM staging system. Cancer is staged (classified) according to three factors by both parties. (i) The size of the tumour (T) (ii) The spread to nearby lymph nodes (N) (iii) The metastasis to distant sites (M).

New strategies

For decades, various histological diagnoses have been combined under the general term "ovarian cancer" and treated in very similar ways. Molecular markers identified in association with specific histologies have led to a more accurate diagnosis. Also, new therapies have been developed based on those molecular markers or mutations. The mutation often occurs during the early stages of tumour development, often with TP53. In the last decade, ovarian cancer treatment has taken a quantum leap, with the approval of many new drugs and experimental therapies. Identifying optimal treatment regimens and improving patient outcomes are new challenges, as new opportunities are created regarding the selection of pharmaceutical agents, the evaluation of those agents, and the treatment regimens that are best evaluated. Current research focuses on developing and applying new agents in several potential directions.

Biomarkers

In light of the high repetition chance and poor conclusions after recurrence, we must develop strategies to identify and prevent recurrence as soon as possible and predict progress as early as possible [74]. The two most commonly used methods for detecting ovarian cancer are cancer antigen 125 (CA-125) and transvaginal ultrasonography [75]. Among the many tumour biomarkers routinely used for surveillance and diagnosis in distinctive clinical practice for illness, detection is CA125, a measurement of the serum level of the tumour cell marker used extensively today [76]. Researches are estimating numerous biomarkers like osteopontin (OPN), HE4, Folate receptor α (FOLR1), mesothelin (MSLN), miRNA, paraneoplastic antigens, cancer stem cells (CSCs) and a mixture of them to appraise their role as prognostic biomarkers for ovarian cancer reappearance.

CA-125

CA125 belongs to the mucin family of glycoproteins. The Mullerian and Coelomic epithelial tissues express these proteins as unspecific markers [77]. CA125 levels correlate with progression and regression of established disease in ovarian tumours and have been used to monitor chemotherapy response [78]. CA125 levels are not elevated in up to 50% of cases of early-stage I and II ovarian cancer [79]. In other words, when the disease is confined to the ovary, CA125 is limited in its usefulness. A higher level of CA125 in the serum is found in up to 80% of women with crucial phase epithelial ovarian cancer [80]. When CA125 concentration is >35 U/mL, there is usually an indication that there is a malignancy, with 47% elevation in EOC early stages and 80–90% elevation in advanced stages [81]. However, some cases of ovarian cancer are silent [82].

HE4

HE4 (Human Epididymis Protein 4) is a new biomarker currently being tested to diagnose ovarian malignant tumours [83]. The FDA has approved HE4 as a tool for monitoring disease progression or the recurrence of EOC [84]. In patients whose tumours do not express CA125, the HE4 level predicts OC recurrence before CA125 [85]. According to Laskshmann et al., serum HE4 had an equal sensitivity (85.3%) but better specificity (81.4%) than serum CA125 in identifying reappearance and an extended lead time of 3 months over serum CA125 [86].

Osteopontin (OPN)

Proteins such as osteopontin, found in the extracellular matrix, inflammation sites, and body fluids, are secreted by activated leukocytes, macrophages, and T-lymphocytes. Further, there is evidence in the literature that osteopontin staining is increased in metastatic lesions of 40 women with stage III ovarian cancer compared with the primary tumour, and metastatic lesions are supported by this independent prognostic indicator [87]. There were significantly higher osteopontin plasma levels in 51 ovarian cancer patients compared to a total of 107 healthy controls, 46 women with the benign ovarian disease, and 47 women with other gynaecological malignancies. [88]. Freshly, a proteomic-based systemrecognised a C-terminal portion of osteopontin in the pre-surgical urine trials of ovarian cancer patients and in patients with the primitive-stagedisease, signifying that it may have prospective as a suitable non-invasive biomarker for theearly discovery and forecast of ovarian cancer [89].

MSLN

According to recent research, MSLN is implicated in cell adhesion and signaling [90], the ERK signal pathway can be activated to facilitate migration and invasion of ovarian cancer cells [91]. MSLN levels elevated in patients with optimal debulking surgery also predict poorer overall survival (OS) [92,93]. Only Shummer *et al.* [94] evaluated the use of MSLN as a marker of remission.The study included 23 women with ovarian cancer who underwent surgery and chemotherapy; the markers (CA125, HE4, MMP7, and MSLN) were assessed after remission before evaluating recurrence.Only four of the 20 patients whose MSLN levels increased showed a recurrence.

Paraneoplastic Antigen

Paraneoplastic antigens have been used to forecastrepetition in ovarian cancer. Various neurological disorders called paraneoplastic syndromes can be caused by the development of these antibodies [95]. Both neurons and tumour cells

express paraneoplastic antigens, resulting in a humoral immune response and onco-neural antibodies. A study conducted by Chatterjee *et al.* [76] determined the warmth of a panel of six paraneoplastic antigens (HARS, CDR2, Ro52, 4B7, 4H4 and 5H6) in predictingthe reappearance of ovarian cancer before the increase in CA125 levels.

CONCLUSION

Women are most likely to die of ovarian cancer, the leading cause of death with a high incidence rate. All types of ovarian cancer have an increased incidence of EOC. EOC can be classified into two types based on the risk factors involved and the stage and genes involved in the development of the tumour. Here is a summary of the magnitude of the problem and analyse of epidemiological studies that have identified risk factors associated with this disease, including genetic, environmental, and lifestyle factors. The most common screening and diagnosis techniques for ovarian cancer are ultrasound, CT, and MRI. Surgery and chemotherapy are combined to treat cancer patients to prevent and detect this deadly disease, and more research is necessary to understand its heterogeneous ethology.

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Table 1: FIGO Staging Of Ovarian Cancer

Stage	Description
I	A tumour that is contained within the uterus
IA	There is a 50% invasion rate of the myometrium
IB	The myometrium is infected to a greater than 50% degree
II	A cervical tumour invades the stroma of the uterus but does not extend beyond it
III	Tumours affecting the local region
IIIA	The invasion of the serosal and adnexal tissues
IIIB	Involvement of the genital region
IIIC	Metastases in the paraaortic or pelvic lymph nodes
IIIC1	Lymph nodes of the pelvis are involved
IIIC2	Lymph nodes in the paraaortic region are involved
IV	This condition may include an expanded pelvic wall, an enlarged lower third vaginal cavity, or a nano functioning kidney.
IVA	Bowel or bladder mucosal invasion
IVB	The presence of distant metastases within the abdominal cavity or in the lymph nodes of the inguinal region

Table 2: Diagnostic parameters of ovarian cancer

Sl no	Name of the test	Procedure	Inference
1	Physical Exam	Health care professionals feel the size, shape, and consistency of the ovaries and uterus during a pelvic exam	Patients having early symptoms should be proceeding for further test
2	TVUS (Trans Vaginal Ultrasound)	An ultrasound wand is put into the vaginal canal to examine the uterus, fallopian tubes, and ovaries with sound waves	Identifying ovarian tumours
3	Imaging Test	Doctors used to take pictures inside of the body	Help to find the pelvic mass and also help to seeif ovarian cancer has spread to other tissues and organs
4	CT Scan	It is an x-ray test that produces a detailed cross-sectional image of the body	Help to find large tumours, a sign of cancer spread to the liver, or it affects to kidney and bladder
5	MRI	Similar to CT scan but does not involve radiation	
6	PET Scan	Imaging test measure tissue activity	
7	Laparoscopy	Through a small incision in the lower abdomen, the tube transmits images of the pelvis or abdomen to a video monitor	It allows doctors to view organs for planning surgery or other treatments and confirming the stage of cancer.
8	Biopsy	The most common way to perform a biopsy is to remove the tumour during surgery and examine cells under a microscope	

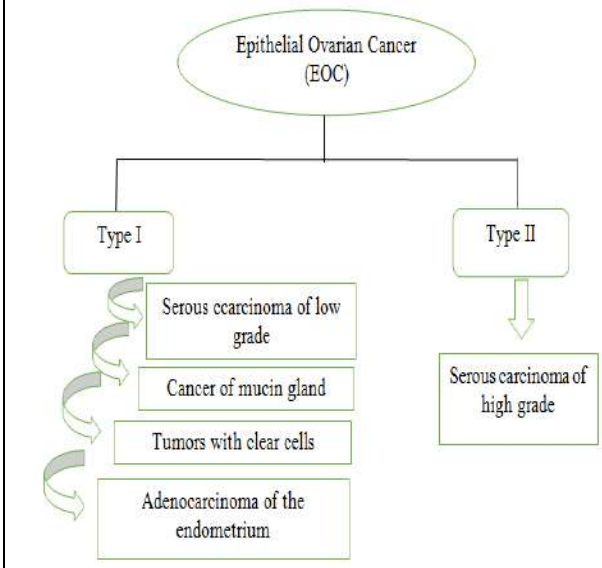

Fig 1: Different types and subtypes of epithelial ovarian carcinoma

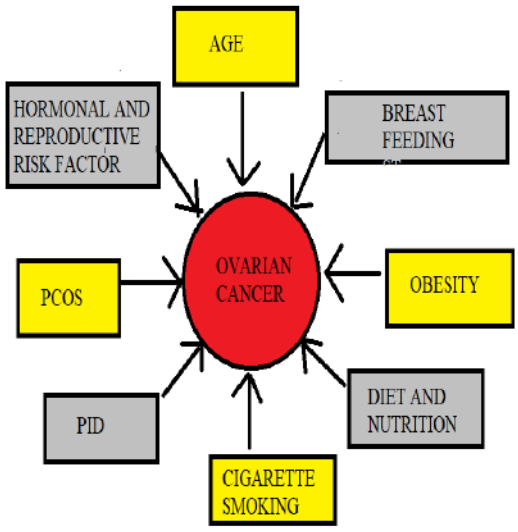

Fig 2: Risk factors responsible for ovarian cancer

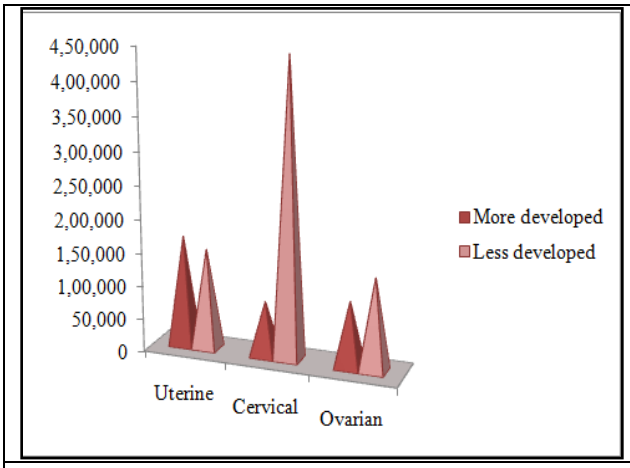

Fig.1. Gynecological Cancer Incidence (2012)

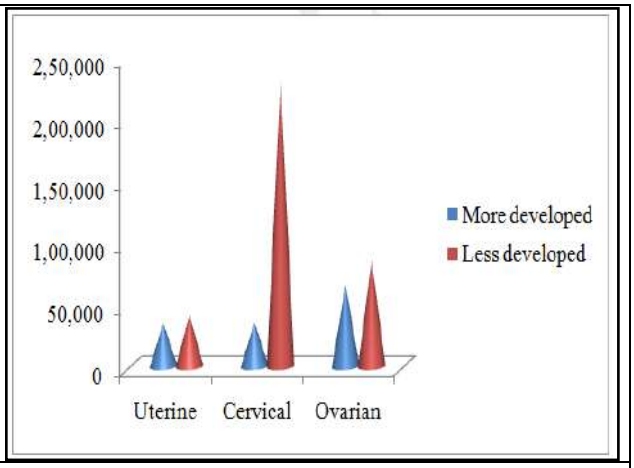

Fig.2. Gynecological Cancer Mortality (2012)

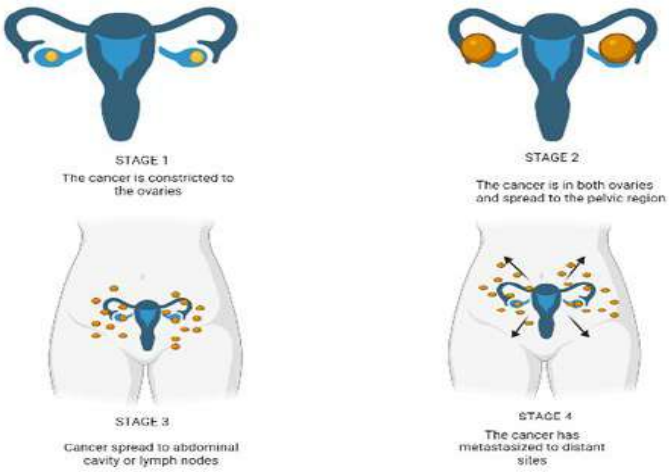

Fig.3. Stages Of Ovarian Cancer

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RESEARCH ARTICLE

Hard Turning of AISI 01 Steel and Process Parameter Optimization

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ABSTRACT

This paper focuses on minimizing surface roughness of AISI 01 steel workpiece using hard, and unalloyed WC/Co grade (ISO K313) inserts in CNC turning. Cutting speed, feed, and depth of cut were taken as input parameters/ factors to evaluate surface roughness as output or response. The experiments were carried out, and the output characteristics were investigated and optimized using Taguchi Method. An appropriate regression model was proposed to predict output as experiments are costly and time-consuming.

Keywords: Dry Turning, Taguchi Method, Regression Analysis.

INTRODUCTION

Dry machining is both eco-friendly and economical. It is also termed green machining and the future of machining. Dry machining is non-toxic, non-polluting, and non-harmful to the skin[1].CNC machining is a sophisticated manufacturing method that produces parts with high accuracy and tight tolerances. Because of a subtractive manufacturing process, CNC machining leaves micro irregularities as surface roughness. Several parameters define surface roughness. Ra (Average roughness) is the most common parameter determined and measured in micrometers or microns [2]. Taguchi's design of experiments methodology allows for faster optimization of cutting parameters. Taguchi proposes an experimental design to make goods more durable – less vulnerable to noise. The experimental design technique can reduce variation in product and process quality [3]. ANOVA can be used to find the most critical factors. [4]. Matsumu Ra et al.[5] (2004) used the design of experiments to determine optimal cutting settings for surface finish and study the machinability in turning steel obtained with coated carbide. Vikram et al. (2007) studied the performance of coated tools during hard turning with the minimal fluid application. Many authors have modeled surface roughness. In turning free machining steel utilizing Taguchi design, Davim [6] found

that cutting velocity has the most influential factor on surface roughness, followed by feed rate. Lin et al. [7] had concluded that feed rate is the critical parameter affecting surface roughness based on their findings. In mild steel turning, Suresh et al. [8] found that cutting speed reduces surface roughness significantly. Surface roughness increases with the depth of cut and feed rate, according to Arbizu and Perez [9]. According to Sahin and Motorcu [10], the feed rate is the critical factor influencing surface roughness while turning mild steel with coated carbide tools. Surface roughness rises with feed rate but lowers with cutting speed and depth. According to the literature review, most research considers the three turning parameters: cutting speed, feed rate, and depth of cut for analysis. There are 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure), and 11 (Sustainable cities and Communities).

This study has two objectives

1. To apply Taguchi's parameter design to find the best parametric combination to reduce surface roughness.
2. To provide a prediction model for assessing surface roughness using data from Taguchi design experiments.

DETAILS OF EXPERIMENT

Workpiece

The workpiece used was AISI 01 steel/ OHNS steel cylindrical bar (D=120 mm and L=300 mm). The chemical composition is in weight percentage as C- 0.85%, Si- 0.35 % Mn-1.20%, P- 0.04%, S- 0.03, Cr- 0.60%, W- 0.70 % and Fe remaining. It is manganese-chromium-tungsten steel excellent for cold work. After hardening and tempering, the steel has good machinability, dimensional stability, and a mixture of high surface hardness and average toughness, making it fit for the manufacture economical tools (blanking and stamping die, punches, thread cutting tools, milling cutters, reamers, woodworking tools, and broaches) with good tool-life.

Tools and Equipment

The cutting tool is K313 cemented carbide inserts (Make: Kennametal) having Insert designation as SNMG 12 04 08. Best for machining titanium, cast irons, austenitic stainless steels, non-ferrous metals, non-metals, and most high-temp alloys. Resistant to thermal deformation and high cutting depth [10]. The turning operations were carried out in Super Jobber (Make- ACE Designer) CNC lathe machine. Surface roughness was measured using a Talysurf profilometer (Make-Taylor Hobson).

METHODOLOGY

Table 1 shows cutting parameters/factors with levels. A L27 orthogonal array was chosen for running experiments [11, 12]. Table 2 shows the runs and response (surface roughness).The option for signal-to-noise ratio (S/N ratio)is lower-the-better. The analysis is carried out by MINITAB 19 software. Table 3 shows the results of ANOVA on the responses. Feed has a significant effect on the surface roughness than other parameters as the results support. The regression equation is

$$Ra = 2.377 - 0.01084v + 0.194d + 27.58f \quad (1)$$

The R^2-value (coefficient of determination) is obtained as 96.2%.

Figure4 shows the residual plots suggesting that the residuals have a normal distribution. It reveals that ANOVA is working correctly.A confirmatory experiment was done using a non-optimal parametric combination. The main effect plot, figure 3, shows that cutting Speed of 200 m/min, feed of 0.03 mm/rev, and depth of cut of 0.3 mm

minimizes surface roughness. The ANOVA predicted values differ by less than 10% from the experimental surface roughness. So the Taguchi empirical analysis was done accurately.

CONCLUSIONS

Analysis of variance indicates that feed is a dominating parameter of surface roughness followed by cutting speed. To minimize roughness, the optimal cutting parameters combination is found to be v=200 m/min, f=0.03 mm/rev, and depth of cut=0.3 mm, while turning AISI 01 steel with carbide inserts.

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Table 1: The cutting parameters with their levels

Input Parameters	Symbols			
Cutting speed (m/min)	v	150	175	200
Feed (mm/rev)	f	0.03	0.06	0.08
Depth of cut (mm)	d	0.3	0.6	0.9

Table 2: Experimental Results

Inputs/ Factors			Output/Response	
V	**F**	**d**	**Ra(μm)**	**SNRA1**
150	0.03	0.3	1.63	-4.244
150	0.03	0.6	1.75	-4.861
150	0.03	0.9	1.83	-5.249
150	0.06	0.3	2.42	-7.676
150	0.06	0.6	2.51	-7.993
150	0.06	0.9	2.63	-8.399
150	0.08	0.3	3.42	-10.681
150	0.08	0.6	3.61	-11.150
150	0.08	0.9	2.1	-6.444
175	0.03	0.3	1.23	-1.798
175	0.03	0.6	1.6	-4.082
175	0.03	0.9	1.63	-4.244
175	0.06	0.3	1.93	-5.711
175	0.06	0.6	2.18	-6.769
175	0.06	0.9	2.32	-7.310
175	0.08	0.3	2.62	-8.366
175	0.08	0.6	2.84	-9.066
175	0.08	0.9	3.03	-9.629
200	0.03	0.3	0.96	0.355
200	0.03	0.6	1.15	-1.214
200	0.03	0.9	1.21	-1.656
200	0.06	0.3	1.8	-5.105
200	0.06	0.6	1.97	-5.889
200	0.06	0.9	2.06	-6.277
200	0.08	0.3	2.5	-7.959
200	0.08	0.6	2.62	-8.366
200	0.08	0.9	2.75	-8.787

Table 3: ANOVA Table

Analysis of Variance for SN ratios

Source	DF	Seq SS	Adj SS	Adj MS	F	P
v	2	26.502	26.502	13.251	10.14	0.001
f	2	162.814	162.814	81.407	62.28	0.000
d	2	4.283	4.283	2.142	1.64	0.219
Residual Error	20	26.142	26.142	1.307		
Total	26	219.742				

Table 4: Response Table

Response Table for Signal to Noise Ratios

Smaller is better

Level	v	f	d
1	-7.411	-2.999	-5.687
2	-6.331	-6.792	-6.599
3	-4.989	-8.939	-6.444
Delta	2.422	5.939	0.912
Rank	2	1	3

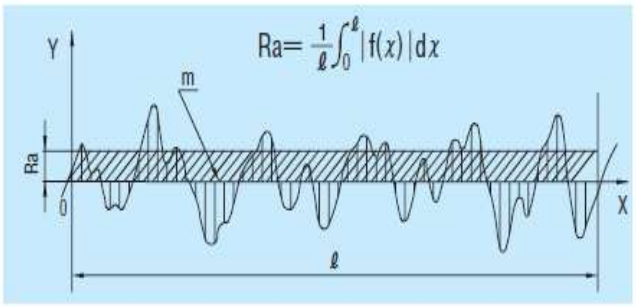

Figure 1:Evaluation of Ra[2]

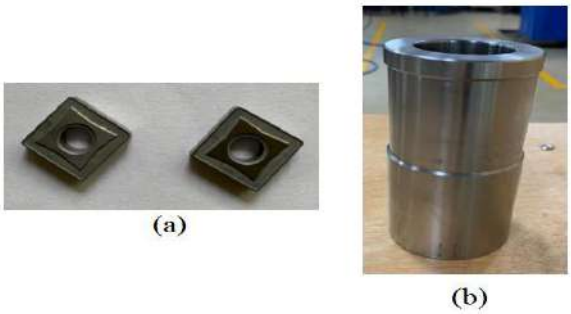

Figure 2 (a) Carbide Inserts; (b) Turned Product

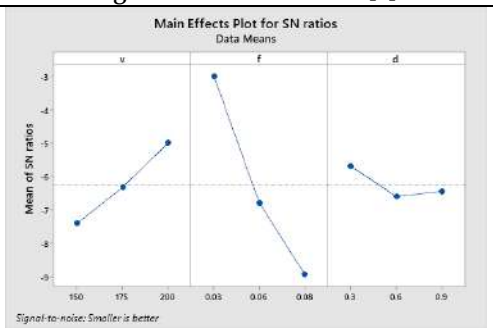

Figure 3: Main effect plot

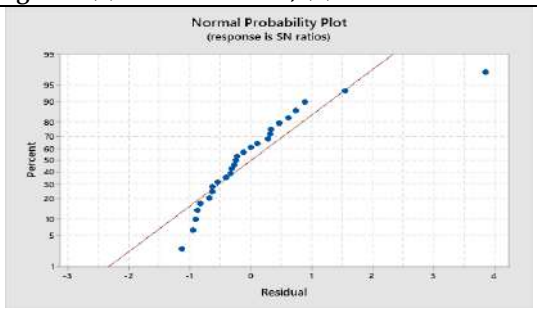

Figure 4 Normal probability plot

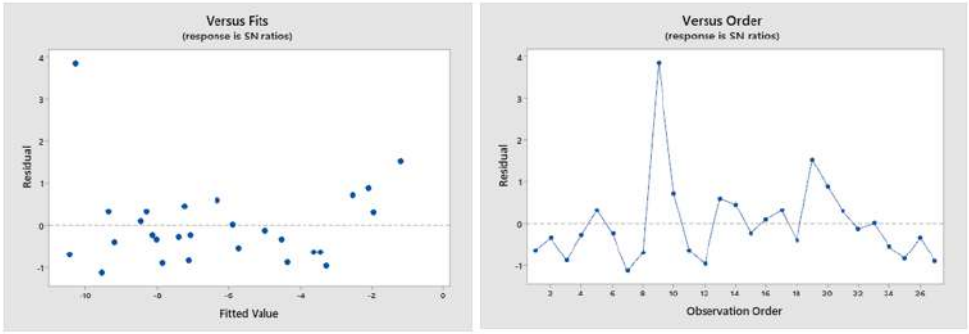

Figure 5. Residual plots

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RESEARCH ARTICLE

Fabrication of Tin Oxide Nanostructure with Enhanced Photo Degradation Efficiency for Hazardous Pollutant

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ABSTRACT

The current research work reveals the degradation study of cationic dye like methylene blue (MB) by using nano tin oxide catalyst. The nano powder was synthesized by wet chemical sol-gel route maintaining calcination temperature of 600° C. The prepared samples were characterized by the help of X-ray diffraction (XRD), UV-Vis spectroscopy, Field emission scanning electron microscopy (FESEM), and FTIR spectroscopy. The X-ray analysis shows the formation of tetragonal rutile structure for SnO_2 nano crystals having crystallite size of 12nm. The morphology of the sample is observed to be particles like of irregular shape. The absorption peak was obtained as 339nm and band gap energy value was calculated as 3.76 eV. The photo catalytic activity of SnO_2 was explored against toxic as well as major water pollutant methylene blue dye with UV-Vis illumination for time period of 180min. The degradation rate was found to be 90% and observed to follow pseudo first order kinetics. The result depicts higher photo catalytic rate for sample in comparison to other production method.

Keywords: Stannic oxide, sol-gel, photo catalytic activity, Methylene Blue

INTRODUCTION

The fast evolution of industries and increase in global population leads to enormous rise of unadulterated fumigated water bodies for the survival of aquatic life. Moreover, progress in agricultural and domestic field ensued in accumulation of huge volume of pollutant in water course. Major source of contaminant was found to carry various dyes. The dyes produced from several industries are hazardous, mutagenic and does not allow dispersion of sunlight and cause imbalance in aquatic biomes. So, treatment of industrial sewage is a serious concern for maintain the marine ecosystem. The various suitable conventional methods for the above purpose were used ranging from adsorption to reverse osmosis process end up with number of limitations. Hence the need of environmentally friendly and sustainable method for complete degradation of contaminant gained attention of researchers. To

develop a novel, powerful and promising method called as advanced oxidation process for elimination of impurities from water bodies is a top priority now [1-14]. Nano semi conductor photo catalyst plays a significant role in the above process. Photocatalysis is one type of advanced oxidation process where a chemical reaction is ignited under the influence of light i.e. photons. For the effective degradation of harmful contaminants, photo catalytic approach is a novel method towards controlling water pollution.

Among different types of semiconductors, metal oxide nano particle is found to be very effective due to its cost effective, non-hazardous nature and higher stability to chemical reaction. It acts as a catalyst and provides larger surface area for reactant to combine and form activated complex which further breaks down to give products. This process is known as contact catalysis. Amid metal nano oxide, tin oxide accumulated huge attention in the field of research owing to its exceptional physical and chemical features. It is a n-type semiconductor mostly used in gas sensor, lithium-ion batteries, solar cell, transistor and electrodes. It was proved to be an efficient photocatalyst as it plays an important role in water splitting, hydrogen production and degradation of organic contaminants [15-30]. The photocatalytic activity in the metal oxide is completely dependent on the electron-hole pair formation through band gap energy differences. Furthermore, tin oxide has less effect on health as it was poorly absorbed through injection. In the study, wet chemical technique such as sol-gel route is used for the fabrication of nano tin oxides. The synthesized nanocatalyst undergoes characterization by X-ray diffraction, Fourier transform infrared (FTIR) spectroscopy, FESEM and UV-Visible spectroscopy. The photocatalytic activity of the prepared sample was studied for the photo degradation of the cationic dye such as methylene blue. The current study satisfy the sustainability development goal 11(sustainable cities and community).

Experimental

Material Synthesis

Stannous tetrachloride pentahydrate ($SnCl_4.5H2O$), isopropylalcohol, sodium hydroxide (NaOH) and methylene blue were purchased from M/s Sigma-Aldrich and used as the reagents in this experiment. We also used double distilled water as the solvent throughout the experiment. The stannous oxide nanoparticles were synthesized by sol-gel route. The preparation of SnO_2 nanoparticles was done by taking different concentration of $SnCl_4.5H_2O$ solution and isopropyl alcohol as precursors. Requisite amount of $SnCl_4.5H_2O$ was taken in a conical flask and 50ml of isopropyl alcohol was added to it with stirring in a magnetic stirrer for 2h until a homogenous solution was obtained. After that 0.1M NaOH solution was added drop wise from a burette till pH reaches from 9 to 11.Then it was stirred for another hour in magnetic the stirrer. The prepared sample was washed by decantation process by using double distilled water and acetone for several times. The sample was kept in oven for drying at 100^o C for 12h. Then sample was calcined for 2 h at 600^o C.Finally,the dried sample was powdered and collected in sample box.

Characterization Of Materials

The as synthesized samples were characterized to understand the structural, optical and photocatalytic properties. The structural property is verified by x-ray diffraction technique (M/s Panalytical, X Pert Pro) and the lattice parameters were ascertained using the data obtained from the measurement. The diffractometer was inbuilt with a Cu Kα (1.5406 Å) radiation source operating at 40kV and 30 mA. The scanning rate was maintained at 0.02°/s with the scanning range of 10°-80°. Scherer formula($D=K\lambda/\beta \cos\theta$) was implemented to estimate the average grain size of the SnO_2nanoparticles. To investigate the morphology of the sample, we took the help of a scanning electron microscope (FESEM, Zeiss Supra). The powdered sample was dispersed in acetone and put inside a UV-Vis spectrometer (Shimazdu 1650PC) to record the absorption spectrum in 200 to 800 nm range. The existence of different functional groups present in the sample can be verified by FTIR measurement which was carried out by a spectrometer (M/s Perkin-Elmer)in 400-4000cm^{-1} range.

The photodegradation ability of the sample is examined from the mineralization study of methylene blue dye under the action of UV-Vis light. Here, SnO_2 nanoparticles were considered as photocatalyst to degrade the above dyes under light irradiation. The reaction was carried out in a photoreactor designed by us with taking1 mg of tin oxide

samplewhich was mixed with 100mL of dye (10mgL^{-1}) in a beaker. To obtain adsorption–desorption equilibrium, the above solution was subjected to continuous stirring for 1h. The detailed process has been described in our previous reports. We used the following equation to estimate the degradation (%).

Degradation (%) $=(C_o - C_t)/C_o * 100$

Here, $C_t$is the dye concentration at time 't' and $C_o$is the initial concentration of dye. By plotting ln (C_0/C_t) against time,the rate constant 'k' was calculated.

RESULT AND DISCUSSIONS

X-Ray Diffraction Study

The structural properties of the tin oxide sample investigated and the diffraction pattern is depicted in Fig.1. It has been observed that tetragonal rutile structure has been developed in the tin oxide sample in correspondence to the diffraction peaks after comparison with the standards JCPDS(card No 14-1445). We have observed x-ray diffraction peaks at various diffraction anglessuch as 26.76, 33.88, 38.05, 51.76, 54.85, 64.8, 65.9, 78.72, which have been attributed to (110), (101), (200), (211), (220), (002), (310), and (301) planes respectively.Figure-1 shows the presence of highly intense and narrow diffraction peaks. We have estimated the average grain size of the sample by Scherer equation as discussed earlier. The lattice parameters of the prepared sample are shown in the Table-1. It is observed that the size of SnO_2 nanoparticles is in 12nm range. From the graph, it has been observed that there is no formation of low temperature monoclinic or high temperature cubic phases are there. The peaks were detected at $2\theta = 20^o$ and 80^o regions of the XRD pattern indicating the formation of rutile structure without any cubic phase having value of a = 4.737Å and c = 3.186 Å. The cubic system having unit cell volume is $V= a^2X\ c = 71.4996$ Å^3. The standard value of the sample is less than the observed value of density reveals that tin oxide powder is compact and densely packed with few unit cells of the material. From XRD spectra, minute line shifting is seen which implies formation of micro strain on the grain [31, 32].

FESEM Study

FESEM measurement was accomplished to investigate the surface structure and morphology of the photocatalyst sample and the image is illustrated in Figure-2. It has been observed that fine nanoparticles of irregular shape have been formed. It is very difficult to ascertain the size of the nanoparticle as we can observe particles of size 5-50 nm are formed with agglomeration causing more no of particles getting overlapped on each other.

FTIR Analysis

FTIR spectroscopic measurement was done by recording the transmittance (%) spectrum of tin oxide nanoparticles which is shown in the Figure-3.It reveals the formation of a broad IR absorption band at 3450cm^{-1} to 1630cm^{-1} which corresponds to the association of stretching and bending vibrations of O-H bonds. The sharp peak at 1398cm^{-1} shows the presence of symmetric C-O bond vibrations. The presence of band at800cm^{-1} indicates the presence of metal-oxygen bond which may arise due to Sn-O bonds[41, 42].

UV-Visible Spectroscopy

To discover the optical properties like absorbance of UV-Vis radiation by the prepared samples, we conducted the UV-Vis spectroscopic studies. Metal oxide semiconductors are specified their band gap values which can be easily estimated by the above study. The absorbance of tin oxide sample was measured by the above process and the spectrum is illustrated in Figure-4. From the absorption spectra, it was observed that size of nanoparticle greatly influence its absorption in UV-region which was found to be 339nm. The value of optical energy gap is evaluated by extrapolation of Tauc's plot. The value of the band gap for SnO_2 was found to be 3.65 eV. The change in the band gap value implies the existence of defects in terms of Sn interstitials, oxygen vacancies, crystal defects which lead to the generation of impurity energy level causing the above change [33-40].

Photo Catalytic Activity

Study on the photocatalytic degradation ability of SnO_2 NPs was carried out recording the changes in the absorption intensity of the MB dye solution. As the contaminant is degraded under dual action of UV-Vis light and tin oxide photocatalyst, we observed a sharp decrease in the intensity of the above peak and gets flattened. This has been depicted in Figure-5. 1 mg/L concentration of catalysts was prepared with 10 ml of dye solution and a mixture was prepared with 10^{-4}M of MB. With the help of a magnetic stirrer, we stirred the sample continuously for half-an-hour before light exposure. To obtain the adsorption–desorption equilibrium, the above process is essentially required. As the absorbance spectra is recorded, we observed an intense peak at λ= 664 nm which loses its intensity gradually. About 90% of degradation was achieved for SnO_2 sample as represented in theFig.5. In dark, no degradation was observed without the catalyst. It has been observed that the dye is not adsorbed on the surface of the catalyst [41-51]. Due to the small size of SnO_2 nanoparticles and check in electron-hole recombination, an enhanced photodegradation is observed. This is the reason why metal oxide semiconductors have been widely studied with novel applications [52-75].

CONCLUSION

In this study, nano structured tin oxide was successfully fabricated by simple wet chemical sol-gel route. The prepared photocatalyst was calcined at 600o C. XRD analysis confirms the formation of tetragonal rutile structure showing peaks in the region between 20º to 70º having average crystallite size of 12nm. The FTIR spectrum reveals the formation of broad IR absorption bands at3450cm-1 to 1630cm-1 which correspond to the association of stretching and bending vibrations of O-H bonds. The FESEM image displays non uniform distribution of finer particles of different size and shape. From UV-Visible studies, the absorption peak was observed at339nm. The band gap value for SnO2 was found to be 3.65 eV. The photocatalytic activity of synthesized tin oxide was examined by taking hazardous pollutant methylene blue dye with UV-Visible illumination for time period of 180 min. The degradation rate was calculated to be 90 % which follows pseudo first order kinetics. From the experiment, it was observed that the prepared photocatalyst exhibits higher photocatalytic degradation rate with comparison to other synthesized route. This leads to the industrial application of removal of unwanted contaminants from aquatic ecosystem. The current study satisfied the sustainability development goal 11(sustainable cities and community)which make cities and human settlements inclusive, safe, resilient and sustainable.

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Table.1.Lattice parameters and average grain size of SnO_2.

Sample	Size (nm)	Stain	Lattice Parameter			Density (gm/cm^3)	Volume(A^0)^3
			a (A^0)	c(A^0)	c/a		
SnO_2	12	0.0012	4.3212	3.187	1.355	6.472	71.0472

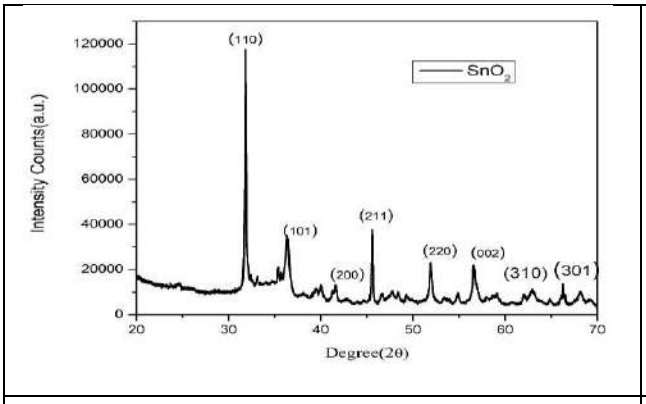

Fig.1: XRD graph of SnO_2 nanoparticles.

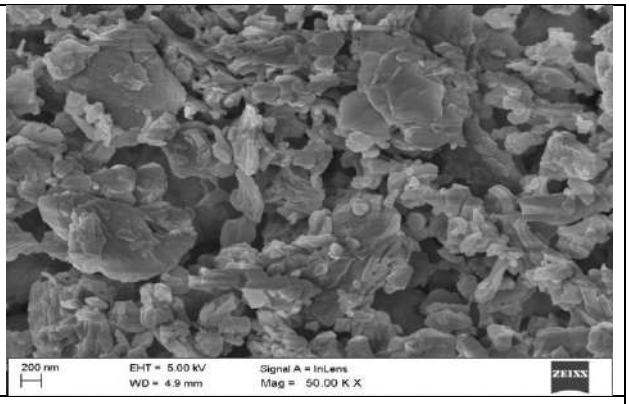

Fig.2: FESEM image of tin oxide nanoparticles.

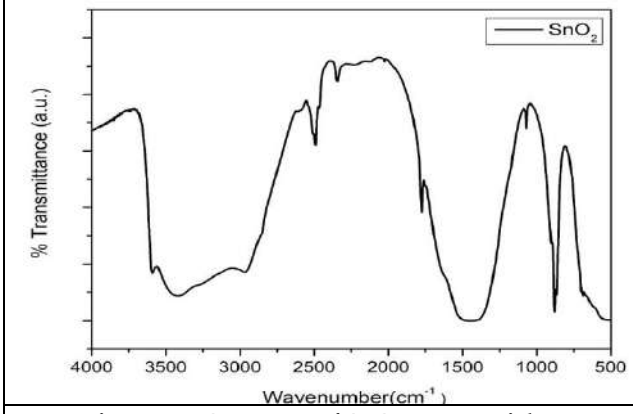

Fig.3:FTIR Spectrum of SnO_2 nanoparticles.

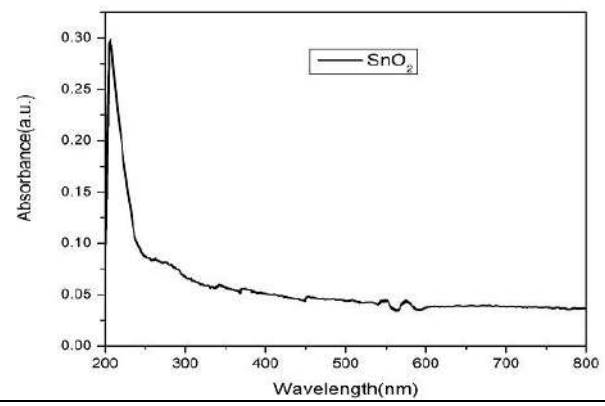

Fig.4: UV-Vis absorbance spectrum of SnO_2nanoparticles.

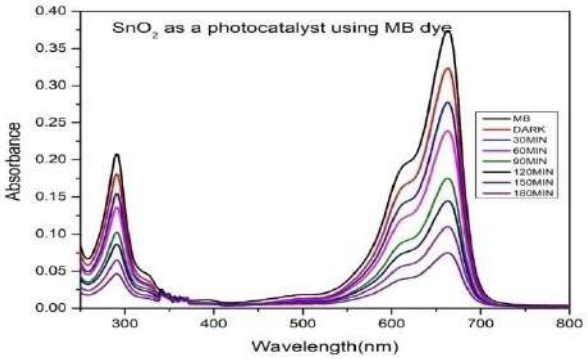

Fig. 5: Absorption spectra of MB dye showing photo degradation by SnO_2.

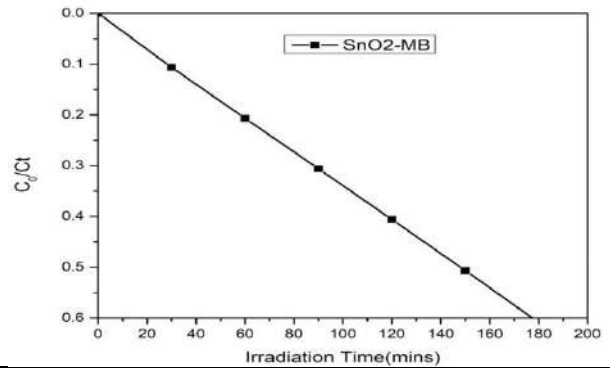

Fig. 6: variation in C_0/Ct with irradiation time showing first order kinetics

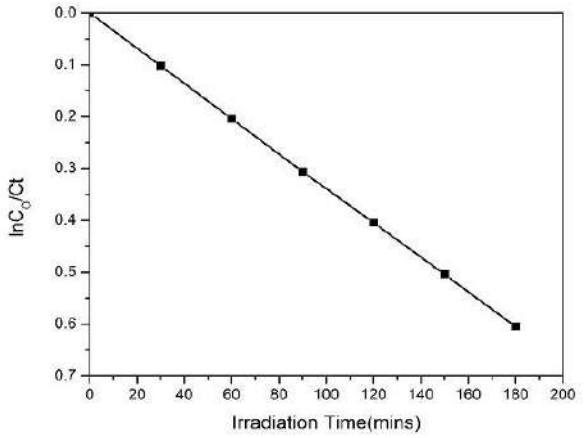

Fig. 7:Variation in ln (Co/Ct) with irradiation time showing first order kinetics.

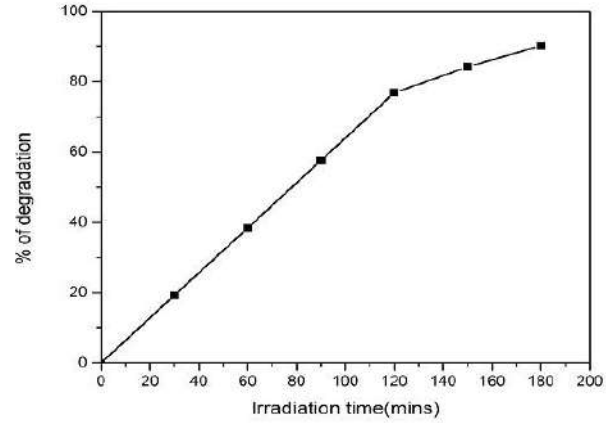

Fig. 8:Degradation of MB concentration at different UV light exposure time.

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RESEARCH ARTICLE

A Mini Review on Classification and Antibacterial Activity of Flavonoids against UTI Pathogens

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ABSTRACT

Urinary tract infections (UTIs) are highly communal illnesses in the society. They are defined as any infection, usually of bacterial origin, that develops in any region of the urinary tract causing urethritis, cystitis, pyelonephritis and vaginitis. Phytochemicals are more commonly thought of as research molecules than as vital nutrients. Phytochemicals come in a variety of forms. The effects of flavonoids are discussed in this paper. Over 25,000 phytochemicals have been discovered in total, with the majority of them located in colourful sections of plants such as fruits, vegetables, nuts, legumes, and whole grains. Phytochemicals produced from medicinal plants have been utilised to cure and control numerous illnesses since ancient times due to their positive benefits. In the present review, the complete focus was on the activity of Flavonoids against the grave UTI causing pathogens.

Keywords: Phytochemicals, urinary tract infection, Flavonoids, Cystitis, Urethritis

INTRODUCTION

Urinary tract infections (UTIs) are highly communal illnesses in the society. They are defined as any infection, usually of bacterial origin, that develops in any region of the urinary tract. Urethritis (infection of the urethra), cystitis (infection of the bladder), pyelonephritis (infection of the kidneys), and vaginitis are the four types of UTIs (infection of the vagina). UTIs are now a major public health concern, accounting for over 150 million illness cases each year around the world(Motse *et al.,* 2019). Most Gram negative (GN) bacteria like*Escherichia coli*, and mixed infections of (Gram positive, GP) *Staphylococcus aureus*, *Enterococcus faecalis*, including other GNs, *Klebsiellap neumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Enterobacter aerogenes*, *Proteus mirabilis, Citrobacter freundii* are causing UTI. The majority of infections are caused by bacteria that are ordinarily found on the skin or in the intestine and infiltrate the urinary tract. With a weakened body defence system and decreased urine flow, the invading bacteria penetrate the urethra and bladder. The bacteria enter the bladder through the urethra, colonise,

multiply, and induce inflammation, resulting in severe pain, burning, frequent and urgent urination, nocturia, foul-smelling, murky urine, and haematuria (Mishra *et al.,* 2013).Bacteriouria, or the proliferation of bacteria in urine within the renal tract, is a common infection. Significant bacteriuria is defined as a concentration of more than 105 organisms/ml. The presence of W.B.C (polymorphous) in the urine is known as pyruria. Hematuria is defined as the presence of RBC in the urine (McMurry& Levy, 2011).

Recurrent infections, particularly in women, permanent kidney damage from an untreated UTI, higher risk of low birth weight or premature newborns in pregnant women, urethral narrowing (stricture) in men, and sepsis, especially in the infection spreads up your urinary tract to your kidneys (Head, 2008). Drinking enough of water allows bacteria to be expelled from the urinary system by diluting the urine. Cranberry juice has been shown to aid in the prevention of urinary tract infections. Deodorant sprays and other feminine products that can irritate the urethra should be avoided in the vaginal area to avoid urinary tract infection (Head, 2008).

Phytochemicals are more commonly thought of as research molecules than as vital nutrients. Phytochemicals come in a variety of forms. The effects of alkaloids, flavonoids, steroids, and tannins are discussed in this paper. Over 25,000 phytochemicals have been discovered in total, with the majority of them located in colourful sections of plants such as fruits, vegetables, nuts, legumes, and whole grains. Phytochemicals produced from medicinal plants have been utilised to cure and control numerous illnesses since ancient times due to their positive benefits(Das *et al.,* 2015). Phytochemicals have grown in popularity and trustworthiness around the world due to fewer reported adverse effects, cost effectiveness, easy availability, lack of bacterial resistance, and tolerance toward patients with UTI even at the dawn of the twenty-first century. Furthermore, according to WHO medicinal plants are used by 80 percent of the world's population and more than 30 percent of pharmaceutical formulations (Taid *et al.,* 2014).

Due to a lack of research, the exact mechanism of herbal medicines used to treat UTI is still unknown, but phytochemical constituents have been reported to act as nutraceuticals and immunomodulators, boost body oxidant status or provide antioxidant compounds, prevent microbe attachment as well as halt the proliferation or multiplication of microorganisms, and some may act as microcidal. Alkaloids, anthraquinones, flavonoids, glycosides, phenols, saponins, steroids, sterols, tannins, terpenoids, triterpenoids, phytosterols, hydrocarbons, mono and sesquiterpenes, phlobatannins, and many other medicinal plant secondary metabolites are responsible for the diverse properties of medicinal plants. Flowers, leaves, bark, fruit, seeds, and even whole portions of medicinal plants have been used to treat UTI, and these parts or extracts are taken orally as a single preparation or coupled with other meals or drinks such as water, honey, milk, juices, and black pepper, among other things (Taid *et al.,* 2014). In the present review, the complete focus was on the activity of Flavonoids against the grave UTI causing pathogens.

Pathogenesis of UTI

Feces contains the germs that usually cause urinary tract infections. The colonisation of the distal end of the urethra occurs when the periurethral region is contaminated with faeces. The anus is near to the urethra, which transports urine from the bladder to the outside of the body. Bacteria from the large intestine, such as E. coli, can sometimes make their way into your urethra through your anus. They can then make their way up to your bladder. Bacteria enters the lower respiratory tract and contaminates it. It colonises the urethra and bladder at first, triggering an inflammatory reaction in the urinary tract, and then neutrophils are recruited, further inflaming the region. When bacteria multiply, they are able to resist the immune system due to virulence factors. If the urinary tract infection is not treated or if the person is immunocompromised, the bacteria may ascend to the kidney and colonise there, resulting in an upper urinary tract infection. If left untreated, the bacteria can migrate into the bloodstream through the renal veins, resulting in septic shock.

Classification of Flavonoids

Flavones

One of the most important flavonoid subclasses is flavones. Flavones can be found in the form of glucosides in leaves, flowers, and fruits. Celery, parsley, red peppers, chamomile, mint, and ginkgo biloba all contain flavones. This flavonoid class includes luteolin, apigenin, and tangeritin. Citrus fruit peels contain high levels of the polymethoxylated flavones tageretin, nobiletin, and sinensetin (Manach *et al.,* 2004).

Flavonols

Flavonols are flavonoids with a ketone group. These basic units make up proanthocyanins. Flavonols are abundant in a wide variety of fruits and vegetables. The most researched flavonols are kaempferol, quercetin, myricetin, and fisetin. Onions, kale, lettuce, tomatoes, apples, grapes, and berries are high in flavonols. Flavonols are also found in tea and red wine, as well as fruits and vegetables. Flavonol consumption has been linked to a number of health benefits, including antioxidant capacity and a lower risk of cardiovascular disease (Iwashina *et al.,* 2013).

Flavanones

Flavanones are another important class of compounds that can be found in citrus fruits including oranges, lemons, and grapes. This group of flavonoids includes hesperitin, naringenin, and eriodictyol. Because of their free radical-scavenging characteristics, flavonones are linked to a variety of health advantages. Citrus fruit juice and peel contain these chemicals, which give them a bitter taste. Citrus flavonoids have pharmacological actions that include antioxidant, anti-inflammatory, blood lipid-lowering, and cholesterol-lowering. The C ring is saturated in flavanones, also known as dihydroflavones; thus, unlike flavones, the double bond between positions 2 and 3 is saturated, and this is the only structural variation between the two subgroups of flavonoids. The number of flavanones has expanded dramatically in the last 15 years (Aoki *et al.,* 2000).

Isoflavonoids

Flavonoids are divided into isoflavonoids, which constitute a big and separate subgroup. Isoflavonoids are found mostly in soyabeans and other leguminous plants and have a limited distribution in the plant kingdom. Microbes have also been found to contain certain isoflavonoids (Matthies *et al.,* 2008). During plant-microbe interactions, they are also discovered to play a crucial function as precursors for the formation of phytoalexins (Diab *et al.,* 2002). Isoflavonoids have a lot of potential in terms of fighting illnesses. Because of their oestrogenic action in animal models, isoflavones like genistein and daidzein are widely classified as phyto-oestrogens.

Flavanols, flavan-3-ols or catechins

Flavanonols are the 3-hydroxy derivatives of flavanones, commonly known as dihydroflavonols or catechins. They are a multisubstituted and highly diverse subclass. Because the hydroxyl group is always attached to position 3 of the C ring, flavanols are also known as flavan-3-ols. There is no double bond between positions 2 and 3 unlike many flavonoids. Bananas, apples, blueberries, peaches, and pears are high in flavanols.

Anthocyanins

Anthocyanins are pigments that give plants, flowers, and fruits their colours. The most studied anthocyanins are cyanidin, delphinidin, malvidin, pelargonidin, and peonidin. They're mostly found in the outer cell layers of cranberries, black currants, red grapes, merlot grapes, raspberries, strawberries, blueberries, bilberries, and blackberries, among other fruits. These compounds' stability, combined with their health benefits, allows them to be used in a range of applications in the food business. The anthocyanin's colour is affected by pH as well as methylation or acylation of the hydroxyl groups on the A and B rings (Iwashina, 2013)

Chalcones

Chalcones are a flavonoid subclass. The absence of 'ring C' of the basic flavonoid skeleton structure depicted in distinguishes them. As a result, they're also known as open-chain flavonoids. Phloridzin, arbutin, phloretin, and chalconaringenin are all examples of chalcones. Tomatoes, pears, strawberries, bearberries, and certain wheat

products all contain substantial levels of chalcones. The simplest and safest strategy to prevent diseases and adjust activities may be to consume flavonoids through food sources.

Activity of Flavonoids against UTI

The antibacterial activity of *Withania somnifera* L. Dunal (Solanaceae) was tested against a variety of diseases in a recent study. The antimicrobial activity of free and bound flavonoids from different parts of *W. somnifera* (root, stem, leaf, and fruit) was investigated using a disc diffusion assay against three Gram negative bacteria (*Escherichia coli* MTCC 46, *Proteus mirabilis* MTCC 3310, and *Pseudomonas aeruginosa* MTCC 1934), one Gram positive bacteria (*Staphylococcus aureus* MTCC 3160), and (*Candida albicans* MTCC 183, *Aspergillus flavus* MTCC 277 and *Aspergillus niger* MTCC 282). The root flavonoid extract with the highest activity against *Candida albicans* was bound flavonoid extract (IZ 30, MIC 0.039, MFC 0.039, respectively). All of the bacteria tested, however, were found to be susceptible to the extracts. *E.coli, P. mirabilis, S. aureus, and C. albicans* all had the same total activity of bound flavonoid extract of root (153.84 ml/g) (Alvarez *et al.,* 2006). To test the antibacterial effects of *Peganumharmala* (*P. harmala*) extracts against pathogens obtained from infected patients with urinary tract infections. The presence of flavonoids, alkaloids, saponins, tannins, glycosides, terpenoids, and steroids, as well as the absence of anthraquinons, were discovered in the leaves of *P. harmala*. Flavonoids isolated from the leaves and seeds of P. harmala were found to be bactericidal against *S.aureus* at both the minimum inhibitory and bactericidal concentrations. The flavonoids extract of *P. harmala* may be effective in the treatment of uropathogenic bacteria, according to the findings of this study (Cushnie & Lamb, 2005).

The antibacterial test of two aqueous extracts and flavonoid, as selective extracts (n-butanolic and ethyl acetate fractions), was carried out by agar well diffusion method against a selection of Gram-positive and Gram-negative uropathogenic bacteria, while the qualitative tri phytochemical screening of Fenugreek (*Trigonellafoenum-graecum* L.) was carried out according to a standard protocol, based on staining method. However, as compared to the antibacterial action of gentamicin, flavonoids had a larger effect, with an activity index (AI) of 1 to 2.5 for *S. aureus* strains at doses of 27 to 223 mg/mL, where Gram-positive uropathogenic isolates were more susceptible. *E. coli, Citrobacter freundii*, and *Pseudomonas aeruginosa* strains, on the other hand, had an activity index of 1 to 1.21 for Gram negative reference bacterial strains (Baron *et al.,* 2013).

CONCLUSION

Despite the diversity of antimicrobial medicines, including antibiotics, multidrug resistance has been steadily emerging in recent years. However, because of the negative side effects they cause, as well as the sometimes prohibitively high treatment costs, as well as adaptation and new resistance mechanisms of microorganisms that emerged and spread globally, many people have turned to bioactive compounds in the form of plant extracts with antimicrobial properties for treatment. According to World Health Organization figures, two-thirds of the world's population uses medicinal herbs as basic medications. Recent research has concentrated on finding plants from all around the world that have the right extract to be used as antibacterial medications. In the present review work, it has been concluded that flavonoid can be an effective drug of choice with best antibacterial activity against the pathogens isolated from urinary tract infection. This review ensures the Healthy lives of people by adopting the use of alternative medicines which acknowledges the development of the social and environmental sustainability following the motto of Sustainable Devlopment Goals 3.

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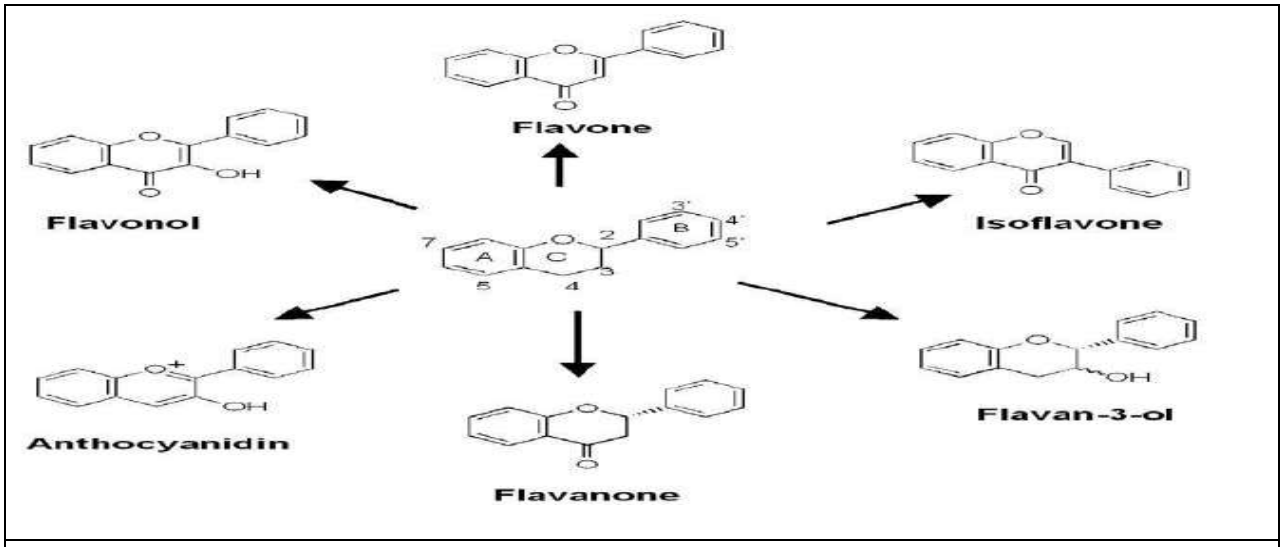

Fig 1: Classification of Flavonoids

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REVIEW ARTICLE

Impact of Salinity Stress on Paddy Production: A Review

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ABSTRACT

Abiotic and biotic stresses are the two important aspects to reduce the crop production. Among the abiotic stresses, salinity plays a major influence on crop production among the abiotic stresses. In this review article, an attempt was taken to explain the effect of salinity stress on rice crop growth and production. The causes of salinity, its impact on crop productivity have also been discussed with an emphasis to use of salt tolerant varieties and coastal land area utilisation to meet the global demand.

Keywords: Abiotic stress, Rice productivity, Salinity stress, *Oryza sativa* L.

INTRODUCTION

Rice is the staple food of majority countries and about 50-80% of people depends on this crop for their daily calorie need (Khush, 2005) and has been predominant in India. Rice contains considerable amount of recommended dose of Zinc and Niacin (Gopalan et al., 2007). According to FAO (2014) India occupies the second in exporting the global wheat and rice production. The yearly production is comparatively less than the growing population. Out of 159,7 million hectares of cultivated field, only 3.77 hectares has been reported to be cultivated with rice, pulses are cultivated in 1.94 ha, coarse cereals 4.74 and oil seeds 8.33, sugarcane 4.96 and cotton 7.16 hectares(3000 Rice Genome Project, 2014). Rice productivity has been affected because of various abiotic stress conditions (Ahmed et al., 2012). Anthropogenic activities are the major reason for environmental stress condition. Stress is the external abiotic or biotic constraint that reduces the plants metabolism and reduces the conversion of energy in to biomass. Abiotic stresses like salinity, cold, drought and temperature influence the yield of staple food crops. Salinity stress is one of the major limitations in rice production. Global warming leads in rising sea level resulting in raising the salinity along with excessive irrigation have become the major constraints for reducing the rice productivity (Hazra et al., 2002). Approximately 6.73 ha of land in India are reported to have high sodium content i.e. sodicity (Sharma et al.,

2004). Negative impact of excess salt contents on the crop is known as salt stress (Munns, 2005). As a result production of paddy will decrease leading to negative impact on our economics, education, health and social development. Cultivation of resistant rice variety will be definitely one of the ways to attain zero hunger for sustainable development.

Causes of Salinity

Natural Salinity

Salinity of the soil is one of the most important physical factors and is the second most soil problem that affects worldwide rice production. Water body and soil of estuarine and coastal regions of the world contain high salt content that affects the productivity and growth of the crops(Luttge and Lauchli, 2002; Munns, 2002).Salinity is resulted due to hyper osmotic condition causing ion imbalances in the cells leading to oxidative damage (Munns and Tester, 2008). Rice productivity has been delimited because of salinity condition in Indian Coastal belt. Climate change and depletion of natural resources is the cause to rise of sea level and coastal storms lead to salt intrusion in agricultural cultivated fields. Ground water table with high salt content contributes to soil salinity. In India, studies regarding saline rice soils along the coastal regions of India have been neglected (Tilak et al., 2005; Das and Danger, 2008).

Induced Salinity by Anthropogenic Activity

It is revealed from the literature that every year about 2000 million hectares of land is detoriated by salt impregnation across 75 countries. Poor drainage in irrigated areas, poor water management practices is also another factor for secondary sanitization (Ismail et al., 2007; Qureshi and Al- Falahi, 2015)

Responsive Mechanism for Salinity Stress of Rice

Salt stress tolerance is controlled by multiple genes and is recognized as complex quantitative traits (Chinnsamy et al., 2005). At young stage rice crop is salt susceptible and the production efficiency is restricted at maturity (Lutts et al., 1995). Salinity stress can be lessened by crop management practices by planting mature seedlings but salinity stress can be affected at flowering stage. Salinity has impact on the growth of the plant. Salinity is known to induce sterility when it is subjected to pollination (Pearson and Bernstei, 1995). Salt tolerance can also be measured by comparative biomass percentage in both saline and controlled condition for a longer period (Munns et al., 2002). Adopting the two mechanisms viz. osmotic tolerance and ion exclusion, rice plants tolerate the salinity condition (Munns and Tester, 2008). In ion exclusion method, Na^+ flows out to the soil from the xylem. Osmotic tolerance is controlled by long distance signals which are known to reduce the shoot growth before accumulation of Na^+ in shoot. Salt tolerance avoidance mechanisms depend upon early plant vigour and restriction of initial entry of salts to root. Growth vigour is itself a mechanism to avoid salinity toxic effect(Kumar et al., 2013). Sodium ion concentration is lower in fast growing variety than in slow growing variety. Vigour works for producing the produce or yield than tolerance mechanism. Weak areas of roots are the possible sites for Na^+ entry from the soil. Transport of salt in rice plant is controlled by selective uptake of ions by root cells and water transportation through apoplastic and symplastic pathways (Das et al., 2015).

Salt stress on rice growth

Morphology of rice plants is affected by salt stress condition (Joseph et al., 2010). Early seedling stage is more sensitive towards salt stress in comparison with tillering stage (Grattan et al., 2002; Shereen et al., 2005). Symplastic, apoplastic, transcellular and water and solutes transport via apoplastic pathways are vital pathways in rice plant where H_2O and solutes enter by the roots (Ochiai and Matoh, 2002; Kronzucker and Britto, 2011). Na^+ uses apoplastic mode of passages in shoots of rice where as Na^+ uses solvent drag and casparin bands for transportation via apoplast mode(Ranathunge et al., 2005). Meanroot length, root numbers per plant and shoot length decreased in increased salt stress(Jiang et al., 2010). Thus, salt stress condition observed in rice plant by two indicators i.e., root and shoot lengths. Salt stress condition affects cell division and cell elongation of rice which causes root, leaf growth, and yield reduction (Munns, 2002). Tu et al., in 2014 reported the resistance of rice root against salt stress by genome duplication method. They observed that root growth, proline content, stability of nuclei and other organells along

with epidermal cell frequency, H+ efflux on root tip was improved and Na+ malondialdehyde (MDA) contents was decreased in tetraploid rice roots (HN2026-4x and Nipponbare-4x) than diploid rice (HN2026-2x and Nipponbare-2x) might be because of protective gap exposure between cortex and pericycle cells in tetraploid rice (HN2026-4x and Nipponbare-4x) and is the reason which causes increase in root resistance against salt stress and improves H+ transport to the root surface and Na+ contents decreases in the rice roots (Tu et al., 2014). At early seedling stage increase in salt stress increases leaf mortality of rice in all rice cultivars (Shreen et al., 2005). Reduction of growth and development observed during salt stress condition in few months (Munns, 2005). It leads to leaves death and leaf area reduction which ultimately causes reduction in rate of photosynthesis (Amirjani, 2011). Senescence of leaf is also affected by salt stress. It causes injury in the cells of transpiring leaves, and inhibition in growth of rice plant. Death of leaves caused by salt concentration in the old leaves is influencial in determining for the survival of the crops (Munns et al., 2006).

Salt stress on rice grain development

Under salt stress condition, reduction in rice grain yield is because of the panicle sterility (Flowers and Yeo, 1981). In some rice cultivars, at pollination and fertilization stages panicle sterility is caused by salt stress condition associated with some molecular mechanisms resulting in nutrient deficiencies condition (Khatun and Flowers, 1995; Hasamuzzaman et al., 2009). Research data reported that the sterility of panicle may be caused by salt stress during fertilization period which leads to grain setting, pollen bearing capacity reduction (Abdullah et al., 2001). Lack of carbohydrates transformation to vegetative growth and spike lets development is considered as the main cause of grain yield reduction under stress condition. In many yield components negative linear relationships was observed. This negative relationship leads to increase in salt stress (Khatun and Flowers, 1995). The main reasons behind lower grain yield of rice under stress condition is the translocation reduction of the soluble sugar contents to superior and inferior spikelets and starch synthetase activity inhibition during grain development (Abdullah et al., 2001). Increase salt stress severely affects yield components which include spike lets per panicle, length of the panicle, tillers per plant, florets per panicle, and 1000-grain weight (Khatun and Flowers, 1995). Salt stress showed influence on the phenotypic characteristics of rice plants and the interrelationship among rice yield parameters was also studied.

Salt stress on crop yield

Literature data revealed that abiotic stresses viz. drought and salinity are responsible in reducing the crop growth and productivity. Plants adjust to the abiotic stresses for their survival. Abiotic stresses such as salinity stresses are responsible in decrease in crop production in peninsular South East Asia and India (Behera et al., 2014). Salinity causes ion imbalances in the cells and causes oxidative damage (Munns and Tester, 2008). It causes decrease in plant growth and productivity of glycophytes and seedling and flowering stages are also reported to be highly susceptible to salinity condition (Singh, 2008).

Transgenic plants in combating salinity stress

Therefore, improvement in salt tolerance of major food crops is one of the best ways of proper utilisation of coastal areas (Jini et al., 2017).Rice (*Oryza sativa* L.) production is affected by salt stress condition in all the growing stages and thereby it becomes the major constraint of crop productivity. Rice seedlings are sensitive to salinity. Coastal region agricultural crop fields are either uncultivated or produce relatively low yields because of unavailability of appropriate salt tolerance varieties (Mass and Hoffman, 1977).

CONCLUSION

The rice crop growth and yield has been affected by salinity stress. All the growing stages are affected by salt stress condition and therefore reduce the crop productivity. Improved salt tolerant varieties should be cultivated in salt stress conditions for proper utilization of coastal area which in turn will justify the benefits of proper utilization of the salt stress area and also will contribute towards the crop yield to meet the global requirement.

CONFLICT OF INTEREST

There is no conflict of interest.

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RESEARCH ARTICLE

Single Objective Optimization of Die-sink EDM with Graphite Tool Electrode by Taguchi Method

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ABSTRACT

Die-sinking EDM machines have been used to maximize reliability and flexibility. Using Taguchi-based single-objective optimization, the present work optimizes the process parameters to minimize surface roughness in the die-sinking electrical discharge machining of EN31 steel. Taguchi's method works well for single-objective optimization because the observed values of surface roughness outperform the predicted values.

Keywords: Electrical Discharge Machining; EN 31 Steel, Minitab

INTRODUCTION

EDM-Electrical Discharge Machining is one of the most widely used non-traditional machining processes in the manufacturing sector. The EDM is commonly employed in the die and mold making, aerospace, automotive, microelectronic, and biomedical healthcare industrial sectors. The use of EDM has extended dramatically in recent years, owing to the widespread use of difficult-to-cut materials. As a result, substantial study & research has been done on EDM. Today, around 75% of the industry prefers graphite electrode materials over copper due to low wear, better surface finish at faster speeds, functioning extremely well at a high current density even with intricate geometry, and significant cost and time savings in electrode production. Again graphite is available in a variety of material qualities, allowing you to match the electrode material to the EDM application. The right electrode material selection, flushing conditions, and power supply settings produce a fine surface finish. High frequency and low power create the best finish.

The EDM process is widely recognized for cutting DTM- Difficult-to-machine materials and producing tougher geometrical shapes with more accuracy than conventional machining methods [2], [3].The prediction of SR and MRR in die sink EDM has been extensively studied utilizing various materials and optimization methodologies [4,5].For Al6063 silicon powder mixed EDM, Singh et al [6] studied the influence of powder concentration, Ipeak and TON on SR. The Taguchi technique yielded optimal process conditions, and all chosen parameters had substantial effects on SR. Recently, [7] examined the influence of three input process parameters on H13 die steel machining: electrode material, Ipeak, and TON. Also, output responses like MRR, SR, and EWR ratio were used to evaluate and optimize using Taguchi method. Many explanations have been proposed to solve the optimization problem in Die-sink EDM, such as Taguchi, RSM, ANN, etc. [8], [9]. Taguchi is the most appropriate approach for deriving optimal process parameters. Hence It has been proposed in this experimental analysis. There are 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure), and 11 (Sustainable cities and Communities).

EXPERIMENTAL DESIGN AND METHODOLOGY

Fine-grain graphite (~10 μm) of high density (1.82 g/cm^3) of cylindrical shape (D= 10 mm)was used as the electrode material in the study. Other properties are: Hardness- 10 HB, Thermal Conductivity- 80 W/m.k, Melting Point 3300^{0}C. The work piece material used was an EN31 Plate having a thickness 20 mm. Composition % wt(C-1.10, Si-0.35, Mn-0.50, P-0.035, S- 0.050, Cr-1.60, rest Iron); Properties (Tensile

a) Strength- 750 N/mm^2, Density- 7.8 Kg/m^3 and Hardness- 63 HRC.
b) ZNC-25 (JK Machines) die-sinking EDM machine was used for the experiment.
c) Hydrocarbon-based oil was used as dielectric fluid.
d) Portable stylus-type profilometer, Talysurf (Taylor Hobson, Surtronic 3+, UK) was used for measuring roughness.
e) The Taguchi strategy is precise for researching unknown machining processes, especially unique machining methods that are still in the early stages of study. The L16 orthogonal array was chosen for this study since it has four input parameters (Pulse Current, Flushing Pressure, Pulse on time, and Pulse off time)and four levels. Operating time for each run is 5 minutes.

Minitab 19 was used as the data analysis and process improvement tool

EXPERIMENTAL RESULTS

Table- 2: L16 OA with Experimental outputs

RESULT ANALYSIS

From the results we observed that ''the smaller-the-better" option for roughness is supposed as a characteristic of quality. The Ton and I are the most substantial parameter for reducing surface roughness

a) Figure 4 shows the residual plots suggesting that the residuals have a normal distribution. It reveals that ANOVA is working correctly.
b) A confirmatory experiment was done using the optimal parametric combination. The main effect plot, figure 3, shows that Toff of 45 μs, Ton of 20 μs, Flush Pressure of 6 MPa and Pulse Current of 5 amp is the optimum condition. The surface roughness was found to be 2.976 μm.
c) The ANOVA predicted values differ by less than 10% from the experimental surface roughness.

d) Regression equation Ra= 2.693-0.01488T_{off}+0.03648T_{on}+0.0101P+0.06045I was used to get predicted values if surface roughness.

CONCLUSIONS

Analysis of variance indicates Ton is a dominating parameter of surface roughness followed by I. To minimize roughness, the optimal cutting parameters combination is found to be Toff=45 μs, Ton=20 μs, Flush Pressure= 6MPaand Pulse Current= 5 amp

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Table- 1: Input EDM parameters with their levels

EDM Parameters	Levels			
Pulse Current, I, amp	5	10	15	20
Flushing Pressure, P, MPa	2	4	6	8
Pulse on time, Toff, μs	15	25	35	45
Pulse on time, Ton, μs	20	35	50	65

Table- 2: L16 OA with Experimental outputs

Run	Toff	Ton	P	I	Ra	SNRA1
1	15	20	2	5	3.426	-10.6957
2	25	35	4	5	4.056	-12.162
3	35	50	6	5	4.256	-12.58
4	45	65	8	5	4.586	-13.2287
5	25	50	2	10	4.696	-13.4346
6	15	65	4	10	5.256	-14.4131

7	45	20	6	10	3.256	-10.2537
8	35	35	8	10	4.346	-12.7618
9	35	65	2	15	5.446	-14.7216
10	45	50	4	15	5.056	-14.0761
11	15	35	6	15	4.856	-13.7256
12	25	20	8	15	3.696	-11.3546
13	45	35	2	20	4.446	-12.9594
14	35	20	4	20	3.976	-11.9889
15	25	65	6	20	5.676	-15.0808
16	15	50	8	20	5.756	-15.2024

Table- 3: Response Table for S/N Ratios

Smaller is better

Level	Toff	Ton	P	I
1	-13.51	-11.07	-12.95	-12.17
2	-13.01	-12.90	-13.16	-12.72
3	-13.01	-13.82	-12.91	-13.47
4	-12.63	-14.36	-13.14	-13.81
Delta	0.88	3.29	0.25	1.64
Rank	3	1	4	2

Table 4. ANOVA

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Regression	4	8.26749	2.06687	44.77	0.000
Toff	1	0.44253	0.44253	9.59	0.010
Ton	1	5.98965	5.98965	129.73	0.000
P	1	0.00820	0.00820	0.18	0.682
I	1	1.82710	1.82710	39.57	0.000
Error	11	0.50786	0.04617		
Total	15	8.77534			

Table-5: Regression Model Summary

S	R-sq	R-sq(adj)	R-sq(pred)
0.214870	94.21%	92.11%	88.17%

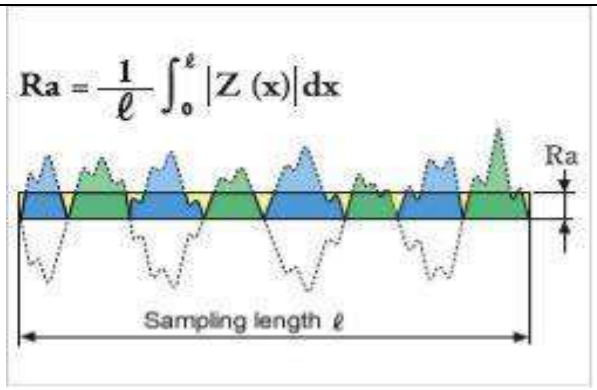

Figure-1: Measurement of Ra[1]

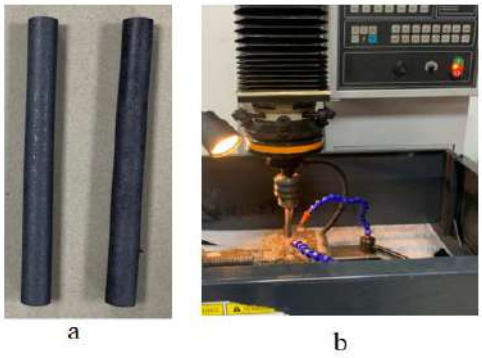

Figure 2 (a) Graphite Electrode,(b) Experimental Setup

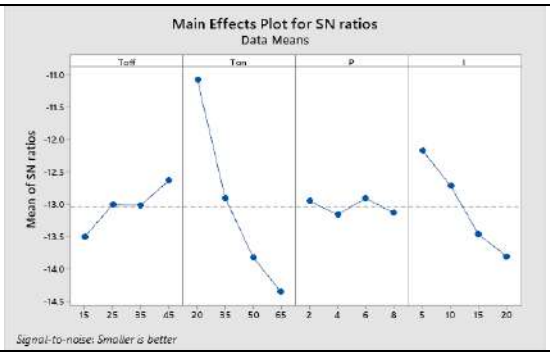

Figure 3 Main Effect Plot

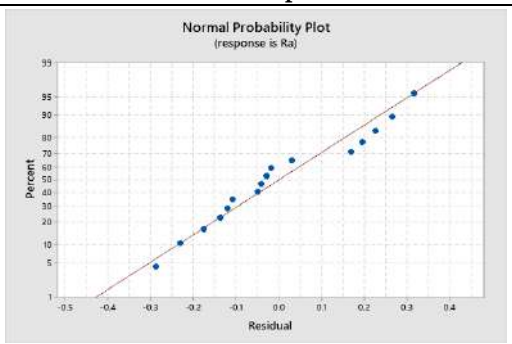

Figure 4 Residual plot

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REVIEW ARTICLE

A Review on the Health Benefits of *Helianthus annuus* L.

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ABSTRACT

The plants are the beauty of our earth. The importance of plants can never be denied. They are valuable and serve an essential purpose with many benefits of planting trees. The countless benefits of plants cannot be neglected. Plants maintain a balance in the ecosystem. They also help to purify the air that we breathe. Humans depend on plants for their needs. One reason we rely on plants is for consumption. They provide food by the process of photosynthesis. The importance of plants is not just limited to being a source of food or oxygen. Plants are also used for various medicinal purposes. These medicines are safer because of lower side effects. This review article throws light on the importance of *Helianthus annuus* (sunflower) in the aspect of health. This essential herb has multiple benefits. The tiny seeds of this plant have a lot of value. It is a boon for reducing heart disease, high cholesterol and high blood pressure. Also, it is rich in antioxidants and significant vitamins, which protect the cell from damage and helps in lowering chronic disease. It also has essential minerals such as magnesium, zinc, copper, etc., excellent for our immune system.

Keywords: Antioxidant, *Helianthus annuus*, Cholesterol, Blood pressure,

INTRODUCTION

Ethnobotany is the study of people and the study of plants. Every year, the food sector produces and discards large amounts of biodegradable trash and leftovers (1, 2). The conservation of the environment must be the top concern of international politics (3). Suffering, disease outbreaks, and even death from starvation have occurred from the continual rise in the human population and high demand for food; thus, there is a need to intensify agricultural methods for maximum food production for the human population (4). Overall, sunflower is valued for its nutritional

and therapeutic properties. Sunflower has been recognized as a functional food or nutraceutical due to its good health impacts, while its full potential has yet to be realized. Sunflower contains dietary fibre, manganese, vitamins, tocopherols, phytosterols, triterpene glycosides, -tocopherol, glutathione reductase, flavonoids, phenolic acids, carotenoids, peptides, chlorogenic acid, caffeic acid, alkaloids, tannins, and saponins, all of which contribute to their healthy and functional development (5). The medical advantages of sunflower seeds/oils are credited to its major healthful constituents, which incorporate high monounsaturated and polyunsaturated fats, proteins, tocopherols, phytosterols, copper, zinc, folate, iron and vitamin B having antimicrobial, antidiabetic, calming, antihypertensive, and cancer prevention agents

Various uses of *Helianthus annuus*

For healthy skin

Studies have shown that the skin is severely affected and gradually loses its appearance due to a lack of critical fatty acids. So, for this reason, consuming sunflower seeds with omega-6 fatty acids can improve skin condition and delay ageing (6).

Cholesterol control

This oilseed crop is very rich in fatty acids such as linoleic acid ($C_{18}H_{32}O_2$) and oleic acid(($C_{18}H_{34}O_2$), which decreases the LDL (Low-density lipoprotein) cholesterol and keeps heart disease away (7).

Anti-cancer effect

Due to the presence of the compound phytosterol, the seeds of this plant are used as a preventive step against breast cancer and reduce the spreading of specific types of tumour cells (8).

Anti-inflammatory agent

Sunflower oil has Anti-inflammatory activity, which has been reported in the experiment on laboratory rats where indomethacin, when given along with sunflower oil, decreased paw edema, which is provoked by carrageenan by nearly about 80 per cent on the other hand when diclofenac and also indomethacin when given singly lessened paw edema by 50 per cent and 56 per cent accordingly (9).

Anti-fungal action

Tinea pedis (also known as Athlete's foot) is a fungal infection that usually begins between the toes and is triggered by a fungus of specific genera. Oleozon (ozonized *H.annuus* oil) does an extraordinary job curing this disease. The experiment was carried out on 200 people, and the positive results were seen by applying two times every day for about 42 days (10).

Antidiabetic properties

The research was done to determine the outcome of sunflower seeds on diabetic rats. The rats were fed with sunflower seed extracts for about three weeks. This led to a boost in glycogen levels in the liver, which showed improvement in the diabetic condition of the rats. It was presumed that these seed extracts' antidiabetic effects were due to the heightening of insulin release from pancreatic alpha cells due to the presence of chlorogenic and caffeic acid (11).

For heart health

H. annuus seeds contain monounsaturated and polyunsaturated fats, excellent for heart and cardiovascular diseases (12).

CONCLUSION

This review article represents the beautiful advantage of the vital plant Helianthus annuus and how it is used to cure specific day-to-day occurring diseases. The above finding clearly shows that the beneficial effects of Sunflower plants have a logical and scientific basis. The information mentioned in this review assures that the plant can be used as a multipurpose agent. All existing disease prevention strategies are compatible with this plant's medicinal properties. These new approaches to studying medicinal plants offer a wealth of further information. This review contributes to the health application and fulfils the SDG goal of good health and well-being.

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REVIEW ARTICLE

A Review on Herbal Formulation in the Management of Vitiligo

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ABSTRACT

Dysfunction or death of pigment-producing cells causes vitiligo. As a result, white patches or macules can appear on anywhere on the body including the mouth, eyes, hair, and other areas. Vitiligo is more noticeable in darken skin people. It is not contagious or life-threatening but may lead to mental stress or get down to one's self-confidence. It occurs in both males and females. There is a wide variety of medical treatments available for those suffering from vitiligo. The treatment range from steroid creams to phototherapy, to surgery. Plant-based therapeutic preparation is recurrent to complement dermatological therapy. There is the use of traditional herbal drugs in vitiligo treatment. Some herbs are used topically on one's skin or orally consumed which helps in minimizing or decreasing the white patches or macules. Herbal drugs constituents like capsaicin, piperine, curcumin, khellin, green tea polyphenols having antioxidant, anti-inflammatory, anti-necrobiosis properties are found to have very effective treatment options for vitiligo.

Keywords: Vitiligo, Melanin, Herbal formulation, Segmental vitiligo, Non-segmental vitiligo

INTRODUCTION

Vitiligo is an idiopathic depigmenting disorder characterized by melanocyte loss on the skin in areas with hypo-melanism. It is amelanotic, non-flaky, and has lighter macules with distinct margins. It is seen in the areas like skin, eyes, innerear, leptomeninges, and hair bulb. Vitiligo patients also may have eye abnormalities, pernicious anemia, diabetes, and thyroid disease. Prior to the appearance of a new patch, people may experience itching and it also affects good health and well-being of human. It is not contagious. In comparison to normal melanocytes, melanocytes from vitiligo patients die more easily from oxidative stress, with elevated levels of reactive oxygen

species and greater stress on endoplasmic reticulum. [1, 2, 3, 4]. There are two major classes of Vitiligo, Segmental Vitiligo (SV) and Non-Segmental Vitiligo (NSV). It is thought to be an autoimmune disease caused by a combination of genetic and environmental factors with metabolic, oxidative stress, and cell detachment abnormalities. The Segmental vitiligo is characterized from other types depending upon its prophecy implications whereas Non-segmental vitiligo includes acrofacial, mucosal, generalized, mixed, universal, and rare variants [5, 6, 7].

Epidemiology

A customariness of 0.5% to 2% is estimated for Vitiligo, the most common skin disorder. Its incidences range from 0.1% - 8.8% the worldwide. Approximately half of all vitiligo cases appear during active growth; 70% - 80% of cases appear before age 30.The segmental vitiligo seen at younger age i.e., before 30years of age in 87% of cases and before the age of 10years in 41.3% [8, 9] while symptoms of non-segmental vitiligo are seen at any age but they typically develop between 10 and 30 years of age. About 70% - 80% of vitiligo patients develop the signs before the age of 30 years and 25% before the age of 10 years.[14, 15, 16]. Different studies have been done to know the customariness of vitiligo. Vitiligo prevelance ranges from 0.004% to 9.98%.A summary of the included studies is shown in Table 1. Characteristics of studies on the prevalence of vitiligo.

Hospital Base Studies

Males and females are equally affected, but females are often seeking consultation more frequently, possibly due to the greater negative social impact than for men.

Biosynthesis of Melanin Pigment

The skin pigment melanin is synthesized by specialized cells known as melanocytes, formed through series of oxidative reactions which involve the amino acid tyrosine in the presence of an enzyme tyrosinase. Melanocytes synthesize the melanin within the membrane-bound organelles called melanosomes later on which transferred through dendrites to surrounding keratinocytes. The type and amount of melanin synthesized by the melanocytes and its distribution in the surrounding keratinocytes determine the actual color of the healthy skin. There are four important steps involved in the melanogenesisprocess, they are a) Development of melanoblasts and their migration from the neural crest to peripheral sites b) Differentiation of melanoblasts into melanocytes c) Survival and proliferation of melanocytes and) Formation of melanosomes and melanin production. Any disturbance in the melanin pathway shows either hyper pigmentation like Addison's disease and melisma or hypopigmentation like albinism and vitiligo. [9,10,11,13]

Classification

Vitiligo is classified into following basing upon its clinical forms.

Types	Subtypes
1.NON-SEGMENTAL VITILIGO	**A. Acrofacial**
	B. Mucosal
	C. Generalised
	D. Universal
	E. Mixed
	F. Rare
2.SEGMENTAL VITILIGO	**A. Uni segmental**
	B. Bi segmental
	C. Multi segmental

Non-Segmental Vitiligo

It consists of a group of mucosal, generalized, universal, acrofacial, and mixed types.

a) **Acrofacial** – It affects the parts of the body like the hand, feet, face, and head. Mainly involve the perioral region and the extremities of digits. A distinctive feature is de pigmentation of the distal fingers and facial orifices. Later it may progress to other body surfaces which can be categorized as generalized vitiligo or universal vitiligo. [Figure 1] [9,10,12]

b) **Mucosal:** it affects the oral and genital mucosae. It May also be affected in patients with acrofacial, common, or universal forms; when it involves only one mucosal site it is classified as indeterminate. [Figure 1.]

c) **Generalized or common**: Generalized vitiligo is characterized by bilateral, often symmetrical, depigmented macules or patches occurring in a random distribution over the entire body surface likehands, fingers, face, and trauma-exposed areas. It may begin in childhood or early adulthood. [Figure .1]

d) **Universal:** is the form that affects the largest extent of tegument (80-90% of body surface), and it is the most common form in adulthood. The generalized or common form usually precedes it. [Figure 1.]

e) **Mixed:** it is the concomitant involvement of segmental and non-segmental vitiligo. Most often, the segmental form precedes NSV.

f) **Rare forms:** vitiligo punctata, minor and follicular. These types were also considered unclassifiable.[11]

Segmental Vitiligo

Segmental is non-uniform Vitiligo, spreads rapidly, more constant and stable when compared to Non-segmental vitiligo. This type of vitiligo is very rare and seen in only 10% of the cases, mainly occurs in the areas where the skin is attached to nerves and occurs at a younger age.Typically present with unilateral depigmented macules surrounded by normal skin and the macules are white with more irregular border and less homogenous pattern of pigment loss than NSV. In rare cases, SV involves two or more different segments with the homolateral distribution. Lee and Hann reported that in 5 of 240 SV cases show bilateral on the same that appears on both sides of the body. [24,25,26] It is mostly seen on the face. [Fig.2]According to the Lee and Hann study 25% of SV involved the trunk [Fig.3], 5% involved the face,11% the extremities, and an additional 17% had both face and neck. [Fig.4]

SV is also associated with the occurrence of white hair known as poliosis, leukotrichia in lesional skin.
Several conditions are difficult to classify the two forms of SV and NSV.
a)Punctate vitiligo – It occurs as sharp demarcated depigmented puncti form of 1 to 1.55mm macules in any area of the body.
b)Hypochromic vitiligo – It is characterized by the presence of hypopigmented macules in seborrheic distribution on the face and neck, trunk, and scalp.
c)Follicular vitiligo – It occurs with leukotrichia in the absence of depigmentation of the surrounding epidermis.

Treatment

Vitiligo cannot be cured but it can be managed by different medical treatments by creating a different skin tone by repigmentation. Till now vitiligo treatment is the most difficult dermatological challenge. There is different treatment for it which includes phototherapy, topical and systemic immunosuppressant surgical techniques, stabilizing depigmented lesions and stimulation of repigmentation. Vitiligo treatment depends upon different factors like patient's age, disease's subtype, rate of extent, disease's activity and its distribution, phototype, and effect on the quality of life. For the treatment at least 12 weeks is needed to determine the efficacy of the treatment.

Vitiligo shows a less optimal with either poor response or with continued progress in the field of medical therapy and surgical treatments. As per current views in medical therapies, high potency topical steroids and narrowband ultraviolet B(NB-UVB) irradiation are considered to be an effective form of mono-therapy. But steroids and phototherapy cannot be used for prolonged medication because of their side effects. [31,32,33]. As different medical therapies are available the high repigmentation percentage are effective on the neck and face lesion but it is less effective on limbs and trunk part and poorly effective on the acral part of the extremities .narrow band UVB and psoralens and UVA isthe most effective treatment for generalized vitiligo which affect more than 10% -20% of the cutaneous surface whereas calcineurin inhibitors are a most effective treatment for localized vitiligo.[33,34,35].With

different research on the various pathomechanism of vitiligo related to cutaneous blood flow, cytokine mechanism, and others.[41,42,43] Topical therapies have been a centerpiece of vitiligo treatment, with or without phototherapy. Topical treatments used in the treatment of vitiligo include steroids, calcineurin inhibitors, vitamin D analogues, pseudocatalase, and depigmenting agents. Sometimes combination therapies are done to improve the pigmentation. Some topical agents have been developed to incite the pigmentation mechanism in herbal. Since ancient times, herbal products of different nature and effects had been used for the treatment of vitiligo.[44,45] So here is a list of herbal drugs andtheir main active chemical constituents used in the treatment of vitiligo:

Ginkgo biloba: It is known as the maidenhair tree, belongsto the family Ginkgoaceae. The extract of its leaves and seeds has been used in medicine for a very long time. Its extract is very effective in the treatment of vitiligo, pre-menstrual syndrome, distended vein, and others. The drug is formulated into a tablet of different dosages and taken orally once or thrice a day for more than 3 months but its exact mechanism is unknown in the treatment of vitiligo. [39,40]

Cucum ismelo: It is known as Muskmelon, a species of Cucumis that belongs to the Cucurbitaceae family. Its extract is rich in antioxidants containing high superoxide dismutase (SOD) which have the activity of melanocyte deconstruction by oxidative stress. The combined use of Cucumismelo extract with phenylalanine and acetylcysteine in a gel formulation was observed to be effective and safe showing a better repigmentation of cutaneous lesions. [41,42].

Piperine: Piperine is the main alkaloidal content of the species Piper nigrum (black pepper) which shows growth stimulatory action in melanocyte proliferation in mouse models. It is observed that piperine does not stimulate melanin synthesis but it can be effective in repigmentation when associated with UV radiation. [45,46,47]

Curcumin: Curcumin is a polyphenol obtained from the plant species Curcuma longa belonging to the family Zingiberaceae, used in the treatment of different diseases because of its properties like antiviral, anti-inflammatory, anti-oxidant, anti-proliferative, anti-fungal, and anti-viral. In recent studies, a cream known as tetrahydrocurcumide has been used in the vitiligo treatment association with nb-UVB. The phototherapy was performed twice a week for 12 weeks. The overall degree of repigmentation was slightly better in the group at 8 and 12 weeks. Patients showed a slightly effective repigmentation compared to the ones treated only with nb-UVB. Finally, as with other antioxidants, curcumin may be orally administered as adjuvant therapy in vitiligo patients. [48,49]

***Polypodium leucomotos*:** Polypodiumleucomotos is a species of tropical fern belonging to the family Polypodiaceae. It has antioxidant and photoprotective activity, used in the treatment of different skin diseases like atopic dermatitis, psoriasis, atopic dermatitis, vitiligo, post-inflammatory hyperpigmentation, and others. The oral administration of Polypodiumleucomotos therapy in combination with psoralens plus UVA and nb - UVB show a significant improvement in vitiligo. [51,52,53]

Khellin: Khellin is obtained from the plant Ammivisnaga which is a furanochromonederivative. It is used in the treatment of different diseases like kidney stones, renal colic, coronary disease, asthma, psoriasis, and vitiligo. Khellin may be used topically or orally. In these two types of therapy When Khellinis applied topically in combination with UVA light it stimulates melanocytes in hair follicles but when given orally it induces elevated liver enzyme and photosensitivity. In this therapy twenty-five vitiligo, patients were given Khellin orally and three patients were treated topically, treatments were done three times weekly. Its better results depending on the number of treatments. [54,55,56,57,58]

Pyrostegia venusta: It is popularly known as "flame vine'' or ''woody vine'' belonging to the family Bignoceae. P. venusta have different properties like antioxidant, antipyretic and anti-inflammatory, used in the treatment of diarrhoea, dysentery, immoderate menstrual flow cold and flu, leukoderma and vitiligo. The hydroalcoholic extract of its leaves and flowers were found to be increased the melanin content in a concentration dependent manner in

incubation of four days on melanoma cells. Its leaves extract enhances the melanogenesis with maximum effect then its flower extract [64,65,66]. Green tea :green tea polyphenols are extracts of green tea leaves use as medicine since ancient time. They have anti-inflammatory , anti-oxidants and immunomodulatory agents because of its epigallocatechin components. It may be useful in the treatment of vitiligo by inhibiting the oxidative stress of the melanocyte. [67,68].

Psoralea corylifolia : The seeds of Psoraleacoryfolia are used in the form of paste and as an ointment for both external and internal use for treatment of alopecia, inflammation, vitiligo, leprosy, psoriasis etc due to its chemical constituents like flavones, coumarins, monoterpenes , flavonoids , antioxidants like psoralidin ,astragalin etc.[69,70]
Capsaicin: Capsaicin is a natural irritant belongs to the vaniloid family which is obtained from Capsicum (chilli peppers). It's anti-inflammatory, antioxidant and anti-necrobiosis properties has been proposed for the treatment of vitiligo. The pre-treatment of vitiligo with capsaicin in combination with curcumin decrease the reactive oxygen species and increase the cellular antioxidant capacity which inhibits the keratinocyte necrobiosis; thus, this combination promotes the repigmentation in vitiligo. [71]

CONCLUSION

The topical formulation of some herbal drugs in combination with phototherapy is found to be superior to monotherapies regarding efficacy, early response and safety in the vitiligo treatment .In different case studies , observed that it is more effective when applied topically. So some herbal drugs are considered as well founded therapeutic tool in the treatment of vitiligo.

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Table 1. A Summary Of The Included Studies Is Shown

First author	Publication Year	Country	Survey Age (years)	Survey Year	Sample (N)	Vitiligo (n)	Prevalence
Mehta NR [7]	1973	India	All	1971-1972	9065	138	1.52%
Howitz J [8]	1977	Denmark	All	1971-1972	47033	179	0.38%
Johnson MT [9]	1978	USA	Jan-74	1971-74	20749	102	0.49%
Bechelli LM [13]	1981	Brazil	Jun-16	1974-75	9955	4	0.04%
Das SK [15]	1985	India	Above 3years	1978-1982	15685	72	0.46%
Nanda A [17]	1989	India	Below 1month	1986	310	1	0.32%
Schallreuter KU [18]	1991	Germany	14-86	1989	350	2	0.57%
Bhatia V [24]	1997	India	0-14	1988-1989	666	4	0.60%
Wolkenstein P [45]	2003	France	All	2002	18137	51	0.28%
Dogra S [41]	2003	India	6~14	2001	12586	272	2.16%
Abdel-Hafez K [42]	2003	Egypt	All	1994~1996	8008	98	1.22%
Ingordo V [71]	2011	Italy	18	2001~2004	34740	60	0.17%
Reddy J [83]	2014	India	All	-	22037	160	0.73%

Table 2 : Hospital base studies

First Author	Publication Year	Country	Survey Age (years)	Survey Year	Sample (N)	Vitiligo (n)	Prevalence
Anand IS [89]	1998	India	0~12	1994	400	8	2.00%
Nanda A [90]	1999	India	0~12	1992~1996	10000	149	1.49%
Poojary SA [102]	2011	India	-	2002~2008	33252	204	0.61%
Kumar S [107]	2014	India	All	2012	443	44	9.98%

Table.3 : Some herbal drugs and its main active chemical constituents used in the treatment of vitiligo

Herbal drugs	Active chemical constituents
Polygala tenuifolia	Lipopolysaccharide, phenylpropanoids
Piper nigrum	Piperine
Green tea	Epicatechin, epicatechin -3 – gallate, epigallocatechin
Cucumismelo	Superoxide dismutase
Picrorrhizakurao	Picriside I and II
Polypodium	p-coumaric,ferulic,vannilic
Pyrostegiavenusta	Allantoin,sterols
Ammivisnaga	Khellin

a. Acrosomal

b. Mucosal

c. Generelised

d.Universal Vitiligo

e. Mixed Vitiligo

f. Rare Vitiligo

Fig.1. Non-Segmental Vitiligo

Fig.2.Segmental vitiligo on face

Fig.3.Segmental vitiligo on the trunk

Fig.4. segmental vitiligo on face and neck

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RESEARCH ARTICLE

Fabrication of Zinc Oxide Nanoparticles Showing Appreciable Antibacterial Activities against Human Pathogen

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ABSTRACT

Novel ZnO nanoparticle samples were prepared by wet-chemical method. Nanoparticles were structurally and optically characterized by different analytical methods. The aim of this study is to prepare the above functional nanoparticles of ZnO and check their effectiveness towards the inhibition of bacterial growth/activity. Sol-gel route was followed to synthesize the nanoparticles with maintaining a calcination temperature of 600^{o} C. The X-ray analysis reveals the growth of polycrystalline hexagonal wurtzite structure of ZnO having crystallite size of 28 nm. Morphology of the ZnO sample was investigated by FESEM and shows the formation of hexagonal crystallites. The sharp absorption peak was obtained from UV-Visible spectrum and we have calculated the band gap energy value of zinc oxide. This is found to be 3.42 eV. The goal of present work is to assess the antibacterial activity of ZnO against both gram-positive as well as gram-negative microbes such as; Staphylococcus aureus and Escherichia coli respectively. From the antibacterial experiment, it was observed that gram-negative Escherichia coli bacteria exhibits maximum zone of inhibition of 19.5 mm in comparison to gram-positive bacteria S. aureus. This confirms the higher defence mechanism of ZnO nanoparticles against the above bacterias and can be treated as a good antibacterial agent.

Keywords: Zinc oxide, sol-gel, antibacterial activity, Staphylococcus aureus, Escherichia coli

INTRODUCTION

The natural lifecycle on this earth is facing fierce threat by exposure to bacteriological contagion which has become prime concern of the present time. In global level, microbial agents being resistance to antibiotics leads to birth of many contagious diseases [1, 2]. In this context, nanotechnology plays a significant role in handling bacterial contamination. Nanomedicine is considered as an alternative active material for antibacterial activity. The development of novel, cost effective bactericidal nanomaterial is recognised as an encouraging approach to solve

above problem due to its exclusive physiochemical properties [3-11]. Nanomaterials are materials having at least one dimension in the nanometre scale range. Nanoparticles show antibacterial properties against gram-positive as well as gram negative bacteria [12-21]. Among numerous nanomaterials, zinc oxide is proved to be efficient one, owing to its diverse striking properties and wide spectrum of applications. ZnO has wide band gap energy value of 3.3 eV. ZnO being effectual and a notable material which has gained huge attention in the field of science and technology for combining various properties, safe, simple fabrication process, cost effective and non-toxicity in nature. ZnO expresses bio-compatibility with human cell due to its crystalline shape, size of particle, morphology and surface area ratio [22-31]. ZnO metal oxide is environment friendly having biodegradability properties. Though ZnO has high ratio of surface to volume, it exhibits superior antibacterial activities which enables improved dissolution and penetration on bacteria. The nano size of metal oxide is the main factor for enhancing antibacterial activities [32-36]. In this study, wet chemical technique such as sol-gel route is used for the fabrication of zinc nano oxides. The synthesized nano metal oxide undergoes characterization by X-ray diffraction and UV-Visible spectroscopy. The goal of the present work is to assess the antibacterial activities of zinc oxide against both gram-positive as well as gram negative human pathogen Staphylococcus aureus and Escherichia coli respectively.

Experimental Section

Chemicals Required

Zinc acetate dihydrate (Zn $(CH_3CO_2)_2.2H_2O$), methyl alcohol, sodium hydroxide (NaOH) were purchased from Sigma-Aldrich and double distilled water was used throughout the experiment. Muller Hinton Agar was obtained from Hi-Media, Mumbai, India.

Fabrication of Zinc Oxide

The zinc oxide nanomaterial was synthesized by sol-gel route. The preparation of ZnO nano particles was done by taking different concentration of (Zn $(CH_3CO_2)_2.2H_2O$) solution & methyl alcohol as precursors. Required amount of (Zn $(CH_3CO_2)_2.2H_2O$) were taken in a conical flask and 50ml of methyl alcohol was added to it & undergo stirring in magnetic stirrer for 2hr until a homogenous solution was obtained. After that 0.1M NaOH solution was added drop wise from burette till pH reaches between 9-11. Then it was stirred for half an hour in magnetic stirrer .The mixture solution was allowed to settled down for 2-3hr. Then it was washed by decantation process by using double distilled water and acetone for several times. The prepared sample was put it in Petridish and kept in oven for drying at 100^{o}centigrade for 12hour. Then sample undergo calcination for 2 hour at 600 degree Celsius. Finally dried sample was powdered & collected in sample box.

Bacterial Sources

For the experiment, two pathogenic bacterial strains specifically Staphylococcus aureus (MTCC3100) and Escherichia coli (MTCC400) were obtained from ITER, BBSR, and Odisha, India and maintained in nutrient agar slants at 4^{0}C.

Preparation Procedure

For antibacterial activity analysis, Muller Hinton Agar (MHA) medium was prepared and autoclaved at 121 degree centigrade and 15psi pressure. The synthesized nanoparticle was examined against two bacterial strains such as Staphylococcus aureus (MTCC3100) and Escherichia coli (MTCC400) through agar disc diffusion method. After solidification, the isolated colony was smeared over the medium by using sterile swab. Well were prepared at the centre of the inoculated MHA medium by using gel puncture. The sterile discs were taken of diameter 5mm and filled with various concentration of nanoparticle (10 and 20 mg/ml) and control tetracycline (10mg/ml) was carefully placed in the prepared well. The swabbed plates undergo incubation for 24 hours at 37 degree centigrade. After this, the zone of inhibition was measured.

Characterization

X-ray diffraction is a non-destructive and analytical method for identification and quantitative analysis of various crystalline forms of ZnO, also known as phases of the compound present in the samples. X-ray diffraction measurements (Pan Analytical made) was used to study structural properties of ZnO nano-powder using the Cu Kα (1.5406 Å) as a radiation source, operated at 40kV and 30 mA with a scan rate of 0.02°/s over the range of 20°-70°. The average crystallite size D (hkl) of all crystal planes for ZnO powder was estimated from the classical Scherer

formula: $D=K\lambda/\beta \cos\theta$

Where K is the shape factor usually has a value 0.9, is the X-ray wavelength and the Bragg angle gives the full width of the half maxima (FWHM). The absorbance measurements were obtained using UV-VIS spectrometer (Shimadzu 1650PC) in the spectral range of 200 nm to 800 nm. The X-intercept obtained by extrapolating the linear portion of the exponential curve from of the graph of ($h\nu^2$) versus photon energy ($h\nu$) is the band gap energy of the material.

RESULT AND DISCUSSIONS

X-Ray Diffraction Studies

The structural properties of the zinc oxide were studied by XRD and the spectrum has been shown in Fig.1. The sample having diffraction peaks shows the development of hexagonal wurtzite structure and well agreed with powder diffraction standards (JCPDS) card No 14-1445. The diffraction peaks at various diffraction angles 31.8, 34.5, 36.33, 56.63, 62.82, 66.4, 67.95 attributed to (100), (002), (101), (110), (103), (200) and (112) respectively. The fabricated sample with sharp diffraction peaks specifies good crystallinity value. The average crystalline size was estimated by the Scherer equation given by $D=K\lambda/\beta Cos\theta$, where D is the crystallite size, K is the shape factor, (being taken as 0.9), λ is the X-ray wavelength, β is the full width at half maximum of the diffraction peak, and θ is the Bragg diffraction angle in degree. It is observed that the size of ZnO is found to be 28 nm. From the graph, presence of number of XRD peaks ascribed to various crystalline orientations reveals growth of ZnO with polycrystalline nature [37-39]. Some of the additional peaks have also been appeared in the XRD spectrum of ZNO which may belong to the hydroxide phases.

FESEM Measurement

The morphology and chemical composition (elemental analysis) of the as synthesized sample was accomplished by FESEM. The image has been depicted in Fig.2 which tells that nanoparticles of hexagonal morphology have been formed. The size of the particles varies from 15 – 80 nm as observed from the FESEM photograph. The elemental analysis of ZnO sample gives us the information about the existence of Zn and O elements in the samples along with C and Au which are incorporated due to the experimental process.

UV-Visible Spectroscopy

UV-Visible spectrophotometer is used to discover the optical properties of prepared nanosample. The band gap energy value is one of the optical properties which describe the semiconducting nature of zinc oxide. From the absorption spectra, it was observed that size of nanoparticle greatly influences its absorption in UV-region which is found to be 363 nm. The value of optical energy gap is evaluated by extrapolation of Tauc's plot. The band gap value for ZnO was found to be 3.42 eV. The absorption spectra of pure ZnO is shown in Fig.3.The nanosized ZnO leads to the appearance of sharp absorption peak and good absorption value in UV region which makes it an suitable tool in medical field as an UV absorbent [40, 41].

Antibacterial Activity

The synthesized nanoparticle exhibits prominent antibacterial activity against gram-positive as well as gram negative human pathogen Staphylococcus aureus and Escherichia coli respectively. The agar disc diffusion method

was employed at various concentrations (10 to 20 mg/ml) and zone of inhibition was recorded shown in Table no.1. It was found that E. coli exhibits maximum zone of inhibition of 19.5 mm compared to the S. aureus due to the variation of structure of cell wall of microbes [42-44]. Commonly, cell membrane in microbes contains negatively charge due to presence of small amount of teichoic acid in gram-positive bacteria and phospholipids in gram-negative bacteria. So, the attractive force exists in between negatively charged bacteria and positively charged prepared zinc oxide might end up in superior bacterial inhibition [45-47]. From the above study, it has been verified that metal oxide semiconductors like ZnO possesses novel structural, optical, photocatalytic and antibacterial properties for different applications [48-71].

CONCLUSION

In the current work, nano structured zinc oxide was successfully fabricated by simple wet chemical sol-gel method. The prepared zinc oxide underwent calcination at 600º C. XRD analysis confirms the formation of hexagonal wurtzite structure showing peak in the region between 20º to 70º having average crystallite size of 28 nm. It also reveals the poly-crystallinity growth of zinc oxide. From UV-Visible studies, sharp absorption peak was observed at 363 nm. The band gap value for ZnO was found to be 3.42 eV. From the antibacterial studies, it was found that the gram-negative bacteria exhibits superior zone of inhibition of 19.5 mm in comparison to gram-positive bacteria owing to their permeability proficiency into the cell wall. The current study satisfied the sustainability development goal 11(sustainable cities and community) which make cities and human settlements inclusive, safe, resilient and sustainable.

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Table-1: Antibacterial activity of ZnO: zone of inhibition against E. coli and S. aureus

Bacterial Strain	**Concentration (mg/ml)**	**Zone of inhibition (mm)**
E. coli	10	11
	20	19.5
Control	10	8
S. aureus	10	10.5
	20	19
Control	10	9

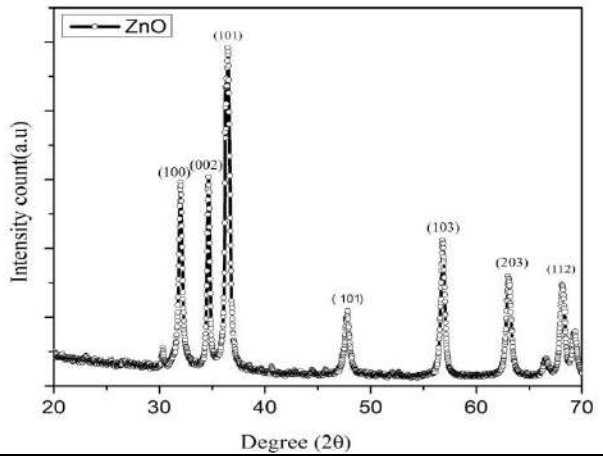

Fig. 1: XRD graph of ZnO nanoparticles.

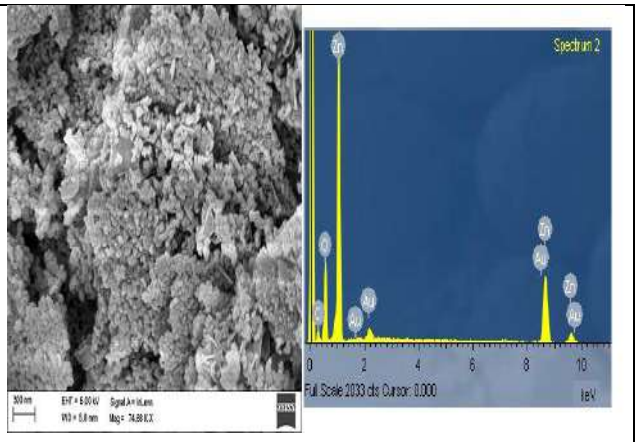

Fig.2: FESEM and EDAX images of ZNO nanoparticles.

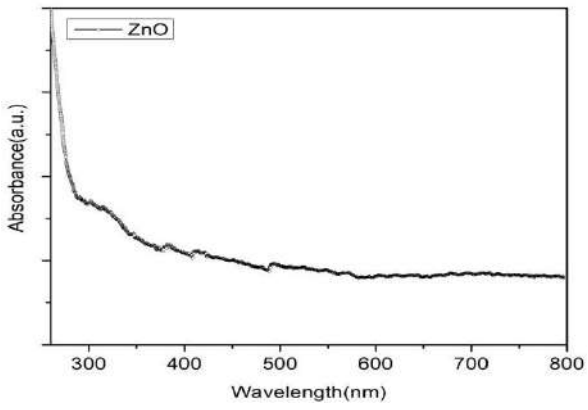

Fig. 3: UV-Visible absorbance spectrum of ZnO nanoparticles.

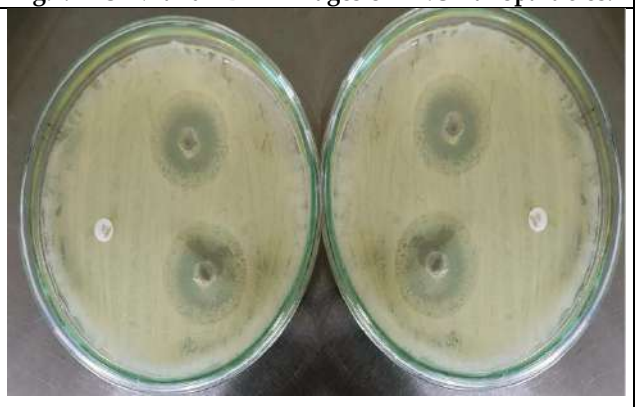

Fig. 4: Antibacterial activity of ZnO against E. coli and S. aureus at various concentrations (10, 20 mg/ml).

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RESEARCH ARTICLE

Prediction of Solar Radiation using Machine Learning Regression Models

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ABSTRACT

Owing to its recent advance, machine learning has spawned a large collection of solar forecasting works. In particular, machine learning is currently one of the most popular approaches for hourly solar forecasting. Nevertheless, there is evidently a myth on forecast accuracy-virtually all research papers claim superiority over others. Apparently, the "best" model can only be selected with hindsight, i.e., after empirical evaluation. For any new forecasting project, it is irrational for solar forecasters to bet on a single model from the start. To ensure a fair comparison, no hybrid model is considered, and only off-the-shelf implementations of these algorithms are used. Moreover, all models are trained using the automatic tuning algorithm available in the package. It is found that tree-based methods consistently perform well in terms of overall results. Increasing penetration of distributed renewable power means that reliable generation forecasts are required for grid operation. The present work aims at combining state of the art implementations of the Weather Research and Forecasting (WRF) model with multivariate statistical learning techniques to provide the most accurate forecasts of day-ahead hourly irradiance.

Keywords: Solar radiation forecasting, machine learning, linear regression, decision tree regressor, random forest regressor.

INTRODUCTION

An electrical operator should ensure a precise balance between the electricity production and consumption at any moment. This is often very difficult to maintain with conventional and controllable energy production system, mainly in small or not interconnected (isolated) electrical grid. Many countries nowadays consider using renewable energy sources into their electricity grid. This creates even more problems as the resource (solar radiation, wind, etc.)

is not steady. It is therefore very important to be able to predict the solar radiation effectively especially in case of high energy integration [1].There are 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure), and 11 (Sustainable cities and Communities).

The necessity to predict solar radiation or solar production

One of the most important challenge for the near future global energy supply will be the large integration of renewable energy sources (particularly non-predictable ones as wind and solar) into existing or future energy supply structure. An electrical operator should ensure a precise balance between the electricity production and consumption at any moment. As a matter of fact, the operator has often some difficulties to maintain this balance with conventional and controllable energy production system, mainly in small or not interconnected (isolated) electrical grid. The reliability of the electrical system then become dependent on the ability of the system to accommodate expected and unexpected changes (in production and consumption) and disturbances, while maintaining quality and continuity of service to the customers. Then, the energy supplier must manage the system with various temporal horizons (Fig. 1).

The integration of renewable energy into an electrical network intensifies the complexity of the grid management and the continuity of the production/consumption balance due to their intermittent and unpredictable nature [1, 2]. The intermittence and the non-controllable characteristics of the solar production bring a number of other problems such as voltage fluctuations, local power quality and stability issues [3, 4]. Thus forecasting the output power of solar systems is required for the effective operation of the power grid or for the optimal management of the energy fluxes occurring into the solar system [5].

Forecasting Methodologies:

The solar power forecasting can be performed by several methods; the two big categories are the cloud imagery combined with physical models, and the machine learning models. The choice for the method to be used depends mainly on the prediction horizon; actually all the models have not the same accuracy in terms of the horizon used. Various approaches exist to forecast solar irradiance depending on the target forecasting time. The literature classifies these methods in two classes of techniques:

One is the extrapolation and statistical processes using satellite images or measurements on the ground level and sky images are generally suitable for short-term forecasts up to six hours. This class can be divided in two sub-classes, in the very short time domain called "Now casting" (0–3 h), the forecast has to be based on extrapolations of real-time measurements [5]; in the Short-Term Forecasting (3–6 h), Numerical Weather Prediction (NWP) models are coupled with post-processing modules in combination with real-time measurements or satellite data and 2nd one is the NWP models able to forecast up to two days ahead or beyond (up to 6 days ahead). These NWP models are sometimes combined with post-processing modules and satellite information are often used [2].

Some Machine Learning Methods

Machine learning is a subfield of computer science and it is classified as an artificial intelligence method. It can be used in several domains and the advantage of this method is that a model can solve problems which are impossible to be represented by explicit algorithms. In [6] the reader can find a detailed review of some machine learning and deterministic methods for solar forecasting. The machine learning models find relations between inputs and outputs even if the representation is impossible; this characteristic allow the use of machine learning models in many cases, for example in pattern recognition, classification problems, spam filtering, and also in data mining and forecasting

problems. The classification and the data mining are particularly interesting in this domain because one has to work with big datasets and the task of preprocessing and data preparation can be undertaken by the machine learning models. After this step, the machine learning models can be used info recasting problems. In global horizontal irradiance forecasting the models can be used in three different ways [7]:

- Structural models which are based on other meteorological and geographical parameters;
- Time-series models which only consider the historically observed data of solar irradiance as input features (endogenous forecasting);
- Hybrid models which consider both, solar irradiance and other variables as exogenousvariables (exogenous forecasting).
- As already mentioned machine learning is a branch of artificial intelligence. It concerns the construction and study of systems that can learn from data sets, giving computers the ability to learn without being explicitly programmed.

Linear Regression

Linear Regression is a supervised machine learning algorithm where the predicted output is continuous and has a constant slope. It's used to predict values within a continuous range, (e.g. sales, price) rather than trying to classify them into categories. Early attempts to study time series, particularly in the 19th century, were generally characterized by the idea of a deterministic world. It was the major contribution of Yule (1927) which launched the idea of stochasticity in time series by assuming that every time series can be regarded as the realization of a stochastic process. Based on this simple idea, a number of time series methods have been developed since that time. World's decomposition theorem [8] led to the formulation and solution of the linear forecasting problems. Since then, a considerable amount of literature is published in the area of time series, dealing with parameter estimation, identification, model checking and forecasting.

Support Vector Machines / Support Vector Regression

Support vector machine is another kernel based machine learning technique used in classification tasks and regression problems introduced by Vapnik in 1986 [9]. Support vector regression (SVR) is based on the application of support vector machines to regression problems [10]. This method has been successfully applied to time series forecasting tasks.

Decision Tree Learning

The basic idea is very simple. A response or class Y from inputs X_1, X_2,…., Xp is required to be predicted. This is done by growing a binary tree. At each node in the tree, a test to one of the inputs, say Xi is applied. Depending on the outcome of the test, either the left or the right sub-branch of the tree is selected. Eventually a leaf node is reached, where a prediction is made. This prediction aggregates or averages all the training data points which reach that leaf. A model is obtained by using each of the independent variables. For each of the individual variables, mean squared error is used to determine the best split. The maximum number of features to be considered at each split is set to the total number of features. [11-13].

Random Forest

A random forest is a Meta estimator that fits a number of classifying decision trees on various sub-samples of the dataset and uses averaging to improve the predictive accuracy and control over-fitting.

Dataset

	A	B	C	D	E	F	G	H	I	J	K
1	UNIXTime	Data	Time	Radiation	Temperat	Pressure	Humidity	WindDire	Speed	TimeSunR	TimeSunSet
2	1.48E+09	9/29/2016 0:00	23:55:26	1.21	48	30.46	59	177.39	5.62	6:13:00	18:13:00
3	1.48E+09	9/29/2016 0:00	23:50:23	1.21	48	30.46	58	176.78	3.37	6:13:00	18:13:00
4	1.48E+09	9/29/2016 0:00	23:45:26	1.23	48	30.46	57	158.75	3.37	6:13:00	18:13:00
5	1.48E+09	9/29/2016 0:00	23:40:21	1.21	48	30.46	60	137.71	3.37	6:13:00	18:13:00
6	1.48E+09	9/29/2016 0:00	23:35:24	1.17	48	30.46	62	104.95	5.62	6:13:00	18:13:00
7	1.48E+09	9/29/2016 0:00	23:30:24	1.21	48	30.46	64	120.2	5.62	6:13:00	18:13:00
8	1.48E+09	9/29/2016 0:00	23:25:19	1.2	49	30.46	72	112.45	6.75	6:13:00	18:13:00
9	1.48E+09	9/29/2016 0:00	23:20:22	1.24	49	30.46	71	122.97	5.62	6:13:00	18:13:00
10	1.48E+09	9/29/2016 0:00	23:15:22	1.23	49	30.46	80	101.18	4.5	6:13:00	18:13:00
11	1.48E+09	9/29/2016 0:00	23:10:22	1.21	49	30.46	85	141.87	4.5	6:13:00	18:13:00
12	1.48E+09	9/29/2016 0:00	23:05:23	1.23	49	30.47	93	120.55	2.25	6:13:00	18:13:00
13	1.48E+09	9/29/2016 0:00	23:00:25	1.21	49	30.47	98	144.19	3.37	6:13:00	18:13:00
14	1.48E+09	9/29/2016 0:00	22:55:20	1.22	49	30.47	99	139.8	6.75	6:13:00	18:13:00
15	1.48E+09	9/29/2016 0:00	22:50:19	1.21	50	30.47	99	140.92	2.25	6:13:00	18:13:00
16	1.48E+09	9/29/2016 0:00	22:45:31	1.23	50	30.47	99	147.61	5.62	6:13:00	18:13:00
17	1.48E+09	9/29/2016 0:00	22:40:23	1.22	50	30.47	99	113.78	4.5	6:13:00	18:13:00
18	1.48E+09	9/29/2016 0:00	22:35:19	1.21	50	30.47	99	123.03	10.12	6:13:00	18:13:00
19	1.48E+09	9/29/2016 0:00	22:30:22	1.22	50	30.47	99	173.73	6.75	6:13:00	18:13:00
20	1.48E+09	9/29/2016 0:00	22:25:19	1.22	50	30.47	98	91.43	6.75	6:13:00	18:13:00
21	1.48E+09	9/29/2016 0:00	22:20:22	1.2	50	30.47	98	109.74	6.75	6:13:00	18:13:00
22	1.48E+09	9/29/2016 0:00	22:15:22	1.2	50	30.47	98	143.53	2.25	6:13:00	18:13:00
23	1.48E+09	9/29/2016 0:00	22:10:21	1.2	50	30.47	97	146.76	5.62	6:13:00	18:13:00
24	1.48E+09	9/29/2016 0:00	22:05:20	1.21	50	30.47	97	158.35	4.5	6:13:00	18:13:00
25	1.48E+09	9/29/2016 0:00	22:00:26	1.22	50	30.47	97	166.05	5.62	6:13:00	18:13:00

From the dataset we know that in different times of a day from 1st September 2016 to 31st December 2016 temperature (F), pressure, humidity, wind direction (Degrees),radiation (W/m^2) sunrise and sunset time of solar power system is recorded.

Experimentation/ simulation

For experiment we use Anaconda application where we use Jupyter notebook to write the coding and run it. Here we want to find the model score, r^2 score, median absolute error, explained variance.

R^2Score

Coefficient of determination also called as R2 score is used to evaluate the performance of a linear regression model. It is the amount of the variation in the output dependent attribute which is predictable from the input independent variable(s). It is used to check how well-observed results are reproduced by the model, depending on the ratio of total deviation of results described by the model.

Mathematical Formula

$$R^2 = \frac{1 - SSres}{SStot}$$

Where,

SS_{res} is the sum of squares of the residual errors.

SS_{tot} is the total sum of the errors.

Median Absolute Error

The median absolute error is particularly interesting because it is robust to outliers. The loss is calculated by taking the median of all absolute differences between the target and the prediction. If $\hat{y}$ is the predicted value of the i th sample and y_i is the corresponding true value, then the median absolute error estimated over n samples is defined as follows:

$$MedAE\left(y, \hat{y}\right) = median\left(\left|y_1 - \hat{y}_1\right|, \ldots, \left|y_n - \hat{y}_n\right|\right)$$

Explained Variance

It is used to measure the discrepancy between a model and actual data. In other words, it's the part of the model's total variance that is explained by factors that are actually present and isn't due to error variance.
Higher percentages of explained variance indicate a stronger strength of association.

$r^2 = R^2 = \eta^2$

Explained variance can be denoted with r^2. In ANOVA, it's called eta squared (η^2) and in regression analysis, it's called the Coefficient of Determination (R^2). The three terms are basically synonymous, except that R^2 assumes that changes in the dependentvariable are due to a linear relationship with the independent variable; η^2 does not have this underlying assumption.

RESULTS AND DISCUSSION

	Model Score	R Square	Median Absolute Error	Explained Variance
Linear Regression	62.9433435187304	62.94334351873041	115.35459365005138	0.6295826357372237
Support Vector Regression	86.296261932048	86.29626193204861	0.6400000000000001	0.8629646419967041
Decision Tree Regressor	92.94001236235401	92.94001236235401	0.84787499999999	0.9294004728635185

CONCLUSION

As shown, many methods and types of methods are available. There are a lot of methods to estimate the solar radiation, some are often used (ANN, naive methods), others begin to be used (SVM, SVR, k-mean) more frequently and other are rarely used (boosting, regression tree, random forest, etc.). In some cases, one is the best and in others it is the reverse. Generally, the accuracy of these methods depends on the quality of the training data. The three methods that should be generally used in the next years are SVM, regression trees and random forests, as the results given are very promising and some interesting studies will certainly be produced the next few years. Actually, these methods yield similar error statistics. The implementation of the methods may have more to do with the errors reported in the literature than the methods themselves.

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REVIEW ARTICLE

Magnetohydrodynamic (MHD) Flow and Heat Transfer: A Brief Review

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ABSTRACT

The present paper aims to provide a varied and wide range of recent advancement in Magneto hydrodynamic flow and heat transfer in different flow geometries considering the effects of different flow parameters. Several parameters like "magnetic field (applied as well as induced), porosity of the surface as well as medium, heat source/sink, radiation, free convection, chemical reactions etc." have their impact on the flow. These fluid flow problems have their applications in many engineering as well as astrophysical and geophysical problems of interests. Present study may provide the readers a brief idea about the MHD flow.

Keywords: MHD, heat transfer, porosity.

INTRODUCTION

In nature and man-made processes Magneto hydrodynamics plays an important role not only in our daily lives but, in fact, throughout the entire domain of nature. The problems dealing with Magneto hydrodynamic flows are of great theoretical and practical interest in view of their varied applications in natural sciences, engineering sciences and also in industry. Mass transport phenomena are linked to the study of star structure on the solar surface. Its cause is linked to temperature differences generated by non-homogeneous heat production, which can result not only in the development of convective currents but also in severe explosions in many circumstances. Within the mantle and cores of planets the size of or greater than the Earth, mass transfer is undoubtedly occurring. Investigating this phenomenon, particularly the case of heat and mass transport on Magneto hydrodynamic flows, is therefore quite fascinating. Beauty of this work is it fulfills the SDGs 4 (Quality education), 8 (Decent Work &Economic Growth), and 9 (Industry, Innovation and Infrastructure). Authors are confident enough that the present study will definitely enable the researcher to emphasize their understanding towards sustainable development goals like quality education; economic growth; industry, innovation and infrastructural developments.

Brief Literature Survey

The effect of applied magnetic field on unsteady free convective flow past an infinite vertical porous plate has been given much importance in view of its varied applications in nuclear research and in the study of stars and planets. These problems are of general interest in the field of geophysical and astrophysical studies. In view of these applications Soundalgekar and Haldavnekar[1] analyzed the MHD free convective flow in a vertical channel. Deviand Jothimani[2] discussed the heat transfer in unsteady MHD oscillatory flow. Chowdhuryand Islam[3] have studied the MHD free convection flow of visco-elastic fluid past an infinite vertical porous plate. Singh *et al.* [4] looked into heat and mass transfer in MHD flow of a viscous fluid through a vertical plate at an oscillating suction velocity. Krishna and his associates [5] demonstrated a second order Rivlin-Ericksen fluid's hydromagnetic oscillatory flow in a channel. Pathal *et al.* [6] investigated the unsteady mass, momentum, and heat transfer in MHD free convection flow across an abruptly moving vertical plate.

The problem of MHD convective flow through a porous medium has attracted the attention of several researchers because of its possible applications to several geophysical studies. Gersten and Gross [7] discussed the flow and heat transfer along a plane wall with periodic suction. Choudhury and Das [8] investigated non-Newtonian fluid boundary layer flows past a flat plate using magneto hydrodynamic boundary layer flows. MHD three-dimensional flows past a porous plate were examined by Gupta and Johari [9]. The three-dimensional free convective flow and heat transfer through a porous media with periodic permeability were presented by Singh and Sharma [10]. Using finite difference analysis, Das and his colleagues [11] examined the hydromagnetic flow and heat transfer of an elastico-viscous fluid between two horizontal parallel porous plates.

The problem of MHD flow through porous medium with heat transfer has been given much attention due to its numerous applications. Choudhury and Das [8] investigated non-Newtonian fluid boundary layer flows past a flat plate using magneto hydrodynamic boundary layer flows. MHD three-dimensional flows past a porous plate were examined by Gupta and Johari [9]. The three-dimensional free convective flow and heat transfer through a porous media with periodic permeability were presented by Singh and Sharma [10]. Using finite difference analysis, Das and his colleagues [11] examined the hydro magnetic flow and heat transfer of an elastico-viscous fluid between two horizontal parallel porous plates. In natural sciences, engineering sciences, geophysical and astrophysical studies and also in industry. A porous medium is characterized, most often, by its porosity. Porous media include natural materials like rocks and soil (e.g. aquifers, petroleum reservoirs), zeolites, biological tissues (e.g. bones, wood, cork), and man-made materials like cements and ceramics. Many of their significant qualities can only be explained if they are considered porous media. Porous media is a notion that is used in many fields of applied science and engineering: filtration, mechanics, material science, petroleum engineering, hydrogeology etc. Heat transmission rates in ducts will be improved by porous media that provide high surface area contact. The use of porous medium has two major advantages. First, its heat dissipation area is larger than that of traditional fins, which improves heat transfer. The second factor is the uneven velocity of the fluid flow around the individual beads, which effectively mixes the fluid. Soundalgekar[12] analyzed the free convection effects on steady MHD flow past a vertical porous plate. Kim [13] discussed the unsteady MHD convective heat transfer past a semi-infinite vertical porous moving plate with variable suction. Gupta and Johari[9] explained the MHD three dimensional flows past a porous plate. Sharma and Pareek [14] have reported the steady free convection MHD flow past a vertical porous moving surface. Sarangi and [15] studied the unsteady free convective MHD flow and mass transfer past a vertical porous plate with variable temperature.

Mahanthesh *et al* [16] investigated "Radiated flow of chemically reacting nano-liquid with an induced magnetic field across a permeable vertical plate". The purpose is to study the heat transfer materials with magnetism and nanoparticles. It was found that the velocity decreases with larger v and Q and increases as the Hartman and Prandtl values increase. Magnetic energy distribution decreases Hartman number and Prandtl magnetic numbers. Nanoparticles volume fraction, heat / sink, radiation and chemical reactions are favorable for the expansion of the

magnetic induction boundary layer. The heat transfer rate is decayed by the volume fraction of the growing nanoparticles and the magnetic field.

Huang [17] studied "Lateral mass flux and thermal radiation on natural convection heat and mass transfer from a vertical flat plate in porous media considering Soret/Dufour effects". The work has investigated heat and mass transfer through more regular natural flow in the ground floor apartment under a uniform wall thickness (UWT / UWC) mounted in media focusing on the effects of Soret and Dufour on lateral mass flux and radiation. The results showed that, when the hotter the Rd, the buoyancy rate N and lateral mass flux fw increased, both the local Nusselt numbers and the local Sherwood number. The local Nusselt value is decreasing as the Lewis Le and Dufourparlue D prices increase. In contrast, the local value of Sherwood increases when Le and D increase. Ultimately, upgrading the Soret S parameter increases Nusselt's local value and reduces the local Sherwood value.

Tiwari *et al* [18] investigated "Computational approaches for annual maximum river flow series". In the current analysis, process analysis distribution which can facilitate the flow of major rivers of the strong showing better mobility pitch. It was found that the highest detail of the fillings is approximately the same and the highest accuracy with ANN-Wavelet modelling produces a more probabilistic distribution. Graphical approaches were utilised to choose a probabilistic distribution model, and Kolmogorov– Smirnov (K–S) and chi-square tests were used to assess goodness of fit for the probabilistic models that were chosen.It is suggested that the use of a generalized distribution of regional Logistic analysis of the frequency.

Jyotsna *et al* [19] investigated "Radiation and mass transfer effects on MHD flow through porous medium past an exponentially accelerated inclined plate with variable temperature". The purpose of the study was to analyze the effect of the inclination on the presence of heat source / sink and destructive reaction. It was found that an increase in the radiation parameter lowered the temperature to reach the normal state earlier. Low perturbation types with high chemical reaction rate eliminate the concentration at all points. An increase in the chemical reaction rate gives an increase in skin swelling and an increase in the thickness of the medium decreases the desired skin friction. The absence of a porous matrix mattress and the free current convective reduces the inflammation of the skin, while other fields enhance it. The lack of flow is noted due to the time equivalent.

Ullah *et al* [20] investigated "Effects of slip condition and Newtonian heating on MHD flow of Casson fluid over a nonlinearly stretching sheet saturated in a porous medium". The mathematical scheme is solved mathematically using the Keller box method. Numerical calculations are made of physical parameters that reach the desired level of accuracy. The result has shown that Velocity decreases with increasing b, n, M, K and d. The temperature increases with the increase of b, n, M, K, d and c. Local crack fractures increase with increasing b, k and d. The reduced Nusselt number increases with the increase of b, k, Pr and c.\

Rashidi *et al* [21] investigated "Entropy analysis of convective MHD flow of third grade non-Newtonian fluid over a stretching sheet". The purpose of this study is to analyze the entropy generation due to the elastic sheet containing non-Newtonian water in the presence of magnetic fields. The energy density and the energy used to obtain a linear generation are determined from a very unequal system of differential equations. The results indicated that the magnitude of thermal boundary elasticity decreased with a higher increase in the Prandtl number. Brownian motion plays an important role in enhancing fluid flux. By increasing the magnitude of the magnetic field parameter, the reproductive activity of the entropy increases to a certain distance from the sheet.

Reddy and Chamkha[22] investigated "Hall effects on unsteady MHD oscillatory free convective flow of second grade fluid through porous medium between two vertical plates". Here "the effects of radiation and Hall current on an unsteady magneto hydrodynamic free convective flow in a vertical channel filled with a porous medium" have been studied. It can be seen that the component of the basic flow velocity increases with the increase of the permeability parameter, the Hall parameter, and the Grash of number and decreases with the increase of the

magnetic and parabolic energy. The velocity component of the second flow improves with an increase in the multiplication parameter and is also increased by an increase in the Hartmann number, the Grash of number, and the radiation parameter. The temperature decreases with an increase in the radiation parameter or Peclet number, while increasing at the beginning and then decreasing gradually with increasing oscillation.

CONCLUSION

A brief and concise literature review on "Magnetohydrodynamic flow and heat transfer in different flow geometries considering the effects of different flow parameters" has been carried out. Some of theconclusions are summarized below:

- Applied magnetic field has significant effects on the fluid velocity and fluid temperaturein most of the problems studied.
- Fluid velocity as well as fluid temperature is significantly affected by porosity of the medium as well as porosity of the surfaces.
- Temperature profiles are largely affected by different parameters like, convection (free and forced), radiation, Grashof number, Prandtl number etc.

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REVIEW ARTICLE

A Review on Effectiveness and Biological Activities of Different Mentha Species

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ABSTRACT

Mentha spicata L., also known as spearmint, and *M. piperita*, often known as peppermint, are used in herbal medicine and industry for various ailments.*Mentha* is well-known folk medicine. Some portions of this plant have been employed in traditional medicine in Iranian and other countries. The plant has been shown to have various pharmacological and therapeutic effects in numerous studies. This review aimed to look at the traditional usage of *Mentha* and the pharmacological and therapeutic effects of the whole extract and critical components. Different plant components, including the leaves, flower, stem, bark, and seeds, have been used in traditional folk medicine as antimicrobials, carminatives, stimulants, antispasmodics, and treating ailments like headaches and digestive disorders. *Mentha* is a pharmacologically diverse herb with antibacterial, gastrointestinal, and nervous system effects. Menthone, isomenthone, menthol, 1, 8-cineole, borneol, and piperitenone are the essential plant compounds responsible for most of the plant's pharmacological actions, followed by menthone, isomenthone, menthol, 1, 8-cineole, borneol, and piperitenone. Furthermore, the plant may have harmful effects on several physiological systems in a dose-dependent manner.

Keywords: *Mentha*, Pharmacological Effects, Menthol, Traditional

INTRODUCTION

Mentha spicata L. comes under the family Lamiaceae. Lamiaceae family plants contain many polyphenols and show good antioxidant activity. Spearmint is mainly found in the northern part of England. Spearmint is primarily cultivated in tropical to the temperate area such as China, Europe, South Africa, America and Brazil. Spearmint is a

plant that may be found all over the world. Brown Mint, garden mint, and lady's mint are all varieties of *Mentha spicata* L. The leaves are big and erose sharply. Spearmint is a rhizomatous and perennial herb in nature. Long pink or white flowers adorn the spearmint blossom (1,2). One of the most important essential oil crops is spearmint. Spearmint is used in various meals and beverages, including flavourings, cuisines, spices, and tea. Spearmint oil is used to treat multiple types of human diseases. This herb is used primarily as an aromatic agent. Spearmint is also used to make various products such as dental cream, chewing gum, mouthwashes, sweets, fragrance, pesticides, and antimicrobial agents. This plant contains different essential oils, a phenolic antioxidant, cholinesterase inhibitors, biofilm disinfection, pancreatic lipase inhibitors, antifungal and anti-proliferative agents. Spearmint oil includes a dominant component: R-(-)- carvone; due to this, spearmint shows a unique scent. Spearmint oil contains limonene, dihydrochalcone, and 1,8-cineole. Nowadays, spearmint is used in phytomedicine due to its different bioactivities in Traditional Arabic Palestinian Herbal Medicine. It is used to cure obesity, dementia,hypertension, digestive disorder, abdominal pain, muscle spasm, flatulence, headache, fever, menstrual pain, asthma, cough, cold, depression etc. Spearmint is widely used as a memory enhancer and nerve sedative. Spearmint is also used in animals as a Laxative, diuretic, hypothermia blocker, flea repellent, and sore throat(3). Besides its enormous health benefits, it also has excellent antibacterial, antifungal & insect repellent properties over synthetic drugs and repellents. Mosquitoes, causing deadly diseases like yellow fever, Malaria, Zika virus & dengue fever, are resistant to synthetic insecticides due to their continuous use over the years (4).There is a constant expansion of antioxidants in the food system today. Some of the natural antioxidants like vitamin C. Tocopherols and carotenoids are very important in the food industry and human health. From a safety point of view, herbs and spices are necessary to search for natural oxidants. Mint is the world's third most popular flavour, and it was discovered 2000 years ago. This spice is utilized in cuisine, pharmaceuticals, and cosmetics worldwide. Mint is a perennial herb with aromatic qualities that grows primarily in warm climates. Peppermint, maize mint, and spearmint all use it as an essential oil. It is observed that antioxidant properties are found by examining *Mentha spicata* and *M.piperita.* Then these properties and all the composition of the extract are reported. A recent experiment is done on the extraction of mint by surveying the pH temperature and storage stability. The extraction of *Mentha spicata* is done to study the quality improvement ability and fruit juice application in fruit juices. The mint has also been used in traditional medicines, reports the property of lipid oxidation inhibition on baked mint products. One study directs the utility of mint as a source of antioxidants in biscuit preparation and the storage capacity of antioxidants and sensory attributes (8). The opinions of the experiment, The seasonal effect on the constitution of spearmint cultivation in Palestine and the essential oil content. Some of the potential benefits of essential oils focus on treating antibiotic-resistant infections, dermatophytosis, obesity, and Alzheimer's disease(3). For repellence against arthropod species, essential oils are extracted from various plant families(4).

Humans, particularly in developing nations, rely heavily on medicinal plants for life-saving pharmaceuticals. According to estimates from the World Health Organization, more than 80% of the world's population in developing countries rely on herbal medicine for primary health care. The difficulties surrounding the usage of synthetic pharmaceuticals and antibiotics and the renewed interest in plant-based medicines. Over the last few decades, there has been a rise in research on medicinal plants and their traditional therapeutic uses in various parts of the world. It is critical to document indigenous traditional knowledge through ethnobotanical studies to conserve and utilize biological resources. As a result, it is recognized that plants can be employed in their natural or enhanced state (5). Medicinal plants that have been separated from plants and applied based on ethnobotanical expertise and licensed medications from medicinal plants are known to have a variety of physiologically active components[10].

Plants' biological functions are evaluated based on their chemical profile or ethnobotanical information about a specific ailment. Finding a particular molecule that can fight a particular disease is a time-consuming and challenging task. Various herbal medicines have been researched utilizing cutting-edge scientific methods. Mentha (Mint) is a member of the Lamiaceae family, subfamily Napithoidae, with roughly 38 species found in all agro-climates worldwide. Essential oils are produced from a variety of Mentha species. Mint oils are one of the most precious essential oils on the market, with over $400 million. The most important commercial species for necessary

oil production are *Mentha condensis* L., *Mentha aquatica* L., *Mentha spicata* L., and *Mentha piperita*. For centuries, Mentha leaves, stems, and blossoms have been used to flavour and fragrance herbal teas and various foods.

Mentha spicata L. (Spearmint) is a perennial plant that is commercially farmed all over the world. Teas and aromatic agents are made from spearmint leaves, both fresh and dried. *Mentha spicata* treats gastrointestinal, respiratory, and bad breath problems and carminative, antispasmodic, diuretic, and sedative properties. Spearmint has been used to treat flatulence disorders in traditional Iranian medicine in various forms (decoctions, tinctures, and tablets). Spearmint leaves are utilized in conventional Iranian treatments to strengthen the stomach and relieve dyspepsia symptoms. Spearmint oil is a flavouring ingredient used in chewing gum, cosmetics, and toothpaste formulations(6). The fresh and dried plants and their essential oils are widely used in the food, cosmetic, confectionery, chewing gum, toothpaste, and pharmaceutical industries. This species is also often used in Indian and Italian cuisine and is usually added fresh or dried to fish and shellfish plates before or after cooking. *M. spicata* possesses several biological activities and is used in folkloric medicine as a carminative, antispasmodic, diuretic, antibacterial, antifungal, and antioxidant agent and for the treatment of colds and flu, respiratory tract problems, gastralgia, haemorrhoids, and stomachache(7).

Taxonomy

Mentha spicata L. is a member of the Lamiaceae (mint) family, including 260 genera and 7000 species that thrive in various agroclimatic settings. *M. spicata* L. (Spearmint) is a herbaceous, rhizomatous perennial plant with hairless to hairy stems and foliage and a wide-spreading fleshy underground rhizome that grows 30–100 cm tall. The leaves have a serrated border and are 5–9 cm long and 1.5–3 cm wide. The mint family of herbs is known for their square-shaped stems. Spearmint blooms in thin spikes with pink or white flowers 2.5–3 mm long and wide. The leaves are widely used to flavour tea, and the entire plant is used as a carminative. Mentha has 42 species, hundreds of subspecies, 15 hybrids, cultivars, and variations in its genus.

Types of Mentha [11,12,13]

1. **Spearmint [Botanical Name:** *Mentha spicata*]: When it comes to culinary usage, spearmint or common mint is arguably the most popular. It has slender, green leaves with a pleasant, gentler aroma than peppermint. The herb is also known as Lamb mint because of its use in lamb and potato dishes.
2. **Pepper Mint** [**Botanical Name:** *Mentha piperita*]: It's a hybrid of spearmint and water mint. It's utilized in pastries and drinks because of its strong flavour, sweet scent, and cooling, spicy aftertaste.
3. **Apple Mint** [**Botanical Name:** *Mentha suaveolens*]: Woolly or Pineapple Mint are some other names for this plant. It features pale pink blooms from early to mid-summer and has light green circular leaves. Its fruity aftertaste distinguishes it. It's used in tea and as a salad garnish.
4. **Banana Mint** [**Botanical Name:** *Mentha arvensis* 'Banana']: The perfume of this fragrant herb is similar to that of a banana, which attracts bees. It has small lilac-coloured flowers that bloom all summer. It can be used in ice creams, biscuits, muffins, and fruit salads, among other things.
5. **Chocolate Mint**[**Botanical Name:** *Mentha piperita*' Chocolate Mint']:Chocolate Mint is well-known for its minty chocolate scent. Shakes, sweets, and ice creams all benefit from it. Summers provide lovely lavender flowers on its spherical spear-shaped leaves.
6. **Water Mint [Botanical Name:** *Mentha aquatica*]: Watermint, also known as *'Mentha citrata,'* grows primarily along rivers and waterways. It has scented foliage that is oval and toothed. This wild plant spreads by runners.
7. **Lavender Mint**[**Botanical Name:** *Mentha piperita*]:One of the most attractive mint varieties available for aesthetic applications. Make an informal hedge out of this 2 ft tall cultivar in your landscape.
8. **Slender Mint** [**Botanical Name:** *Mentha diemenica*]:This frost-hardy, 6 cm tall mint is an Australian native. Slender Mint differs from other mints in appearance. It can be used as a regular mint. Here's where you can learn more about it.
9. **Egyptian Mint [Botanical Name:** *Mentha niliaca*]: Egyptian mint dates back to the period of the Pharaohs. The flavour is gentler than peppermint and spearmint, and the fragrance is similar to the apple mint. It has a sturdy upright stem with fuzzy leaves that can be used in savoury recipes, drinks, and skin toner.

10. **Pennyroyal Mint** [**Botanical Name:** *Mentha pulegium*]:Pennyroyal Mint is mentioned in several Roman cookbooks. It is now primarily utilized as a herbal cure and insect repellent rather than in kitchens. It can be grown in a vegetable garden to help with pest control. It features beautiful pale blue or lavender flowers with small, delicate green foliage.
11. **Horsemint** [**Botanical Name:** *Mentha longifolia*]:This erect plant can grow to about 3-4 feet tall, with lovely pale pink or purple flower spikes and hairy foliage. Silver mint is another name for it. It has a broader range of medicinal applications, making it an excellent addition to a medical garden.
12. **Corsican Mint** [**Botanical Name:** *Mentha requieni*]:Corsican mint is a native of the island of Corsica. It features fragrant flowers and trails of spherical, scented leaves. It's low-growing and invasive, like other mints. Corsican mint is used in teas and salads to enhance the flavour of the vegetable crops that thrive nearby. This cultivar is often used to make crème de menthe, a mint-flavoured alcoholic beverage.
13. **Eau de Cologne Mint** [**Botanical Name:** *Mentha piperita citrate*]: It boasts citrus-flavoured fragrant leaves elliptical in shape on magnificent burgundy stems and is also known as the orange and bergamot mint. Orange mint is used to make jellies, salads, and sauces and is known for its aromatic qualities. The perfume business uses its essential oil.
14. **Strawberry Mint** [**Botanical Name:** *Mentha spicata* subsp. Citrate'Strawberry']:This tiny mint type can be grown inside hanging baskets and pots. It has a fruity scent that is a cross between strawberry and mint. Toss it in salads and desserts, or prepare an iced tea.
15. **Grapefruit Mint** [**Botanical Name:** *Mentha x Piperita*' Grapefruit']:The enticing grapefruit-like smell distinguishes this mint from the rest. Grapefruit mint's deep green leaves have a fruity flavour that pairs well with fruit sweets. You may also use it to add citrus flavour to seafood and lamb salads.
16. **Hemingway Peppermint** [**Botanical Name:** *Mentha nemorosa*]:This delicious wild mint type from the United States can be eaten fresh or cooked into recipes to offer a lovely aroma and flavour. Mint leaves can also make herbal teas and other cold beverages.
17. **Ginger Mint** [**Botanical Name:** *Mentha gracilis*]: Ginger mint is also known as Vietnamese mint because it's popular in Vietnamese cuisine and used to spice beef and chicken meals. Because of the name, it smells like spearmint with a tinge of delicious ginger-like fragrance.
18. **Mojito Mint** [**Botanical Name:** *Mentha villosa*]:Cuban Mint (Yerba Buena) has a pleasant and gentle flavour compared to other types. This mint is the essential ingredient in the well-known Mojito cocktail.
19. **Hart's Pennyroyal** [**Botanical Name:** *Mentha cervine*]: Another one-of-a-kind mint is known for its fragrant leaves, vivid blooms, and a solid minty flavour akin to spearmint. Aside from popular teas and beverages, this is most commonly used to season fish, meats, and other culinary purposes.
20. **American Wild Mint** [**Botanical Name:** *Mentha Canadensis*]:This mint variety is one of the most popular in North American gardens. It is native to most of Canada and the United States. It's delicious in jellies, teas, and candies, and it's also been used to treat hiccups and toothaches.
21. **Margarita Min** [**Botanical Name:** *Mentha margarita*]:This is the mint variety you should cultivate if you don't like the flavour of mojito. The fragrance of lime in a margarita makes it the ideal garnish.
22. **Red Mint** [**Botanical Name:** *Mentha rubrararipila*]: This excellent hybrid of water mint (*Mentha aquatica*), spearmint (*Mentha spicata*), and maize mint (*Mentha arvensis*) is another superb mint type. The flavour is comparable to spearmint and can be used in cocktails, as a garnish in lemonade or other cool beverages, and refreshing teas, sweets, and ice creams.
23. **Lemon Balm** [**Botanical Name:** *Melissa officinalis*]:Lemon balm is a perennial mint plant that grows in the mint family. People use it to make pleasant, lemony drinks because of its citrus-like aroma, similar to lemongrass but with a tinge of mint. It's also used to treat mental illnesses and as a medicine.
24. **Calamint** [**Botanical Name:** *Calamintha nepeta*]:This mint type has a strong aroma, comparable to Pennyroyal, and a flavour that is a cross between marjoram and spearmint. Calamint has several therapeutic properties and is utilized in meat dishes and beverages.
25. **Catnip** [**Botanical Name:** *Nepeta cataria*]:Catnip contains a chemical called nepetalactone, which attracts almost 70% to 80% of cats. Growing catnip is an excellent option for your feline's enjoyment if you're a cat parent. Catnip is also good in salads and mint teas.

26. **Licorice Mint [Botanical Name:** *Anise hyssop*]:This mint cultivar has beautiful purple blooms. Fresh leaves are commonly used in baked goods like scones and pastries and custards, ice creams, drinks, vinegar, jams, and salad dressings.
27. **Catmint** [**Botanical Name:** *Nepeta racemose*]: Catmint, unlike catnip, is a decorative herb that can be used as a border plant in vegetable gardens to prevent insects. Catmint has a similar chemical that makes cats happy.

Harvesting

Spearmint should be harvested when the weather is bright and sunny. In roughly 100-110 days, the crop sown in December gets ready for the first harvest during the last week of April; in some varieties, such as Neer Kalka (the most popular Indian spearmint variety), the second harvest occurs 60–70 days after the first harvest. The green herbage should be shed for a day after harvesting to ensure good oil recovery. Fresh herb yields are primarily determined by crop growth. A good spearmint crop can yield 20–30 t of fresh herb per hectare. The output of spearmint essential oil varies between 100 and 175 kg/ha, depending on the crop growth and cultivars used (7).

Phytochemicals Content [6, 28]

The successful utilization of plants in the agribusiness, food, and pharmaceutical industries is predicated on a thorough understanding of their physiologically active secondary metabolites. Many Mentha species have been researched for their phytochemical and pharmacological properties. The volatile oil, phenols, and flavonoids in *M. spicata* leaves are abundant.

Essential Oil Composition

Essential oils are natural, volatile secondary metabolites with a distinctive odour and complicated chemical makeup. They are often extracted by steam or hydro-distillation from various aromatic plants in temperate to warm climates such as the Mediterranean and tropical regions. They constitute a significant element of traditional pharmacopoeia [7,14,15].

Phenolic Compounds

Phenolic compounds, or secondary metabolites, are a broad collection of biologically active compounds containing about 8000 molecules, both small and large and complex structures, with at least one aromatic ring with one or more hydroxyl groups attached. Esters and glycosides are common forms of these chemicals in nature [29]. Mentha species include a range of components, including cinnamic acids and aglycon, glycoside, and acylated flavonoids [30].Water extracts from Mentha have been shown to include esters of phenolic acids and flavonoid derivatives and glycosidic flavonoids that have been hydroxylated in position 3 or 5 [31].Flavonoids, specifically flavones and flavanones, are abundant in Mentha plants. The primary flavones found in Mentha species are Luteolin and its derivatives[32].In aqueous extracts from Mentha species, hybrids, variations, and cultivars, the components eriocitrin, luteolin-7-O-glucoside, naringenin-7-O-glucoside, isorhoifolin, eriodictyol, Luteolin, and Apigenin were detected. Furthermore, the glycoside eriocitrin has been identified as the primary component in aqueous Mentha preparations[33,34].

Biological Activities

Over the past several years, research has shown that mint and its constituents possess different biological activities, including antioxidant, antimicrobial, insecticidal, anticancer, and anti-inflammatory properties[62].

Antimicrobial Activity

Mentha species have been researched for their antibacterial and antifungal properties against various bacteria and fungi [32].Essential oils are more potent antifungals and antibacterials than polar extracts, according to these studies. Mentha essential oils have been discovered to have antibacterial activity against bacteria and other microbes such as yeasts and periodontopathogens. Mentha essential oils have been found to have antimicrobial activity against bacteria and other organisms such as yeasts and periodontopathogens. The presence of oxygenated monoterpenes in their chemical makeup is the primary cause. *Bacillus subtilis, Bacillus cereus, Escherichia coli, Proteus mirabilis, Salmonella typhimurium,* and *Staphylococcus aureus* were all found to be susceptible to *M. rotundifolia* oils. *M. suaveolens*

essential oils effectively inhibited all examined bacteria (20 stains). In contrast, *M. rotundifolia* essential oils had better antimicrobial activity than *M. pulegium* oils against all microorganisms studied (three Gram+, three Gram, two fungal, and one yeast). Despite this, *M. pulegium* oil was good antibacterial action against 11 bacteria (3 Gram+ and 8 Gram) and two yeasts. *Streptococcus pyogenes, E. coli, S. aureus, S. pyogenes*, and *Candida albicans* are all susceptible to the essential oil of *M. spicata*. *Mentha longifolia* oils were found to have significant antibacterial action against all 16 pathogens tested, including *E. coli, Shigellasonnei*, and *Micrococcus flavus*. Essential oils from *M. aquatica* and *M. piperita* also inhibited these bacteria. Furthermore, essential oils from Mentha spp. are a safe ingredient in creating antibiofilm agents that could be used in the pharmaceutical business[63, 74]. Microbes are changing their metabolic and genetic structure to become resistant to medications used to treat prevalent infectious diseases in the contemporary medical and pharmaceutical era. These drug-resistant candidates are more pathogenic and have a higher mortality rate, posing a significant challenge to the pharmaceutical and healthcare industries. Scientists are looking forward to discovering alternative and novel medications to combat microbial drug resistance. Plants, algae, and animals contain various natural therapeutic substances that can be used to treat a variety of infectious diseases. Plants have been used as a source of medicine since the dawn of time. According to several studies, plants have been proven to be one of the vital medication discovery and development sources. Antibacterial, anticancer, anti-diabetic, antioxidant, and other activities have been reported. Anti-bacteria refer to anything that kills bacteria or inhibits their growth or reproduction. The antibacterial effect is the effect of anti-bacteria on various bacteria (or diseases) (72, 75).

Effects on Nervous System

The antinociceptive and antipyretic effects of *M. longifolia* aqueous leaf extract were discovered in a study. The plant extract's oral and intraperitoneal injection yielded comparable high L.D.(50) values, indicating that the plant extract is non-toxic to mice[64]. In another study, methanolic extracts of *M. longifolia* were evaluated for their antioxidant activity (as measured by 2, 2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid) (A.B.T.S. and xanthine/xanthine oxidase methods) and neurochemical properties (MAO-A inhibition, acetylcholinesterase inhibition, and affinity to the gamma-aminobutyric acid(A) receptors. The antioxidant and MAO-A inhibitory properties of this plant were discovered. The essential oil of *M. longifolia* has a more robust central nervous system C.N.S. depressive effect. C.N.S.function has also been studied using *M. longifolia* crude ethanol extract and fractions high in apigenin glycosides, luteolin glycosides, and phenolic acids. Phenolic acids have been discovered to have unique spasmodic, choleretic, and C.N.S.simulative properties[65].

Effects on Gastrointestinal System

The leaves of *Mentha longifolia* are employed in herbal remedies for gastrointestinal problems. The leaves of *M. longifolia* are boiled in water with cardamom seed or powdered leaves given to children and green tea. It's utilized as an antiemetic, especially in cases of chronic diarrhoea. In treating gas problems, *M. longifolia* is used as a carminative and is consumed as chutney, especially in the summer, with butter to prevent diarrhoea. It's also used to relieve pain in the abdomen[66]. *M. longifolia* leaf extract relaxes intestinal smooth muscle, consistent with the plant's traditional use to treat gastrointestinal diseases like diarrhoea and colic. Due to calcium channel blocking components, this plant exhibits a spasmolytic effect primarily through variable calcium mobilization and somewhat through potassium channel activation. In a castor oil-induced diarrheal model, the crude extract of *M. longifolia* gave 31-80% protection, similar to loperamide, at doses of 100-1000 mg/kg. Pretreatment of the tissue with *M. longifolia* crude extract generated a rightward shift in the Ca++ concentration-response curves, similar to verapamil, confirming the calcium channel blocking activity. After activity-directed separation, the petroleum spirit fraction was more potent than the parent crude extract and aqueous fraction. In a castor oil-induced diarrheal model, the crude extract of *M. longifolia* gave 31-80% protection, similar to loperamide, at doses of 100-1000 mg/kg. Pretreatment of the tissue with *M. longifolia* crude extract generated a rightward shift in the Ca++ concentration-response curves, confirming the calcium channel blocking action. The essence of *M. longofolia* (0.1-100 g/mL) had a modest spasmogenic impact in isolated ruminal and abomasal preparations, followed by relaxation and total (P 0.05) elimination of spontaneous contraction at the maximum dose (1000 g/mL).

On the other hand, the rat ileum only revealed a dose-dependent relaxation effect, and tissues preincubated with essence attenuated the contraction caused by acetylcholine (ACh). Essence (1000 g/mL) significantly reduced ACh's impact, implying that the effect is mediated through cholinergic receptors on smooth muscle. The essence significantly altered gastrointestinal smooth muscle contraction in a dose-dependent and tissue-specific manner. The essence of *M. longofolia* (0.1-100 g/mL) had a modest spasmogenic impact in isolated ruminal and abomasal preparations, followed by relaxation and total (P 0.05) elimination of spontaneous contraction at the maximum dose (1000 g/mL). On the other hand, the rat ileum only revealed a dose-dependent relaxation effect, and tissues preincubated with essence attenuated the contraction caused by acetylcholine (ACh). Essence (1000 g/mL) significantly reduced ACh's impact, implying that the effect is mediated through cholinergic receptors on smooth muscle. The essence significantly altered gastrointestinal smooth muscle contraction in a dose-dependent and tissue-specific manner[67].

Antioxidant Effect

Due to their radical scavenging characteristics, many aromatic and medicinal plants are attracting particular study. Reactive oxygen species (R.O.S. are highly reactive chemical species that occur in the body during metabolism and may have one or more unpaired electrons. The peroxidation of membrane lipids and the attack on biomolecules are detrimental results of oxidative stress, defined as an imbalance between R.O.S.and antioxidant defence (proteins, membrane enzymes, and carbohydrates[32].Antioxidant activity has been demonstrated in various Mentha species and their extracts or essential oils. The principal antioxidants are phenolic acids (e.g., rosmarinic and caffeic acids), flavones (e.g., luteolin derivatives), and flavanones (e.g., eriocitrinproducts). Vitamin antioxidants (such as ascorbic acid and carotenoids) contribute just a tiny portion of the total antioxidant potential. In essential oils, unsaturated terpenes with a cyclohexadiene structure (e.g., terpinene) and minor cyclic oxygenated terpenes (e.g., thymol) may have antioxidant properties. Still, acyclic unsaturated oxygenated monoterpenes (e.g., linalool) may have pro-oxidant properties[68, 70].

In various functional tests, mentha plants have also been found to exhibit antioxidant properties. The D.P.P.H. test is a frequently used method of determining a person's ability to donate hydrogen atoms. The most studied species are *M. spicata, M. piperita, M. longifolia, M. pulegium, M. rotundifolia, M. arvensis*, and *M. aquatica*. Compared to other species, *M. piperita* and *M. spicata* extract demonstrated good antioxidant activity in numerous in vitro assay techniques. The most studied species are *M. spicata, M. piperita, M. longifolia, M. pulegium, M. rotundifolia, M. arvensis,* and *M. aquatica*. Compared to other species, *M. piperita* and *M. spicata* extract demonstrated good antioxidant activity in numerous in vitro assay techniques(7).

***In vitro* Toxicological Evaluation**

One study looked at the effects of the essential oil from the leaves of *M. longifolia* on a few biochemical measures in Wistar rats. Red blood cells and lymphocytes were reduced (P 0.05) by the oil at 125, 250, 375, and 500 L/kg of body weight, but there was no discernible trend in white blood cells or mean cell volume. The ideal doses raised the population of neutrophils, monocytes, and giant unstained cells significantly. Furthermore, the liver-body weight ratio and serum concentrations of cholesterol, triglyceride, high-density lipoprotein-cholesterol, and inorganic phosphate increased; however, the heart-body weight ratio and serum levels of low-density lipoprotein-cholesterol, Na(+), Ca(2+), Cl (-), K(+), creatinine, and uric acid did not change. The oil enhanced the kidney-body weight ratio by 500 L/kg of body weight.

On the other hand, the oil lowered serum urea and the atherogenic index. Only oil at 125 L/kg of body weight increased total conjugated bilirubin and total protein and albumin in the serum. Serum alkaline phosphatase activity increased, whereas gamma-glutamyltransferase, alanine, and aspartate aminotransferase remained unchanged. The findings reveal the essential oil's dose and parameter-specific effects. Although the essential oil from *M. longifolia* leaves does not cause atherosclerosis, it increases the rat liver's practical activity at the lowest amount tested. As a result, at the levels tested, the essential oil from *M. longifolia* may not be totally "safe"[69].

The brine shrimp lethality bioassay was also used to perform an in vitro cytotoxicity test. The oil was not hazardous at 40 g/mL, the lowest concentration employed; all brine shrimps survived. While the highest mortality rate was 200 g/mL, the lowest mortality rate was 40 g/mL. The brine shrimp lethality bioassay was also used to perform an in vitro cytotoxicity test. The oil was not hazardous at 40 g/mL, the lowest concentration employed; all brine shrimps survived. While the highest mortality rate was 200 g/mL, the lowest mortality rate was 40 g/mL. Because oven-drying reduces the amount of potentially hazardous pulegone and menthone, it is recommended that this herb be oven-dried or cooked before ingestion to avoid toxicity. Raw plant consumption is not recommended, especially in people with a history of liver illness or those on cytochrome P450-inducing medications.The acute toxicity of flavonoids isolated from *M. longifolia* was investigated, and quercetin-3-O-glucoside had the lowest results, with an LL.D.of 5 mg/kg. With an LL.D.of 4 mg/kg, Apigenin and luteolin-7-O-glucoside, luteolin-7, 3'-O-diglucoside exhibited the same effect. The most hazardous flavonoids were kaempferol-3-O-glucoside and kaempferol-3-O-glucoside, with an LL.D.of 3 mg/kg.

Insecticidal Activity

Mint has been shown to have insecticidal properties against a range of insects. Mentha has traditionally been employed as an insecticide in the form of essential oils. In contact and fumigation bioassays, *M. spicata, M. pulegium*, and *M. rotundifolia* oils showed insecticidal activity against adults of Rhyzopertha Dominica, as well as repellency. In a contact toxicity test against the same insect, *M. pulegium* and *M. rotundifolia* oils were highly hazardous in the first 24 hours[22]. In fumigation bioassays, the essential oil of *M. microphylla* showed exceptional effectiveness against adult insects. Piperitenone oxide has also been linked to the insecticidal activities of *M. longifolia* essential oil against this pest[71].

Cytotoxic Activity

Several investigations have found that Mentha plants contain cytotoxic components that could be useful in developing anticancer drugs. Methanolic and aqueous extracts of *M. arvensis, M. longifolia, M. spicata,* and *M. viridis*, for example, had an anti-proliferative activity in vitro against several cancer cell lines at a concentration of 100 g/Ml.The M.T.T.assay was used to determine the cytotoxicity of essential oils from four Mentha species (*M. arvensis, M. piperita, M. longifolia,* and *M. spicata*) on breast cancer (MCF-7) and prostate cancer (LNCaP) cell lines. The essential oils of Mentha were found to have significant cytotoxic action against both cancer cell lines (IC50s ranging from 43.5 2.1–95.7 4.5 g/mL)[73]. In another investigation, *M. spicata* aqueous extract significantly inhibited Wehi-164 and U937 cell proliferation dosage and time-dependently (LD50s ranging from 4.63 to 5.97 mg/mL).

Medicinal Uses

Spearmint has long been used as a medicinal and aromatic plant in both western and eastern cultures. Insecticides, antispasmodics, and anti-platelets are all biological uses for spearmint. In terms of medical applications, spearmint is used in folkloric treatments to cure colds and flu, respiratory tract disorders, gastralgia, haemorrhoids, and stomachaches[2]. Spearmint oil is extracted and utilized in medicine regularly. According to Bensabah et al., spearmint leaves are commonly consumed as tea, and its carminative characteristics can helptreat digestive issues, fever, and mild diseases. Spearmint has also been used to treat a variety of ailments. Nausea, vomiting, and gastrointestinal problems are just a few examples[2]. Spearmint is utilized in the culinary, confectionery, and chewing gum industries, among other things. Spearmint aids in food preservation and enhances the flavour and scent of foods. Spearmint is utilized in the culinary, confectionery, and chewing gum industries, among other things. Spearmint aids in food preservation and enhances the flavour and scent of foods[2]. In Iran, spearmint is used as a flavouring agent in foods like cheese and dough. In addition, spearmint is added to fish and shellfish platters in Indian and Italian cuisine, either fresh or dried, before or after cooking[2].

Because of its antioxidant, antiradical, and chelating capabilities, spearmint in food can assist in maintaining redox balance in the body and increasing safety and effect on human wellness. Spearmint is commonly used in cosmetics and soaps, toothpaste, breath fresheners, and antiseptic mouth rinses[2]. According to spearmint, many traditional remedies are utilized in a different cultures. Spearmint has been used in traditional Iranian medicine for diarrhoea,

antidote, indigestion, intestinal weakness, abdominal discomfort, cold, influenza, sinusitis, headache, and flatulence[6]. *M. spicata* leaves have been advised by traditional Iranian medical practitioners to cure digestive problems and flatulence [6]. Gas, indigestion, nausea, diarrhoea, upper gastrointestinal tract spasms, irritable bowel syndrome (I.B.S., bile duct and gallbladder edoema (inflammation), and gallstones are all treated with spearmint. It's also used to treat sore throats, colds, headaches, toothaches, cramps, cancer, and respiratory tract irritation. Some people use it as a stimulant, germ killer, local pain reliever, and anti-spasm drug. Spearmint is administered directly to the skin for swelling inside the mouth, arthritis, local muscle and nerve discomfort, and skin diseases like pruritus and urticaria. Spearmint is used as a flavouring agent in foods and beverages. Spearmint is utilized to create healthy foods, cosmetics, and oral hygiene products like mouthwash and toothpaste. Spearmint is used to develop healthy foods, cosmetics, and oral hygiene products like mouthwash and toothpaste[9].

Usage and Applications

According to several historical texts, Caraway, dill, and spearmint are among the oldest plants known and utilized. They're not just used in cuisine but also in herbalist and pharmaceutical treatments. Dill is a galactagogue and has anti-hyperlipidemic, anti-hypercholesterolemic, and antioxidant properties. Caraway seeds can all have antispasmodic, carminative, emmenagogue, expectorant, galactagogue, stimulant, stomachic, and tonic properties.Heartburn can be relieved by chewing the seeds after a meal. There have also been reports of new pharmaceutical uses, such as antihyperglycemic potential. The characteristics of spearmint include stimulant, carminative, and antispasmodic. Furthermore, carvone can boost detoxifying activities in murine cells, making it a potential chemoprotective drug.

The essential oils extracted from these three species are widely used in the perfumery, cosmetics, and perfuming agents. Spearmint essential oil, in particular, is in high demand and is being used in toothpaste and other oral care products. Even aromatherapy uses this oil now. Carvone can even be used as a parasiticide and pesticide safe for the environment. Termites, ants, and carpenter ants are controlled by this monoterpene with other essential oil components. Mentha essential oil has been studied for its insecticidal, fumigant, and repellant properties. *Triboliumca staneum*, *Musca domestica*, and *Spodoptera littoralis* are controlled effectively with Mentha spicata oil(9).

Research Gap

There isn't a comprehensive evaluation of spearmint's traditional applications, phytochemicals, or pharmacological investigations (*M. spicata*). We believe that this review paper will provide access to more in-depth usage of spearmint's traditional medicinal expertise and phytochemical and biological data for future research. This study focuses on updating botanical data, conventional medical applications, chemical and pharmacological activities, and further scientific evidence. Based on a review of several studies, *M. longifolia* appears to be a viable natural source for the development of novel medications. However, more research is needed to confirm the exact quality and safety of the plant before doctors can utilize it. More research and advanced studies are required to improve its rates and expand its uses.

CONCLUSION

Mentha spp. has many antibiotic actions against bacteria, yeasts, insects, and other pathogens. The antibacterial activity of the essential oil is greater than that of the hydroalcoholic extract. It also has antinociceptive and carminative properties. This review validates that this plant has the potential to be utilized as a novel source for the development of new medicines; however, additional research is needed to determine the exact quality and amount of this plant before it can be used as a therapeutic source in humans. Spearmint phenolic chemicals have a wide range of biological functions. As a result, this plant has potential for medicinal and functional food applications, and also it fulfils the SDG goal of good health and well-being.

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Table 1: Phytochemical Constituent of Mint Leaves

Name of the plant part	Name of the Phytochemical
Leaf	Alkaloid
	Tannins
	Flavonoid
	Cardiac glycosides
	Terpenoids
	Phenol
	Saponin
	Coumarin
	Diterpenes

Table 2: Essential Oil Composition of Mint Leaves

Plant Species	Component	Reference
M. spicata, *M. pulegium,* *M. rotundifolia,* *M. longifolia*	Carvone, Pulegone, Piperitenone oxide, Piperitone, Menthone, Piperitenone, Carvone, Trans-piperitone oxide, Cis-piperitone oxide, Piperitol, Lippione, Pulegone, 2,4(8),6-p-Menthatrien-2,3-diol, Trans-piperitone epoxide, Cis-piperitone epoxide, carvone and limonene, followed by 1,8-cineole, β-pinene, cis-dihydrochalcone, and dihydrocarveol, iso menthone, and β-caryophyllene, α-terpinene, limonene, 1,8-cineole, and β-myrcene, cis-iso pulegone, pulegone, β-pinene, α-cadinol, and α-pinene	[16,17,18,19, 20,21,22,23, 24,25,26,27]

Table 3: List of Identified Metabolites [28]

Sl.No	Compound
1	2-[2-(Octylamino)ethoxy]ethanol
2	Hesperidin
3	Eriodictyol
4	Methyl 4-(4-methoxyohenyl)butanoate
5	1,8-Diazacyclotetradecane-2,7-dione
6	Apigenin-7-O-glucoside
7	Meprednisone
8	Eravacycline
9	Eriodictyol-7-O-glucoside
10	Allamandin
11	Ferreirin
12	(5Z)-5-Tetradecen-1-ol
13	1-(Methoxymethyl)cyclododecanol
14	Kaempferol
15	Demethylsulochrin
16	Rhamnocitrin
17	2,2′-(Dodecylimino)diethanol
18	Ginkgolide C
19	Trans-5-O-(4-coumaroyl)-D-quinate
20	4-Hydroxycoumarin
21	Chrysosplenetin
22	Decuroside III
23	Erucic acid
24	1-Isobenzofuranone
25	16-Hydroxyhexadecanoic acid
26	Gibberellin A44 diacid
27	Retusin
28	2-Hydroxyethyl 12-hydroxyoctadecanoate
29	Z-9-hexadecen-1-ol

30	2-Hydroxyethyl hexadecanoate
31	7-Methylene-1,3,5-cyclooctatriene
32	2-[(9Z)-9-octadecen-1-yloxy]ethanol
33	2,2′-(Octadecylimino)diethanol
34	Stearamide
35	2,3-Dihydroxypropyl palmitate
36	Phosphatidylethanolaminelyso 16:0

Table 4: Phenolic Compound Present in Mentha Species

Name of the Species	Name of the Phenolic Acids	Reference
M. spicata	Rosmarinic acid, trans-hydroxycinnamic, Veratric acid, 4-hydroxy cinnamic, ferulic acids, syringic, hydroxybenzoic, 2-hydroxy cinnamic,	[35,36,37,38]
M. piperita	Rosmarinic acid, lithospermicacids,protocatechuic acid glucoside, prolithospermic acid, Caffeic acid, isosalvianolic acid A, salvianolic acids (E and H/I), danshensu, Rosmarinic, salvianolic, and dehydro-salvianolic acids, Caffeic, syringic, gallic, salvianolic acid B, vanillic, p-coumaric, and ferulic acids, hydroxybenzoic, o-coumaric,	[39,40,41,42]
M. pulegium	Caffeic acid, vanillic, and ferulic acids, caffeic, p-coumaric, chlorogenic, and rosmarinic acids, 4-Hydroxy benzoic	[43,44,45]
M. rotundifolia	Caffeic, p-coumaric, p-hydroxybenzoic, p-coumaric acids, chlorogenic,ferulic and rosmarinic acids	[45,46]
M. longifolia	Rosmarinic, dedihydro-salvianolic acid, salvianolic acid	[47]
M. australis	Caffeic acids, chlorogenic, Rosmarinic	[48]
M. haplocalyx	Rosmarinic acid, lithospermic acid B, sodium lithospermate B, Cis-salvianolic acid J, salvianolic acid J, ithospermic acid, rosmarinic acid, caffeic acid and Rosmarinic	[49,50]

Table 5: Phenolic Acids of Mentha Species

Name of the Species	Name of the Flavonoid Compound	Reference
M. spicata	Naringenin, Chrysoeriol, Rutin, quercetin, Diosmetin, diosmin, diosmin-7-glucoside Luteolin, Naringenin, thymosin, 5-Desmethoxynobiletin, 5,6-dihydroxy-7,8,3′,4′-tetramethoxyflavone, sideritiflavone,Aapigeninrutin, catechin	[51,52,53,54]
M. piperita	Luteolin 7-O-rutinoside, isorhoifolin, eriocitrin, narirutin, diosmin, Luteolin 7-O-β-glucuronide, pebrellin, eriodictyol 7-O-glucoside, tetramethoxyflavone, luteolin 7-O-rutinoside, isorhoifolin, eriodictyol, eriodictyol 7-O-β-glucoside, Rutin,Catechin, hesperidin, eriocitrin, narirutin, naringenin-7-O-β-glucoside	[55,56].
M. pulegium	Thymonin, jaceosidin, 7-O-α-rutinosides of Apigenin, pectolinaringenin, Luteolin, vicenin, 5-hydroxy-6,7,3′,4′-tetramethoxyflavone, ladanein, sorbifolin, pedalitin, Diosmin, Luteolin	**[57]**
M. rotundifolia	Apigenin, luteolinidin, Thymonin, thymosin,Lluteolindiosmin, elargonidin, cyanidin, delphinidin, petunidin, Luteolin,Esculetin, nNaringeninkaempferol, and diosmetin	[58]

M. longifolia	Luteolin-glucuronide, luteolin-glucopyranosyl-rhamnopyranoside, eriodictyol- glucopyranosyl-rhamnopyranoside, luteolin-diglucuronide, methylated luteolin-glucuronide	[59]
M. australis	Neoponcirin, apigenin, biochanin A, hesperetin, narirutin,andnaringenin	[60]
M. haplocalyx	Isoraifolin, menthoside, Eriocitrin, luteolin-7-O-glucoside, luteolin-7-glucoside	[61]

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RESEARCH ARTICLE

Change in Refraction after One Week and One Month of Phacoemulsification Cataract Surgery

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ABSTRACT

Now days, Management of cataract and surgical outcome of cataract surgery become very much predictable due to development of surgical techniques. However, the change in refraction after cataract surgery always remains a challenge, though there is an advancement of biometry calculation.Itremains uncertain when to prescribe glasses after cataract Surgery. There is very little literature available that change in refraction after cataract surgery happens till how many days of cataract surgery. As a result, there is always a hesitation, when to prescribe glasses after cataract surgery and adjustment of IOL Power of other eye surgery when desired or target refraction is not achieved in surgical eye.Identify the change in refraction in one week and one month of cataract surgery. Spectacle to be dispensed after one week or one month of cataract surgery. Adjustment of IOL power for other eye cataract surgery after one week or one month of refraction.Sample size: 90. A perspective, single centric, study conducted in the Department of Ophthalmology at corporate multispecialty hospital. Inclusion Criteria: All patients with clinically significant cataract and /or complaining blurring of vision due to cataract. Age > 40years both Male and Female. Exclusion Criteria:Ocular Pathology that could lead to miscalculation of IOL power calculation. Surgical complication. Dropouts to follow up during study period. Corneal Astigmatism based on K vale (>1.5D).

At Preoperative evaluation Axiallength, Lens-power calculation and Keratometry were measured with IOL Master (Carl Zeiss Meditec,Germany). Target refractive Error for spherical equivalent Emmetropia, the Surgeon selected value between 0 to -0.50DS. All Cataract Surgery will be performed by an experienced ophthalmologist in topical or local anaesthesia using a 2.8mm limbal incision Phaco with Alcon infinity machine. In the bag insertation of Acrys of IQ, Acrys of Single Piece(ALCON)Aurovue

EV(Aurolab). Postoperative treatment will be consisted of topical steroid and topical antibiotic or a combination of both steroid and antobiotic installed every 4hrly till 1 week of cataract Surgery and tapered thereafter in dosages of 4,3,2,1 in every 1week interval. Follow up examination will be carried after 1week(5-9 days) and 1 month(4 weeks-5 weeks) of cataract surgery. Auto refraction will be performed by Topcon Autorefractometer. Average of 3 readings will be taken into consideration. Subjective refraction will be carried by two of the Optometrist of the department. A refractive error shift was defined as the change in refraction in One week and one month (5 weeks) of cataract surgery.Automated refraction in terms of spherical equivalent shows a good correlation between one week and one month after uneventful cataract surgery(P=0.08) however there is a refractive instability noticed in spherical and cylindrical error between one week and one month after surgery.

In our study, neither nor spherical nor the cylindrical refraction were stable after one week. This difference could rely on differences in the study design and patient material. We conducted our study on varying patient material. With mixed age group, varying axial length and degree of cataract, this makes comparison difficult with other studies.One week after cataract surgery, eyes are often hyperopic compared to refractive target and a myopic shift is often observed later in one month. This early shift may be related to change in anterior chamber depth and IOL position within the eye. It is possible that IOL has slight posterior location immediate after surgery and IOL moves anteriorly with progression of week till one month. The myopic shift can be due to reduce in corneal swelling after one week.

Keywords: Cataract, Phaco, refractive error, IOL, Sustainable, SDG 3

INTRODUCTION

The removal of crystalline lens and putting the intra ocular lens is known as cataract surgery.It is known as an age related process.The crystalline lens of the eye became cloudy and causing the loss of vision. Some cataracts are developed from the childhood and some are developed due to some certain injury factors. Blurring of vision and glaring of lights in night time are the common symptoms. In cataract surgery an eye surgeon removes the cloudy crystalline lens from the patient's eye by emulsification or by cutting and putting the artificial intra ocular lens it.it is only done by the ophthalmologist.in surgical procedure the topical anesthetic drops are used as the patient feel comfortable. In all over India 90% surgeries are successful and patient have good vision with a very few complications rate.Giving a day care, high volume, small incision phacoemulsification is very popular in all over world. Very quick recovery occurs in this process.Thus ensuring healthy lives and promoting well-being at all ages is essential to sustainable development which also satisfies the SDG 3 goal. Currently, the world is facing a global health crisis unlike any other — COVID-19 is spreading human suffering, destabilizing the global economy and upending the lives of billions of people around the globe.

Types

There are two types of surgical procedures which are used most commonly through the world.The first method is phacoemulsification and the second one is extracapsular cataract surgery and it is involves in two different types.The foldable lens is used for 2-3mm phaco incision and the non-foldable lenses are placed by large extracapsular incision.The smallest incision is 2-3mm and it is suture-less incision.In ECCE the incision is 10-12mm and it's a very larger and it is usually require stitching.The modify of ECCE is MSICS cataract surgery.In Phacoemulsification cataract surgery the developed procedure and the high-cost instrument are used.

Operation Procedures

In phacoemulsification cataract surgery the procedure of implantation of IOL lens is happen by different types of steps which is follows one by one carefully by the ophthalmologist and the assistants.The steps are shows one by one.

- Anaesthesia;
- Exposure of the eyeball using an eyelid speculum;
- Entry into the eye through a minimal incision (corneal or scleral);
- Viscoelastic injection to stabilize the anterior chamber and to help maintain the eye pressurization;
- Capsulorhexis
- Hydrodisection
- Hydro delineation
- Ultrasonic destruction or emulsification of the cataract after nuclear cracking or chopping (if needed), careful aspiration of the remaining lens cortex (outer layer of lens) material from the capsular bag, capsular polishing (if needed);
- Implantation of the, usually foldable, intraocular lens (IOL);
- Viscoelastic removal;
- Wound sealing / hydration (if needed).

Before the cataract surgery the dilation of pupil is necessary to implant the IOL behind the iris.The constricting drops are used for secondary implantation of IOL in front of iris.Anesthesia is given topically by eye drops or by injecting in the peri bulbar or behind the eye.If the patient having anxiety to reduce the anxiety have to give oral or intravenous sedation.And for the children the general anesthesia is used sometimes in some cases for children and adults with particular medical issues like psychiatric the surgery may occur on a stretcher or chair.The eye lids are open with speculum and clean with swabbed also cleaned the surrounding skin.The face is full covered with sterilize cloth with an opening for the operative eye.There is no much pain in the eye operative eye as it is anesthetized.The discomfort due to the bright light of the microscope is common.The ocular surface is remained moist by using sterile saline water or eye drops for moisture.The discission into the lens is performed on the limbus area which is the middle part of the sclera and cornea.This procedure is very shortened and early recovery and the most advantage is in this procedure there is no stitches or a few in complicated cases.In capsulotomy procedure by using the cystotome instrument open the lens capsule portion.In anterior capsulotomy the front portion of lens capsule is remain open and in posterior capsulotomy the back portion of lens capsule is remain open.The surgeon while doing phaco surgery performs a curvilinear Capsulorhexis to do a round and smooth opening by which the IOL inserted.

In ECCE procedure the intraocular lens is usually inserted and the insertion of IOL.The ophthalmologist often check that the incision does not leak fluid.And this is a very important step which may cause a high risk of unwanted growth of microorganisms entering into the eye and predisposing and cause of endophthalmitis.In operated eye the eye drop is used which is the combination of antibiotic and steroid.Antibiotics are used as pre-operative,intra-operative and post-operative procedure.The corticosteroid is a combination of antibiotic and steroid used in post operative cases.Most cataract operation are performed under topical anesthetic drops and discharge the patient in the same day with giving eye drops and black specs.The patient is instructed to start using the eye drops after 2hours of the surgery to control the inflammation and prevent the infection.99.9% in united states are performed cataract surgery.After cataract surgery the refractive errors are often found.As the accurate biometric analysis, selection and calculation of the IOL and modern techniques for cataract surgery all contribute to achieve the perfect cataract surgery either no refractive error.The most common goal in cataract surgery is emmetropia which is achieved in only 55% of eye in some cases.The refractive error occurs due to the unsatisfactory cataract surgery which is an unpleasant and frustrating situation for patient and surgeon.The most common Target of cataract surgery is emmetropia(spherical equivalent -0.5 to +0.5D and <1.0 D astigmatism).To achieve target refraction may be a good objective of surgical outcomes.The vision may be decrease after post operative due to some retinal disease or optic nerve disease.To achieve the target refraction is mostly depend upon the accuracy of the IOL calculation and the

appropriate surgical procedure.The main focus to improve the calculation for the IOL power in biometry.Cataract surgery is not having the aim to achieve a post operative refractive error with no astigmatism.UP to 1.0 D astigmatism may also be considered as physiological measure to reduce uncorrected presbyopia which is anage-related disease.Cataract surgeons should consider ways of dealing with preexisting corneal astigmatism when aiming for emmetropia. Approaches to reduce corneal astigmatism include incision placement on the steep axis, peripheral corneal relaxing incisions, and implantation of a Toric IOL.We can benefit from residual refractive error in patients undergoing bilateral sequential cataract surgery in which the refractive error in the first eye exceeds 0.50 D; in these cases, the refractive error in the second eye can be improved by modifying the IOL power

While reviewing the it was found that Automated refraction is highly repeatable and can be used to monitor post surgical refractive changes. Whereas corneal swelling becomes stable 2 weeks after cataract surgery, automated refraction becomes stable after 1 week and can be used to accurately prescribe corrective lenses at that time [12]. The day after cataract surgery, eyes are often slight hyperopic compared to their refractive target, and a minor myopic shift is often observed the week after cataract surgery (Sugar et al. 2001; de Juan et al. 2013). This early shift may be related to changes in anterior chamber depth and IOL position within the eye. It is possible that the IOL has a slight posterior location immediate after implantation after which the IOL moves anteriorly during the first week. Such a model would explain the early refractive shift, if the refractive changes caused by varying degree of corneal swelling are ignored. This study shows that automated refraction is stable with regard to spherical equivalent 1 week after uncomplicated cataract surgery [13]. In a similar study by de Juan et al. from 2013; both spherical refraction and cylinder refraction were stable after 1 week, even though the corneal swelling significantly continued to diminish past the first week after surgery (de Juan et al. 2013). In our study, the amount of cylinder refraction was not stable after 1 week. The difference could rely on differences in study design and patient material. We conducted our study on a mixed patient material with varying age, axial length, corneal astigmatism and degree of cataract including hard cataracts. In the study by de Juan et al., the ocular and demographic characteristics of the patients are not described in detail, which makes comparison difficult. In any case, our material is somewhat larger in terms of patients. De Juan et al. reported in 2013 that automated refraction stabilized 1 week after cataract Surgery(De. Juan et al.2013, sugar et al.2001)

Aim and Objectives

Aims of the Study-To calculate change in refraction after one week and one month of Phacoemulsification cataract surgery in eastern India.

Null Hypothesis (H0)

There will be change in refraction after one week and one month of cataract surgery

Alternate Hypothesis (H1)

To study the Change in refraction after one week and one month of cataract surgery. Refractive power stables after one week of Phacoemulsification cataract Surgery

Objectives

- Identify the change in refraction in one week and one month of cataract Surgery
- Spectacle to be dispensed after one week or one month of cataract surgery
- Adjustment of IOL power for other eye cataract surgery after one week or one month of cataract surgery

MATERIALS & METHOD

This is a prospective cohort study, carried out between October 2021 to April 2022 at Ophthalmology department of a corporate specialty hospital, Bhubaneswar, Odisha.

Study Design

A prospective, single centric cohort study.

Inclusion Criteria

We recruited patients randomly those who visited to our outpatient department, during the study period with a senile cataract.Age group more than 40 years both male and female are included in the study.

Exclusion Criteria

Any ocular pathology that could lead to miscalculation of IOL power calculation, any surgical complication, dropouts to follow up during study period any corneal astigmatism (>1.5D based on K value) were excluded from analysis.

Sample Size

On reviewing literature De Juan et al.reported in 2013that automated refraction stabilized after 1 week of uneventful cataract surgery of 79 patients(de Juan et al.2013). We set out these findings in a patient material. In addition, we wanted to analyse predictive factors for a refractive error shift beyond the first week after surgery in order to guide patient selection in a possible IOL power correction study. Therefore, we designed a study to compare change in refraction after 1 week and 1 month of phacoemulsification cataract surgery.

Methodology

All patients who visited to ophthalmology department meeting the inclusion criteria were enrolled in the study. A comprehensive eye examination includes detail clinical history, Visual acuity measurement, objective and subjective refraction, Intraocular Pressure measurement, non dilated Slit lamp examination, Pupillary reaction details including RAPD, were examined by two of the optometrists of the department.Subsequently Patients were dilated for cataract grading to ensure Patient should undergo Phacoemulsification Cataract surgery. Fundoscopy was done to ruled out any posterior segment Pathology by the Surgeon (Senior Ophthalmologist). After the confirmation of diagnosis patient were counseled for surgery (Phacoemulsification with foldable IOL) with the single surgeon of the hospital. At the Preoperative evaluation, Axial length and Keratometry values were measured with the IOL Master 500 (Carl Zeiss MeditecAG,Jena Germany) to calculate the IOL Power.The Holladay II formula was used if the axial length was 22.00 mm or more and the SRK-II was used if the axial length was less than 22.00mm. Refractive Target for spherical equivalent was emmetropia; the surgeon selected a value between 0D to -0.5D

Surgical Procedures

Preoperative Checklist

Patient with normal blood investigation,(Hb%,BT,CT,RBS/FBS/PPBS,HIV,HBsAG,HCV) were taken for surgery.Informed consent to be taken from patient and relative, after the procedure details, risk and benefit, Surgical complication explained to patient in his/her words.Dilation done with Tropicamide eye drop. After dilation,topical anesthesia(Proparacaine Hydro chloride)was applied 3-4 times in 5 minutes interval before surgery.Those who can focus at bright light(less Photo phobic) and have good fixation were consider for topical anesthesia. Nonoperative Patients were undergone surgery with local anesthesia using lignocaine 2%.

Surgical Process

Surgery was assisted by ophthalmic Nurse. Cleaning of eye surface done with 5% betadine solution. Surface left to dry for 5 minutes.Draping is done,Speculum is applied,eye is flushed with normal saline.Two Side port is done with 20-gauge MVR knife.Applied Trypan blue to Stain the anterior capsule depending on degree of cataract.Hydro is done to remove the excess amount of blue.Viscoelastic applied and anterior Capsulorhexis is done with 26G needle.Globe integrity was maintained with viscoelastic.Corneal entry is done with 2.8 mm keratome knife.Hydro dissection and hydrodeliniation is done with 26G canula and Balanced Salt Solution.Nucleus fragmentation is done by direct chopping method. Nuclear Fragments are removed by phaco hand piece.Cortex is removed with irrigation and aspiration probe(Bi-Manual)To maintain globe integrity Viscoelastic is applied further.Implantation and proper positioning of Foldable intraocular lens in the bag.Viscoelastic is then removed with bi-manual.At the end of the

surgery corneal wound were hydrated if needed.In the bag insertion of hydrophobic foldable IOLs (Acrysof IQ, Acrysof Single piece (Alcon) Aurovue EV (Aurolab) were used in the study.Patch of the surgical eye is done if surgery was performed under local anesthesia and patient left with black goggle if surgery was performed under topical anesthesia.

Post Operative Care

The first Post operative care was given either on same day after 6 hrs of cataract Surgery or on the next day. Post Operative treatment consisted of topical steroid, topical antibiotic or a combination of both the drug installed every 4 hourlies till 1 week of cataract surgery.After One week, a steroid of lower strength was recommended in tapering dosages of 4,3,2,1 in every one-week interval for next 4 weeks or one month.Follow up examination were carried after 1 week (5-9 days) and 1 month (4-5 weeks) of cataract surgery. Auto refractometer was performed by two of the optometrists of the department by Topcon RM 800 auto refractometer.Average of 3 reading was considered for subjective verification. Details of unaided visual acuity in operated eye, Details of subjective acceptance in terms of Spherical, cylindrical and axis details were recorded in the data sheet, in one week and one month of cataract surgery.An Excel sheet containing Patient Demographic, Date of visit,age, gender and operated eye are recorded.Pre-Operative Keratometry value of surgical eye (K1 & K2) and axial length (mm) were entered.The refraction details were entered in one week and one month with spherical equivalent of both the visit was maintained in the excel sheet. Surgical site(incision) was entered into the data sheet

RESULTS

A refractive shift was defined as the refraction difference between two examinations. Statistical significance of refractive shifts was tested with a paired t-test. We have included 90 consecutive patients in our study, meeting the inclusion and exclusion criteria during the study period of 8 months (3rd August 2020 to 3rd May 2021).Out of which one patient had a keratitis post viral fever which was resolved spontaneously by one month follow-up with leaving any corneal lesion was included in the study.Out of which Male and Female ratio was 63% and 37% respectively. The ratio of right eye (OD) and left eye (OS) was 58% and 42% respectively. Age group of patients were varied from 40 years to 84 years with a mean age of 63 years.Mean Keratometry value (K1) recorded from IOL master was varied from 40.81 mm to 47.34 mm with a mean keratometry (K1) value of 44.15mm. Mean Keratometry value (K2) recorded from IOL master were varied from 41.72 mm to 47.80 mm with a mean keratometry (K2) value of 44.78mm Average axial length was recorded to be 23.16mm which ranges from 20.88 mm to 27.77 mm. The observation of one week and one month refraction is shown in table-2. It shows range of refraction varies between the two visits and P value is not statistically significant. The observations are scattered in diagram1. There was no difference between subjective acceptance in 1 week and 1 month after surgery regarding spherical equivalent, although the mean refractive shift in spherical equivalent for the cohort was not statistically significant. The scattered diagram shows a good correlation between 1 week and 1 month of post operative subjective acceptance of the Patients. However. there was a trend towards instability noticed in spherical and cylindrical value showing a non significant P value (Paired t test).

DISCUSSION

One week after cataract surgery, eyes are often hyperopic compared to refractive target and a myopic shift is often observed later in one month. This early shift may be related to change in anterior chamber depth and IOL position within the eye. It is possible that IOL has slight posterior location immediate after surgery and IOL moves anteriorly with progression of week till one month. The myopic shift can be due to reduced in corneal swelling after one week.
This study shows that automated refraction is stable and good correlation noticed with regard to spherical equivalent one week and one month of cataract surgery similar to study done by Ostri et al. from 2018.How ever similar study by de Juan et al. from 2013 both spherical and cylindrical refraction were stable after one week even though the corneal swelling reduced thereafter.In our study, neither nor spherical nor the cylindrical refraction were

stable after one week. This difference could rely on differences in the study design and patient material. We conducted our study on varying patient material. With mixed age group, varying axial length and degree of cataract, this makes comparison difficult with other studies.The Pathogenesis of corneal swelling after surgery is more complex, Surgeon induced corneal and endothelial change is always questionable. It certainly plays a role how close to the cornea the phaco hand piece is held during surgery and how corneal endothelium behaves after surgery in a given patient.Spectacle Prescription always relays on subjective response of patient. Based on the earlier studies by (sugar et al.2001 and Lake et al. 2005) it is possible to prescribe spectacle as early as one week after surgery. On the other hand, there are reasons to consider waiting, considering corneal swelling hardly subsides by one week time in cases of hard Varity of cataract and secondly the corneal cylinder may not be stable if incision has been hydrated. The axis of cylinder may change as corneal swelling reduced.There is limitation to our study considering there is a large variation in patient age group. Secondly accuracy of surgery induced astigmatism or surgeon induced astigmatism is unknown although surgery was performed by a single surgeon. The repeatability of the subjective acceptance and inter observer variability of subjective acceptance between the two-study optometrist were not tested in the study.

CONCLUSION

As automated spherical equivalent refraction is stable after one week of uneventful phacoemulsification cataract surgery, it is possible to conduct an IOL correction for the second eye depending the refraction in the first eye after one week of surgery.

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List of Abbreviations Used

BT	Bleeding Time
CT	Clotting Time
D	Dioptre
ECCE	Extra Capsular Cataract Extraction
FBS	Fasting Blood Sugar
FDA	Food and Drug Administration
HB	Haemoglobin
IOL	Intra Ocular Lens
ICCE	Intra Capsular Cataract Extraction
K	Keratometry
Mm	Millimetre
PHACO	Phacoemulsification
SICS	Small Incision Cataract Surgery

Table No.1: Characteristics of the cohort

n=90			
Characteristic (unit)	**Value**	**Standard Deviation**	**Range**
Male/Female (%)	63/37		
Eye (OD/OS) (%)	58/42		
Mean Age (Years)	63	9.41	40-84
Avg Axial Length (mm)	23.16	1.14	20.88-27.77
Mean Preop K1 (Diopter)	44.15	1.87	40.81-47.34
Mean Preop K2 (Diopter)	44.78	1.88	41.72-47.80

Table no. 2: Comparison of refraction 1 week vs. 5weeks (1 month)

Refractive shift in dioptre	Mean	Standard deviation	Range	P value (Paired t-test)
Sphere_ 1 week	0.91	0.37	-0.75 to 1.5	0.14
Sphere_5 week	0.69	0.37	-1.0 to-1.50	
Cylinder_1 week	-0.53	0.39	0 to -1.75	0.26
Cylinder_5 week	-0.51	0.42	0 to -1.75	
Spherical equivalent_1 week	-0.18	0.34	0.63 to -1.12	0.08
Spherical equivalent_5 week	-0.20	0.35	0.63 to -1.25	

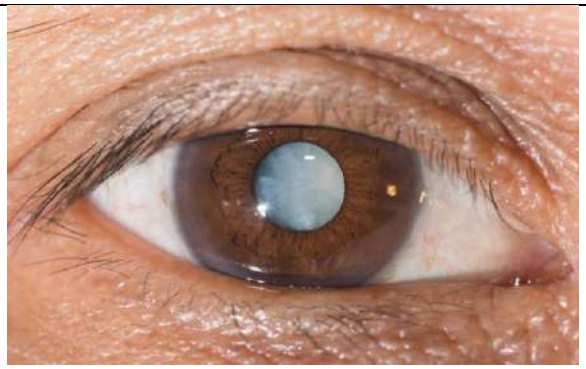


Figure 1: Total Cataract

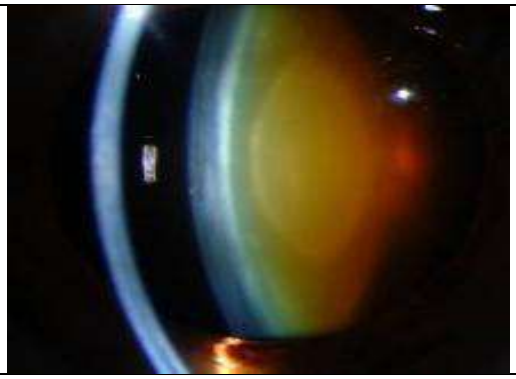


Figure 2: Nuclear sclerosis-4

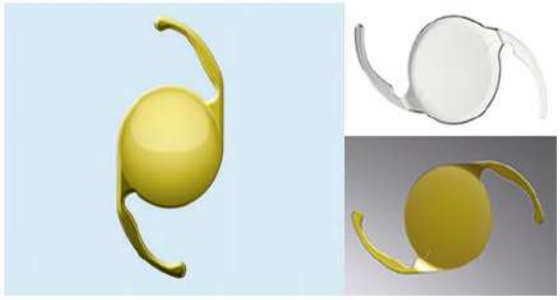


Figure 3: IOL

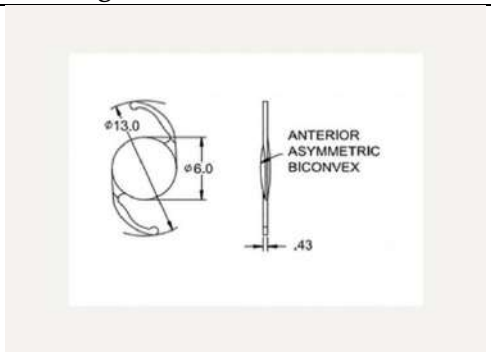
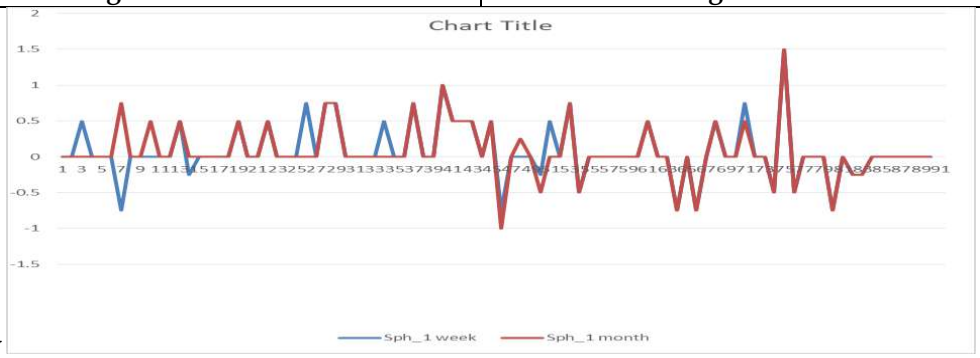


Figure 4: Toric IOL



v

Chart-1: Comparison of change in refraction in terms of spherical refraction in one week vs. one month after Cataract Surgery

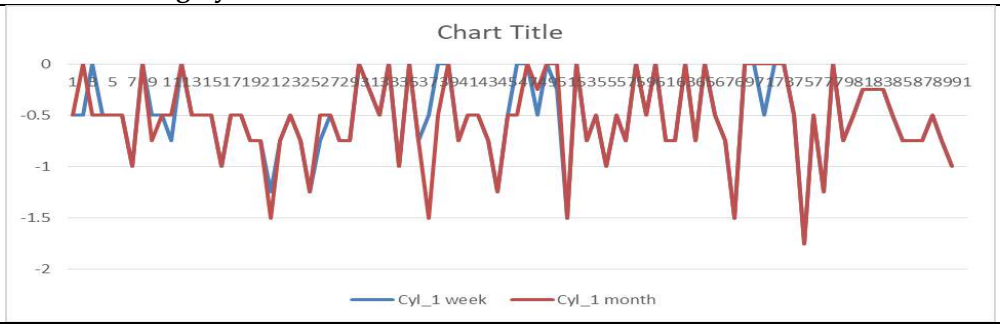


Chart-2: Comparison of change in refraction in terms of cylindrical refraction in one week vs. one month after Cataract Surgery

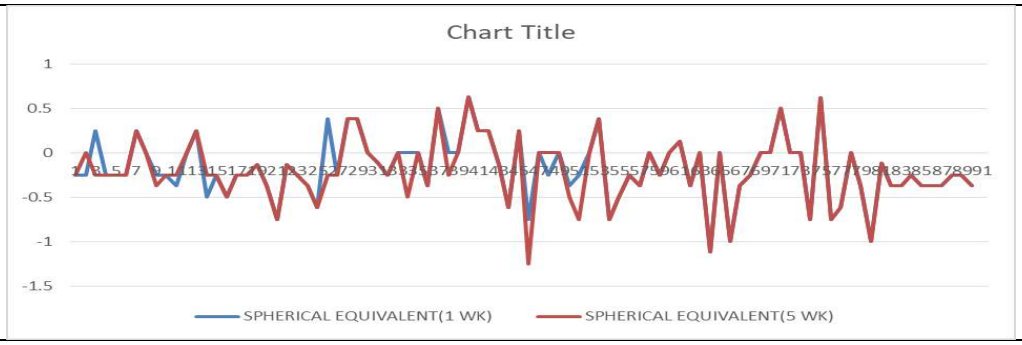


Chart-3: Comparison of change in refraction in terms of spherical equivalent refraction in one week vs. one month after Cataract Surgery

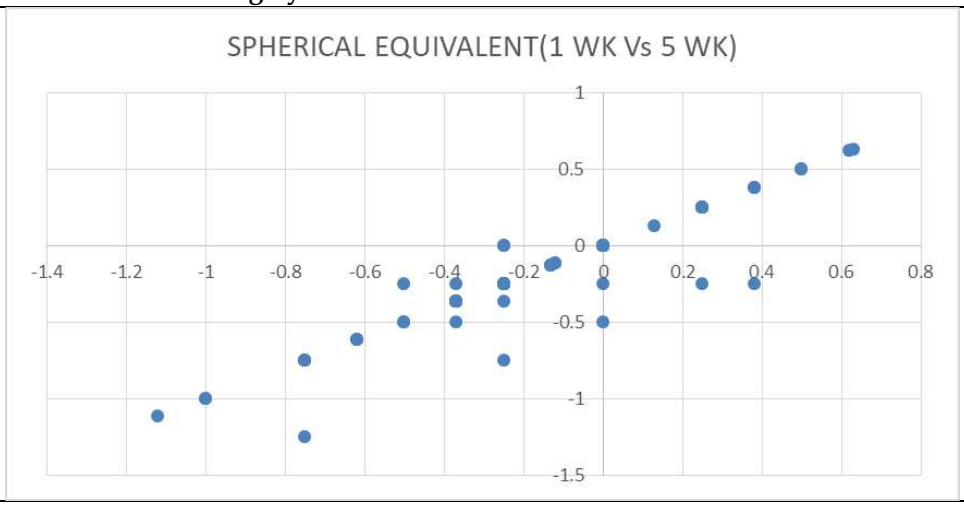


Diagram 1: Scatter Plot comparing correlation of spherical equivalent in one week vs. One month of cataract surgery

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RESEARCH ARTICLE

Promoting Sustainable Tourism in India: The Case of Gorumara National Park, West Bengal, India

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ABSTRACT

Ecotourism a type of sustainable tourism has become a popular phrase in tourism sector very recently. However, the authenticity of ecotourism practice is a big question. The situation is grey for developing countries. The present study examines whether ecotourism in Gorumara National Park of West Bengal achieves its objectives. The study is exploratory in nature and relies on secondary data to examine the linkage of economic benefits and conservation through ecotourism. The study finds that ecotourism has come as an economic rescuer for several villagers and thereby have created a positive attitude towards ecotourism. However, the policy faces problem such as limited income opportunities, lack of coordination between people and policy etc. Thus, proper strategies need to be designed for an inclusive ecotourism approach.

Keywords: Ecotourism; sustainable tourism, economic impact; environmental impact; Gorumara National Park

INTRODUCTION

Ecotourism is a sustainable tourism that has become more popular recently. Ecotourism has been promoted because of its capacity to support preservation of natural resources along with socio-economic incentives to the locals. It is not like mass tourism which mainly focuses on travel. Rather ecotourism is a policy for the preservation of natural capital whose survival is threatened. As a responsible tourism, ecotourism satisfies many sustainable development goals like poverty reduction, biodiversity conservation. The increase in the depletion of natural resources called for a

more sympathetic approach for nature. Global warming, vanishing of several plants, animals, climate change etc. emphasized the need for resource preservation. The situation is worrisome in developing countries particularly because of the ongoing tussle between development and conservation. Until recently, there has been a realization about the gravity of the situation and subsequently there has been a movement for the sustainable use of natural resources. Such a movement has given rise to the birth of ecotourism. It is because tourism and travel industry is a major polluter and ecotourism on the other hand applies green growth strategy for the justifiable use of threatened natural capital (Holden, 2003). Specifically for developing countries Ecotourism provides the imprint of a perfect policy. The developing countries have unique natural capital which is at the verge of extinction. Ecotourism gamut on these issues in the sense that it generates required finance to provide a robust motivation for preservation (Kruger, 2005). The motivations for low-income nations in the adoption of ecotourism rest on the fact that it helps in development of standard of living, social empowerment along with environmental protection (Stone & Nyaupane, 2015).

However, ecotourism is not free from criticisms. There is enormous is agreement and dispute on the effect of ecotourism (Cobbinah, 2015; Das & Chatterjee, 2015). Critics quizzed about the growing thrill of eco-tourism. While supporters claim that ecotourism policies are able to negate the ill effects of mass tourism, critics point out that such policies are only eye wash to increase the demand. Subsequently, income creation outweighs the main motive-protection of natural capital. This is leading directly to environmental degradation. Thus there is a need to go deeper into the issue to examine the efficiency of ecotourism in conservation. It is also required to check whether it dwells on the main mission preservation through betterment of the life style of the inhabitants of these areas. Because of the disputes associated with the policy and particularly for the disagreement in the developing countries, the efficiency of the policy needs an examination. Some of the addressable questions: (1) whether ecotourism policy helps in conservation through economic incentives to the locals

An investigation of an ecotourism site can tell us the positives and negatives of the policy. The present article delves deep to understand the outcome of ecotourism in an important site of West Bengal in India. Specifically, the study inspects the linkage of economic impact with the environmental impact of ecotourism in Gorumara National Park, a widely acclaimed park in the state of West Bengal and also in the country India.

Review of Literature

The negative consequences of mass tourism have paved the path for the development of ecotourism. By permitting tourism in natural areas, ecotourism not only improves the standard of living condition of the locals living in adjacent, but also creates sufficient finance for preservation of threatened natural resources. (Defries et al., 2007). The reason for highlighting the betterment of the inhabitants is that generally these people have been reliant no the natural capital for their livelihood. Poverty of the inhabitants often prompts them to extract resources without thinking of the sustainable use or extinction of these resources. Moreover, because these resources are freely available and lack property rights, there is a problem of 'Free Rider' (Dash & Behera, 2015). It is often claimed that unless these local receive the urge of protection, they won't leave their old habit of dependence. Therefore, the success of the ecotourism necessitates a proper equilibrium of all the patrons. Any imbalance in one will distort the equilibrium.

With the rising cognizance about ecotourism worldwide, the policy has also taken a central role in Indian tourism. Environment consciousness of the tourists (Mihalic, 2000) has been responsible for the introduction of sustainable tourism in India. As a subset of sustainable tourism, ecotourism is having a better acceptance for its policy approaches and missions. The Indian Ministry of Tourism developed the guidelines Ecotourism Policy in 1998. The Government's 12th Five Year Plan (2012-17) also targets to promote ecotourism. The policy document of 12th Five Year Plan emphasized that the finance received from ecotourism should be utilized for the site. At present 868 PAs are there in the country covering 1.65 lakh sq. km i.e., 5.02% of the geographical area (as on January, 2019). With these policy related changes, ecotourism gained momentum in the country with the objective of protecting environment through economic incentives to the locals. There has been an increase in the number of total protected

areas (PA) in the country, where ecotourism is promoted. The following table (Table 1) provides the details of all the types in the country. The ecotourism policy in India attempts to execute the entire missions carefully. The central objective is to fetch an alternative approach to reduce the exploitation of natural capital by the local communities. Engagement prospects are generated for them through ecotourism. They are considered as participants. In the process they feel associated with the policy and encompass the missions. For example in Periyar Tiger Reserve, Kerela, opportunities like rafting, trekking, horse riding, nature camp etc are created. Ecotourism has so far benefited about 40,000 people of 5,540 families (Das & Chatterjee, 2015). With the help of such substitute living, the robbers, smugglers have been transformed as honest followers of preservation of forests [1].

All such facets of ecotourism look appealing and inspiring. But there is a darker side of the story also. The root of the problem is in the execution in developing countries. The concept originated in developed and western countries. The low income countries adopted it blindly. Therefore, the associations between ecotourism and preservation are questionable at the broader level. Themain objective of the present study is to check the positives and negatives of ecotourism. Specifically the study attempts (1) to examine the linkages of financial benefits and preservation of natural capital.

Study Area and Research Methodology

Gorumara National Park (GNP) situated in the in northern part of West Bengal in India. GNP has been selected for the present study. In 2009, the park received the best prize by the Ministry of Environment and Forests for successfully implementing ecotourism. GNP is located in the Dooars region of the Himalayan foothills. Identified for Indian rhinoceros, the park is a major tourist spot. Prior to independence of India, the place was declared as National Park in the year 1949 with the objective of protecting the endangered rhinoceros. From Jalpaiguri town in North Bengal, this place is around fifty kilometers away. From Lataguri, the park is around fifteen kilometers and ten kilometers from Chalsa. With an area of 79.45 sq. km. national park, the place provides relaxation and peace to the travelers and tourists. Figure 1 provides the map of the Gorumara National Park.

As per the report of the park, GNP has both flora and fauna. It is famous for including Indian rhinoceros, gaur, Asian elephant, sloth bear, chital, and sambar deer. Several species of mammals, reptiles, fishes, birds can also be found in the park. Small herbivores such as barking, hog deer and wild boar also attract the attention of the tourists. Sometimes tourists also spot leopard, Tigers. Number of small carnivores animals like various civets, mongooses and small cats are also found inside the park. Critically endangered pygmy hog has also been reported from the park. Moreover, numerous rodents, including giant squirrels, the rare hispid hare has also been reported from the park. Different types of birds including the migratory ones inhabit the park. Large numbers of snakes, both venomous and non-venomous also inhabit the park.

Research Methodology

The study is exploratory in nature. The study has relied on secondary source information for examining the economic and environmental impact of eco-tourism. The study has tried to gain insights from several research articles, documents from ministry of tourism are used for the study. Cross verification of the studies are also done to avoid misrepresentation of the facts.

DISCUSSION

Tourism in West Bengal

The state West Bengals promotes tourism as the sweetest part of India. One of the culturally and literally advanced states in India, West Bengal is a land of divergences. The land has contrasting differences and diversity of landscape, climate, ethnicity, culture, languages and religion. Tourism is exclusive in West Bengal for its grandeur. The gorgeous Himalayas, vast Gangetic planes, tranquil seashores to far stretching mangrove forests, West Bengal is a land of beauty. The state has always been a traveler's happiness. The state has reached 5th position in 2015 with a

total 1.49 million visitors from 6thposition in 2014 (Retrieved from https://www.wbtourismgov.in/files/contents/west-bengal-tourism-highlight.pdf on 12th April, 2019). Ecotourism has been promoted in the state and this offers an occasion to display the state's exclusive natural resources to the tourists. Being rich in in flora and fauna, the state has a great advantage in terms of ecotourism. Protected forests shield 4% of the state area. At present 15 Wildlife Sanctuaries, 5 National Parks and 2 Tiger Reserves are there in the state.

The Case of Gorumara National Park

GNP with the diverse flora and fauna has stimulated ecotourism activity in this area. Since 1895, GNP has been a reserve forest.In 1949, Gorumara was declared as a Sanctuary for the Indian rhinoceros- a critically endangered animal. In 1994, it was given official status of anIndian National Park. Originally the park was as small as 7 km^2. Since then Gorumara has grown by incorporating neighboring lands to about 80 km^2. With the introduction of ecotourism, the park has tried to attract more tourists and thereby provide engagement avenues to the locals staying in the vicinity of the area. In an attempt to maintain a practical breeding community of Indian rhinoceroses, ecotourism was promoted. Attempt was made to interlink livelihood activities and conservation. Being labor intensive industry, ecotourism has created several job opportunities for the indigenous local people. Locals get an opportunity to operate their shops, restaurant, hotels, home stay tourism, cottage etc. and there by earn livelihood from tourism based activities. Some villagers with better education work as tourists guides. The Park authority has also provided employment opportunity to Santals and Oraon people as tourist guides. This represents that ecotourism has tried to make an inclusive development approach.

The guides of safari vehicles are given training. With their sound knowledge about National Park and nature, skill up gradation is an added benefit. Many local tribal man and woman are engaged with flock dance and perform in front of tourist after forest safari and thus opening up avenues of diversified livelihood. Jobs are also created for handicraft industries. All such employment opportunities are helpful to increase the income of the locals and indigenous communities giving them a reason to be associated with conservation process. Some photographs of the park are provided in Photograph 1.

Some photographs of the native folk dancers are given in Photograph 2. Ethnic tribal dance programs are organized in all the ecotourism camps. Such type of involvement helps the indigenous communities in two ways (1) they get associated with ecotourism and thus consider themselves as stake holders and (2) Economic incentive motivate them to preserve these resources rather than exploiting them. Moreover, they are also given the scope to work in souvenir industry. In this manner, ecotourism attempts to provide engagement opportunities and thereby empowering indigenous communities.

Ecotourism has created both direct and indirect opportunities for the locals. Direct employment in tourism paves the path for growth of related industries such as agriculture, handicraft. Inter industry linkages are giving more respite to the locals as one industry cannot absorb all people. (Cooper, 2006:36). In an area where there is no other means of employment except agriculture, ecotourism extends its support to the locals (Ryan 2006:150). Of the total employment, Hall & Boyd et al. (2006:173) report that 62.37% has been engaged in accommodation sector, giving highest employment opportunities. Transport sector employs 14.55% next to accommodation sector. 11.64 % are engaged in folk dancing and 4.16% are engaged in souvenir shops.

Thus as per the secondary source information, the present study finds that ecotourism in Gorumara National Park has the ability to empower local people through earning income and engagement. With an agrarian background when most of the people of the region were engaged in primary sector, ecotourism with its rich natural endowments have done commendable job for the good of the regional economy and society of this economically backward area of India. By this way ecotourism is very helpful to flourish local economy as a whole and therefore it calls for policy makers to formulate policies that can help more villagers to participate in ecotourism in Gorumara National Park.

However, the rapid growth of tourism is also having some negative impact on the environment. For example Karmakar (2011) the increasing construction of resorts, lack of coordination between the forest department and

tourism department, difficulty in bookings for the tourists are the major hurdles in achieving the objectives of ecotourism. Thus if proper policies are devised, ecotourism in GNP will not only be economically effective, but also environmentally sustainable.

CONCLUSION AND RECOMMENDATIONS

With increasing criticisms about ecotourism, the present study has made an attempt to examine positives and negatives of ecotourism policy in Gorumara National Park of West Bengal. With the use of secondary data, the study makes an attempt for an elaborate investigation about the impact of ecotourism on the overall development of indigenous communities and conservation in all four sites. The study finds that ecotourism in Gorumara has been able to generate employment opportunities for the locals. However, ecotourism is limited by limited income opportunities, lack of coordination between the forest officials and the ministry of tourism, lack of coordination between people and policy, existence of a high number of non-ecotourists etc. Thus the study calls for some rigorous policies to make ecotourism an all inclusive approach

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Table 1: Protected Areas in India

Protected Area Coverage	Number	Total Area (sq. km)	Geographical area (in %)
National Parks	104	40501.1	1.23
Wildlife Sanctuaries	550	119776	3.64
Conservation Reserves	87	4286.31	0.13
Community Reserves	127	525.22	0.02
Total Protected Areas	868	165088	5.02

Source: Ministry of Environment, Forest and Climate Change, Govt. of India

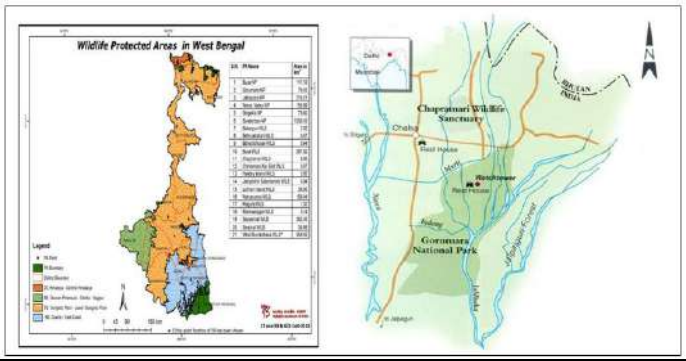

Figure1: Map of Gorumara National Park

Photograph1: Tourism in Gorumara National Park

Photograph 2: Santhal Dance in Gorumara National Park

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RESEARCH ARTICLE

Smart Disease Predictor System using Machine Learning

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ABSTRACT

This Machine Learning project is used to predict or detect the disease based on the symptoms given by the user. For small problems, the users have to go personally to the hospital for check-up which is more time consuming. Also handling the telephonic calls for appointments is quite hectic. Such problems can be solved by using disease prediction application. Over the years, the use of the specific disease prediction tools has been increased due to a variety of diseases and less doctor-patient ratio. Thus, in this system, we are concentrating on providing immediate and accurate disease prediction to the users about the symptoms they enter along with the severity of disease predicted. Best suitable algorithm and doctor consultation will be given in this project. For prediction of diseases, different machine learning algorithms are used to ensure quick and accurate predictions. Disease Prediction is done by implementing four different machine learning algorithms such as Naive Bayes Classifier, Random Forest Classifier, Decision Tree Classifier and K-nearest neighbour Classifier. This Classifiers calculates the probability of the disease. Therefore, average prediction accuracy probability 90% is obtained. "Disease Prediction" system based on predictive modeling predicts the disease of the user on the basis of the symptoms that user provides as an input to the system. The system analyzes the symptoms provided by the user as input and gives the probability of the disease as an output. With big data growth in biomedical and healthcare communities, accurate analysis of medical data benefits early disease detection and patient care.

Keywords : Machine Learning; Naive Bayes Classifier; Random Forest Classifier; healthcare; symptoms; Prediction; Decision Tree Classifier.

INTRODUCTION

Machine learning is one of the most usable techniques which is used in many department of science and technology. This generation is a developing civilization. By using ML we can predict the future which is based on the different algorithm[1] .ML has two phases, one is train data and second one is test data in our project we predict the disease by using ML[2]. Here we use symptoms as our weapon to get predict disease and another one is prognosis, through prognosis we study the accurate part which is the disease columns in our dataset[3]. Basically we collect the data from the health organization .There are too many drawback of ML but if we give perfect suggestion by different type of algorithm then we get more accurate result[4] .By using ML doctors can do more work for patients because Machine learning technology are more efficient, faster & accurate too. Through ML we can improve our healthcare society as well as our people[5].To improve the accuracy from a large data, the existing work will be done on unstructured and textual data. For prediction of diseases the existing will be done on random forest, KNN, Decision Tree algorithm. The order of reference in the running text should match with the list of references at the end of the paper[3].The timely analysis of data and gaining accurate prediction of diseases from symptoms can save many lives[6]. Early detection of diseases helps doctor to give accurate medication. In the field of medicine different algorithms of machine learning are used for predicting different diseases and help the physicians to diagnose fast[7]. Based on the input of data the accuracy of results may vary. There are 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 4 (Quality education), 9 (Industry, Innovation and Infrastructure), and 11 (Sustainable cities and Communities).

Problem Formulation

Now a day's in Health Industry there are various problems related to machines or devices which will give wrong or unaccepted results, so to avoid those results and get the correct and desired results we are building a program or project which will give the accurate predictions based on information provided by the user and also based on the datasets that are available in that machine. The health industry in information yet and knowledge poor and this industry is very vast industry which has lot of work to be done. So, with the help of all those algorithms, techniques and methodologies we have done this project which will help the peoples who are in the need. So the problem here is that many people goes to hospitals or clinic to know how is their health and how much they are improving in the given days, but they have to travel to get to know there answers and sometimes the patients may or may not get the results based on various factors such as doctor might be on leave or some whether problem so he might not have come to the hospital and many more reasons will be there so to avoid all those reasons and confusion we are making a project which will help all those person's and all the patients who are in need to know the condition of their health, and at sometimes if the person has been observing few symptoms and he/she is not sure about the disease he/she is encountered with so this will lead to various diseases in future. So, to avoid that and get to know the disease in early stages of the symptoms this disease prediction will help a lot to the various people's ranging from children to teenagers to adults and also the senior citizens.

The objective of the paper is to predict the accurate disease of the patient using all their general information's and also the symptoms. Using this information, there we will compare with our previous datasets of the patients and predicts the disease of the patient he/she is been through. If this Prediction is done at the early stages of the disease with the help of this project and all other necessary measure the disease can be cured and in general this prediction system can also be very useful in health industry. If health industry adopts this project then the work of the doctors can be reduced and they can easily predict the disease of the patient. The general purpose of this Disease prediction is to provide prediction for the various and generally occurring diseases that when unchecked and sometimes

ignored can turns into fatal disease and cause lot of problem to the patient and as well as their family members. This system will predict the most possible disease based on the symptoms. The health industry in information yet and knowledge poor and this industry is very vast industry which has lot of work to be done. So, with the help of all those algorithms, techniques and methodologies we have done this project which will help the peoples who are in the need.

The features of Disease Prediction Using Machine Learning are as follows.

- In this paper we predicted the diseases of the patients based on the symptoms and other general information using the datasets.
- This is done based on the previous datasets of the hospitals so after comparing it can provide up to 80% of accurate results, and the project is still developing further to get the 100% accurate results.
- With the help of disease prediction, it can predict the disease of the patient and can solve various problems and prevents from various aspects.
- It provides security for the system so that no one can break into that and no one can make any changes in the system.

Literature Survey

Tom Mitchell states machine learning as "A computer program is said to learn from experience and from some tasks and some performance on, as measured by, improves with experience". Machine Learning is combination of correlations and relationships, most machine learning algorithms in existence are concerned with finding and/or exploiting relationship between datasets. Once Machine Learning Algorithms can pinpoint on certain correlations, the model can either use these relationships to predict future observations or generalize the data to reveal interesting patterns. In Machine Learning there are various types of algorithms such as Regression, Linear Regression, Logistic Regression, Naive Bayes Classifier, Bayes theorem, KNN (K-Nearest Neighbor Classifier), Decision Tress, Entropy, ID3, SVM (Support Vector Machines), K-means Algorithm, Random Forest and etc., The name machine learning was coined in 1959 by Arthur Samuel. Machine learning explores the study and construction of algorithms that can learn from and make predictions on data Machine learning is closely related to (and often overlaps with) computational statistics, which also focuses on prediction-making through the use of computers. It has strong ties to mathematical optimization, which delivers methods, theory and application domains to the field. Machine learning is sometimes conflated with data mining, where the latter subfield focuses more on exploratory data analysis and is known as unsupervised learning. Within the field of data analytics, machine learning is a method used to devise complex models and algorithms that lend themselves to prediction; in commercial use, this is known as predictive analytics. These analytical models allow researchers, data scientists, engineers, and analysts to "produce reliable, repeatable decisions and results" and uncover "hidden insights" through learning from historical relationships and trends in the data Machine learning tasks Machine learning tasks are typically classified into several broad categories:

Supervised learning: The computer is presented with example inputs and their desired outputs, given by a "teacher", and the goal is to learn a general rule that maps inputs to outputs. As special cases, the input signal can be only partially available, or restricted to special feedback.

Semi-supervised learning: The computer is given only an incomplete training signal: a training set with some (often many) of the target outputs missing.

Active learning: The computer can only obtain training labels for a limited set of instances (based on a budget), and also has to optimize its choice of objects to acquire labels for used interactively, these can be presented to the user for labeling.

Unsupervised learning: No labels are given to the learning algorithm, leaving it on its own to find structure in its input. Unsupervised learning can be a goal in itself (discovering hidden patterns in data) or a means towards an end (feature learning).

Reinforcement learning: Data (in form of rewards and punishments) are given only as feedback to the program's actions in a dynamic environment, such as driving a vehicle or playing a game against an opponent.

Features of Machine Learning

- It is nothing but automating the Automation.
- Getting computers to program themselves.
- Writing Software is bottleneck.
- Machine leaning models involves machines learning from data without the help of humans or any kind of human intervention.
- Machine Learning is the science of making of making the computers learn and act like humans by feeding data and information without being explicitly programmed.
- Machine Learning is totally different from traditionally programming, here data and output is given to the computer and in return it gives us the program which provides solution to the various problems. Below is the figure.
- Machine Learning is a combination of Algorithms, Datasets, and Programs.
- There are Many Algorithms in Machine Learning through which we will provide us the exact solution in predicting the disease of the patients.

How Does Machine Learning Works?

- Solution to the above question is Machine learning works by taking in data, finding relationships within that data and then giving the output.
- There are various applications in which machine learning is implemented such as Web search, computing biology, finance, e-commerce, space exploration, robotics, social networks, debugging and much more.
- There are 3 types of machine learning supervised, unsupervised, and reinforcement

Existing System

Prediction using traditional methods and models involves various risk factors and it consists of various measures of algorithms such as datasets, programs and much more to add on. High-risk and Low-risk patient classification is done on the basis of the tests that are done in group. But these models are only valuable in clinical situations and not in big industry sector. So, to include the disease predictions in various health related industries, we have used the concepts of machine learning and supervised learning methods to build the predictions system. After doing the research and comparison of all the algorithms and theorems of machine learning we have come to conclusion that all those algorithms such as Decision Tree, KNN, Naïve Bayes, Regression and Random Forest Algorithm all are important in building a disease prediction system which predicts the disease of the patients from which he/she is suffering from and to do this we have used some performance measures like ROC, KAPPA Statistics, RMSE, MEA and various other tools. After using various techniques such as neural networks to make predictions of the diseases and after doing that we come to conclusion that it can predicts up to 90% accuracy rate after doing the experimentation and verifying the results. The information of patient statistics, results, disease history in recorded in EHR, which enables to identify the potential data centric solution, which reduces the cost of medical case studies. Existing system can predict the disease but not the sub type of the disease and it fails to predict the condition of the people, the predictions of disease have been indefinite and non-specific.

Software Description

Python

Python is a multi-paradigm programming language. Object-oriented programming and structured programming are fully supported, and many of its features support functional programming and aspect-oriented programming (including by meta programming and meta objects. Many other paradigms are supported via extensions, including design by contract and logic programming. Python uses dynamic typing and a combination of reference counting and a cycle-detecting garbage collector for memory management. It also features dynamic name resolution (late binding), which binds method and variable names during program execution.

Python's developers strive to avoid premature optimization, and reject patches to non-critical parts of CPython that would offer marginal increases in speed at the cost of clarity. When speed is important, a Python programmer can move time-critical functions to extension modules written in languages such as C, or use PyPy, a just-in-time compiler. Cython is also available, which translates a Python script into C and makes direct C-level API calls into the Python interpreter. An important goal of Python's developers is keeping it fun to use. Python's design offers some support for functional programming in the Lisp tradition. It has filter, map, and

reduce functions, list comprehensions, dictionaries, sets, and generator expressions. The standard library has two modules (itertools and functools) that implement functional tools borrowed from Haskell and Standard ML.

BENEFITS OF PYTHON

- Presence of Third-Party Modules
- Extensive Support Libraries
- Open Source and Community Development
- Learning Ease and Support Available
- User-friendly Data Structures
- Productivity and Speed
- Highly Extensible and Easily Readable Language.

Tkinter Interface

Tkinter is a Python binding to the Tk GUI toolkit. It is the standard Python interface to the Tk GUI toolkit and is Python's de facto standard GUI. Tkinter is included with standard Linux, Microsoft Windows and Mac OS X installs of Python. The name Tkinter comes from Tk interface. Tkinter was written by Fredrik Lundh. Tkinter is free software released under a Python license. As with most other modern Tk bindings, Tkinter is implemented as a Python wrapper around a complete Tool Command Language (TCL) interpreter embedded in the Python interpreter. Tkinter calls are translated into Tcl commands which are fed to this embedded interpreter, thus making it possible to mix Python and TCL in a single application. In Tkinter, the Frame widget is the basic unit of organization for complex layouts. A frame is a rectangular area that can contain other widgets. When any widget is created, a parent-child relationship is created. For example, if you place a text label inside a frame, the frame is the parent of the label. Python offers multiple options for developing GUI (Graphical User Interface). Out of all the GUI methods, tkinter is most commonly used method. It is a standard Python interface to the Tk GUI toolkit shipped with Python. Python with tkinter outputs the fastest and easiest way to create the GUI applications.

To create a tkinter:

Importing the module – tkinter

Create the main window (container)

Add any number of widgets to the main window

Apply the event Trigger on the widgets

Importing tkinter is same as importing any other module in the python code. Note that the name of the module in Python 2.x is 'Tkinter' and in Python 3.x is 'tkinter'.

Hardware Requirements

- System: Pentium 4, Intel Core i3, i5, i7 and 2 GHz Minimum
- RAM: 512Mb or above
- Hard Disk: 10 GB or above
- Input Device: Keyboard and Mouse
- Output Device: Monitor or PC

Software Requirements

- Operating System: Windows 7, 10 or Higher Versions

- Platform: Jupiter Notebook
- Front End: Python Tkinter
- Back End: Python and Files
- Programming Lang: Python

Proposed Methodology

The proposed system of disease prediction using machine learning is that we have used many techniques and algorithms and all other various tools to build a system which predicts the disease of the patient using the symptoms and by taking those symptoms we are comparing with the system's dataset that is previously available. By taking those datasets and comparing with the patient's disease we will predict the accurate percentage disease of the patient. The dataset and symptoms go to the prediction model of the system where the data is pre-processed for the future references and then the feature selection is done by the user where he will enter the various symptoms. Then the classification of those data is done with the help of various algorithms and techniques such as Decision Tree, KNN, Naïve Bayes, Random Forest and etc. Then the data goes in the recommendation model, there it shows the risk analysis that is involved in the system and it also provides the probability estimation of the system such that it shows the various probability like how the system behaves when there are n number of predictions are done and it also does the recommendations for the patients from their final result and also from their symptoms like it can show what to use and what not to use from the given datasets and the final results. Here we have combined the overall structure and unstructured form of data for the overall risk analysis that is required for doing the prediction of the disease. Using the structured analysis, we can identify the chronic types of disease in a particular region and particular community. In unstructured analysis we select the features automatically with the help of algorithms and techniques. This system takes symptoms from the user and predicts the disease accordingly based on the symptoms that it takes and also from the previous datasets, it also helps in continuous evaluation of viral diseases, heart rate, blood pressure, sugar level and much more which is in the system and along with other external symptoms its predicts the appropriate and accurate disease. We are predicting a disease which a person is suffering from depending upon the symptoms he or she is suffering. Here we take five symptoms from the patient and evaluate them by using algorithms such as Random Forest, Decision Tree, Naïve Bayes.

Steps of model building

Collection of raw data

In this we describe dataset which is being use to train the machine learning model. The dataset will contain symptoms of various diseases. The dataset used in this project is real-life Hospital data. The structural data contains symptoms of patients while unstructured data consist of textual format. The dataset used is contains real-life hospital data, and data stored in data center. The data provided by the hospital contains symptoms of the patients.Be it the raw data from excel, access, text files etc., this step (gathering past data) forms the foundation of the future learning. The better the variety, density and volume of relevant data, better the learning prospects for the machine becomes.

Preparing the data

Any analytical process thrives on the quality of the data used. One needs to spend time determining the quality of data and then taking steps for fixing issues such as missing data and treatment of outliers. Exploratory analysis is perhaps one method to study the nuances of the data.

Training of the model

This step involves choosing the appropriate algorithm and representation of data in the form of the model. The cleaned data is split into two parts – train and test (proportion depending on the prerequisites); the first part (training data) is used for developing the model. The second part (test data), is used as a reference.

Evaluation of the model

To test the accuracy, the second part of the data (holdout / test data) is used. This step determines the precision in the choice of the algorithm based on the outcome. A better test to check accuracy of model is to see its performance on data which was not used at all during model build.

Improving the performance

This step might involve choosing a different model altogether or introducing more variables to augment the efficiency. That's why significant amount of time needs to be spent in data collection and preparation.

Implementation of Algorithms

Decision Tree

It is a sort of supervised learning algorithmic program that's largely used for classification issues. Surprisingly, it works for each categorical and continuous dependent variable. In this algorithmic program, we tend to split the population into 2 or a lot of homogenized sets. This is done supported most vital attributes/ freelance variables to form as distinct teams as attainable. A tree has several analogies in real world, and seems that it's influenced a large space of machine learning, covering each classification and regression. In call analysis, a choice tree is wont to visually and expressly represent selections and higher cognitive process. As the name goes, it uses a tree-like model of decisions. Though a commonly used tool in data mining for deriving a strategy to reach a particular goal, it's also widely used in machine learning. Once we completed modelling the Decision Tree classifier, we will use the trained model to predict whether the balance scale tip to the right or tip to the left or be balanced.

Random Forest

Random Forest is a great algorithm to train early in the model development process, to see how it performs and it's hard to build a "bad" Random Forest, because of its simplicity. This rule is additionally an excellent alternative, if you would like to develop a model during a short amount of your time. On prime of that, it provides a fairly sensible indicator of the importance it assigns to your options. Random Forests are terribly onerous to ram down terms of performance. And on prime of that, they'll handle tons of various feature varieties, like binary, categorical and numerical. Overall, Random Forest may be a (mostly) quick, easy and versatile tool, though it's its limitations. Random forests are an ensemble learning method for classification, regression and other tasks that operate by constructing a multitude of decision trees at training time and outputting the class that is the mode of the categories000000000000 (classification) or mean prediction (regression) of the individual trees.Random call forests correct for call trees' habit of over fitting to their training set

Naive Bayes Algorithm

Naive Bayes algorithm is the algorithm that learns the probability of an object with certain features belonging to a particular group/class. For instance, if you are trying to identify a fruit based on its color, shape and taste, then an orange colored, spherical, and tangy fruit would most likely be an orange. All these properties individually contribute to the probability that this fruit is an orange and that is why it is known as "naive". As for the "Bayes" part ,it refers to statistician and philosopher, Thomas Bayes and the theorem named after him , Bayes' theorem , which is the base for Naïve Bayes Algorithm. More formally, Bayes 'Theorem is stated as the following equation: $P(A/B) = (P(B/A)*P(A)) / P(B)$

KNN

K Nearest Neighbor (KNN) could be a terribly easy, simple to grasp, versatile and one amongst the uppermost machine learning algorithms. In Healthcare System, user will predict the disease. In this system, user can predict whether disease will detect or not. In propose system, classifying disease in various classes that shows which disease will happen on the basis of symptoms. KNN rule used for each classification and regression issues. KNN algorithm based on feature similarity approach. A case is classed by a majority vote of its neighbors, with the case being assigned to the class most common amongst its K nearest neighbors measured by a distance function. If K = 1, then the case is just assigned to the category of its nearest neighbor

$$Euclideandistance = \sqrt{\sum_{i=1}^{k}(x_i - y_i)^2}$$

.

It ought to even be noted that every one 3 distance measures square measure solely valid form continuous variables. In the instance of categorical variables, the Hamming distance must beused.It conjointly brings up the difficulty of standardization of the numerical variables between zero and one once there's a combination of numerical and categorical variables within the dataset.

$$HammingDistance = \sum_{i=1}^{k}|x_i - y_i|$$

GUI

- GUI made for this project is a simple tkinter GUI consisting of labels, message box, button, text, title and option menu.
- Root title() is used to set the title as "Smart Disease Predictor System".
- Graphical User Interface is build using tkinter library in Python.
- Rootis used to start the GUI. It is configured with the background that is set to "Black".
- GUI title is given as "Smart Disease Predictor System" using title() function in tkinter
- library. Resizable function is used to fix the size GUI
- The definition of the function "Reset()" which is used to reset the GUI inputs which are given by the user. It is called when user click on the button "Reset Inputs" from the GUI
- The definition of the function "Exit()" which is used to come out from the GUI. It is called when user click on the button "Exit System" from the GUI.

CONCLUSION

The ultimate goal is to facilitate coordinated and well-informed health care systems capable of ensuring maximum patient satisfaction. In developing nations, predictive analytics are the next big idea in medicine –the next evolution in statistics – and roles will change as a result. Patients can get to become higher knowing and can get to assume a lot of responsibility for his or her own care, if they are to make use of the information derived. Physician roles can probably modification to a lot of an advisor than head, who will advise, warn and help individual patients. Physicians might notice a lot of joy in apply as positive outcomes increase and negative outcomes decrease. Perhaps time with individual patients can increase and physicians will another time have the time to create positive and lasting relationships with their patients. Time to assume, to interact, and to really help people; relationship formation is one of the reasons physicians say they went into medicine, and when these diminish, so does their satisfaction with their profession. Hospitals, pharmaceutical corporations and insurance suppliers can see changes furthermore. These changes which will virtually revolutionize the manner drugs are practiced for higher health and unwellness reduction.

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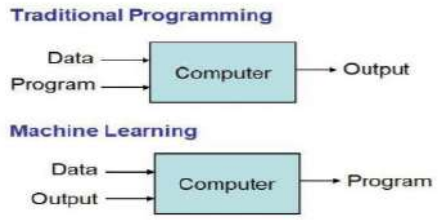

Fig.1.Traditional programming vs machine learning

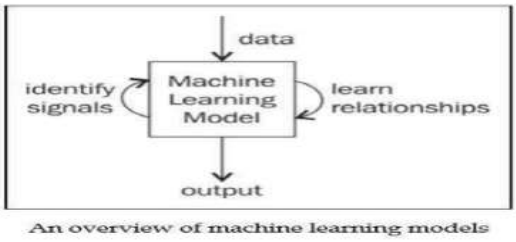

Fig.2.Machine learning model

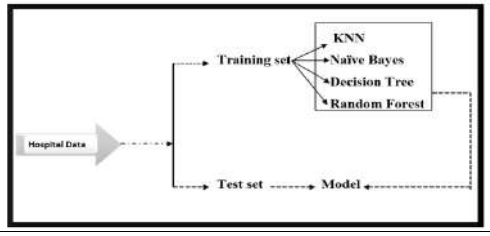

Fig.3. System Architecture

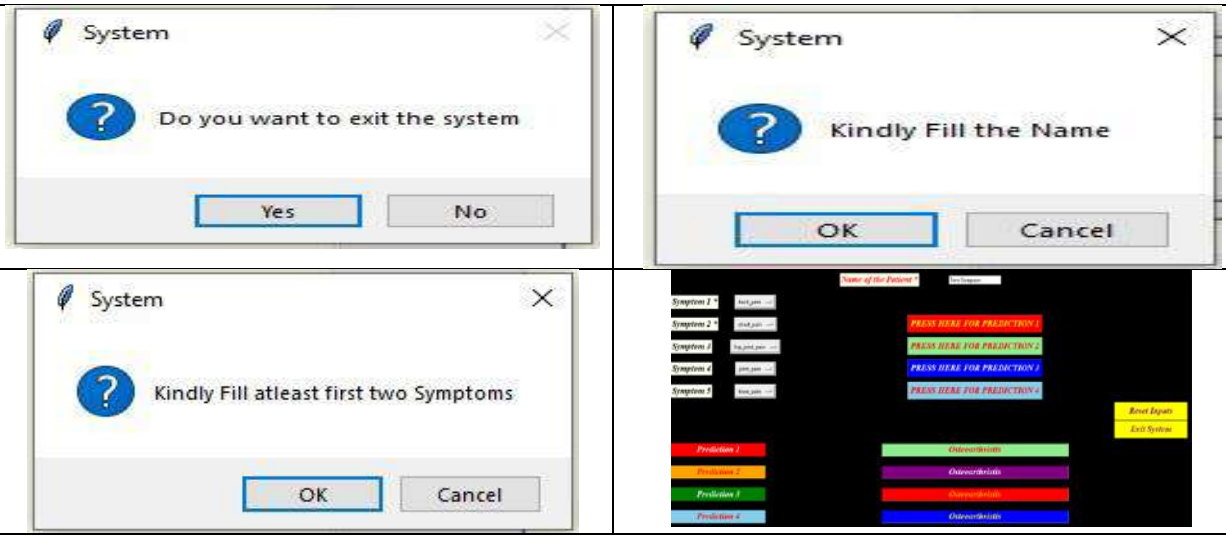
System
Do you want to exit the system
Yes
No
System
Kindly Fill the Name
OK
Cancel
System
Kindly Fill atleast first two Symptoms
OK
Cancel

Fig. 4. GUI

RESEARCH ARTICLE

The Remodelling of Microfilament Actin as a Potential Target for Cancer Drug Development

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ABSTRACT

Along with DNA, microtubules are one of the most reasonable and strategic drug targets for chemotherapy currently available. Tubulin inhibitors as cancer therapeutics have gotten a lot of attention in the last decade, thanks to a clearer appreciation of microtubules and their biological significance in cell activities. Several studies had been conducted, with others ongoing, with the goal of developing novel chemotherapeutics and maintaining the advantages of tubulin inhibition. Actin filaments were discovered to be destroyed in malignant transformed cells around the same time that actin was found in non-muscle cells. In all eukaryotic cells, the actin network is a complex structural and functional system. So according to growing evidence from this and other laboratories, changes in actin polymerization, or actin remodeling, play a key role in regulating malignant cell morphological and phenotypic events. At the moment, there are a number of antitubulin agents in clinical trials. Novel tubulin inhibitors as anticancer therapy are the focus of this review.

Keywords: Microtubules, drug, tubulin, chemotherapeutics, anticancer.

INTRODUCTION

The cytoskeleton is a framework that keeps the cell's shape and inner workings in order while also providing mechanical support. Microfilaments, Microtubules, and intermediate filaments are the three types of fibers that make

up a cytoskeleton structure. Tubulins are considered as important components of microtubules and are globular molecular proteins with α/β chains. Tubulinα and β bind together to form heterodimers, which gradually multimerize to establish a long microtubule filament. Microtubules play an important role in a variety of mobile processes, including chromosome segregation within cells, intracellular transport, cellular motility, and cellular form maintenance [1,2,3]. Actin was first discovered in non-muscle cells about 3 years ago, and actin filaments were discovered to be disrupted or stopped in malignant altered cells around the same time. All eukaryotic cells have an actin network, which is a complex but having essential structural and functional system. Actin filaments are the inspiration for cellular shape and their functions include adhesion, motility, exocytosis, endocytosis and cellular divison. Actin remodelling occurs when oncogenic actin signalling pathways (Ras and Src) are activated or when a number of key actin-binding proteins with tumour suppressor functions are inactivated (e.g., gelsolin). In most cancers and revolutionary carcinogenic processes, some of those genes were discovered to have wonderful protein expression styles. The laulimalide, taxane, vinca alkaloid and colchicine are all used by microtubule targeting agents (MTAs) to interact with tubulin [4]. At the end, tubulin polymerization inhibitors decrease the group of microtubules while polymerization promoters rise the duration of microtubule [5,6].

The cytoskeleton (cell skeletal proteins) provides a simple infrastructure for maintaining cellular form and function. Great efforts have been studied to broaden the scope of so-called "Intelligent Drugs" that focus on the Ras GTPase super family, many of which can be linked to actin dynamics without delay or indirectly. The activities of such GTPases are commonly extended in most cancers cells but not in noncancerous cells. The current study emphasizes the importance of critical proteins in maintaining human cell physiology and thus aligns with the objectives of one of the United Nations formulated Sustainable Development Goals (SDGs); SDG3 which ensures healthy lives and promotes well-being for all at all stages.

Microtubule Destabilizing Agents

Small molecules like Vascular disrupting agents having weakness for the colchicine binding site dominate the microtubule inhibitor category. A number of agents that have already demonstrated clinical potency trials are studied in greater depth.

CA-4P

CA4P is a precursor of CA4 (zyberstat, fosbretabulin). It is dephosphorylate to its active metabolite CA-4 in vivo [7]. CA4P interferes with the mitotic mechanisms of cells. CA-4P interrupts with cytoskeleton and mitotic machinery in cells. Proliferating endothelial cells' morphology and cohesion are also interrupted. In clinical trial-I, CA4P injected intra-cutaneously resulted in a significant reduction in tumour blood flow.

OXI-4503 [CA-1P]

Another phosphorylated prodrug of combretastatin is OXi4503, a second-generation tubulin-binding VDA [8,9]. Compared with CA4P, the tumor model with OXi4053 has a smaller viable edge. Oxi-4053 had a longer-lasting effect on tumour necrosis than CA-4P, indicating that OXi-4053 has therapeutic advantages over CA-4P.

BNC105P

BNC105 is an antiproliferative and tumour vascular disrupting tubulin polymerization inhibitor [10,11]. In preclinical studies, BNC105 showed important binding affinity [80 times higher potential] for activating human umbilical vein endothelial cells over inactive HUVECS. Activated human abdominal aortic endothelial cells showed selectivity (120 fold higher potency) over inactivity cells. In most of the assays, BNC105 outperformed CA-4 by 10 fold greater potential. BNC105 was found to be effective against MDR Cell lines, indicates that it is not a substratum for the efflux pump MDR -1 transporter.

SCB01A

SCB01A is an aroyl indole subordinate that inhibits microtubule polymerization by stable association with tubulin's colchicine binding site with a rise in cyclin B1 polymerization by binding to tubulins colchicine binding site [12]. SCB01A inhibited cancer cell growth in the G2-M phase in human cervical carcinoma cells.

NPI-2358

Itinhibits tubulin and Vascular disrupting agents made from nature diketopiperazine phenylahistin. Like colchicine,it depolymerizes microtubules and destabilises the architecture of tumour vascular endothelial cells, causing selective collapse [13,14]**.** NPI2358 inhibits tumour growth in a diversity of human oncogenic cell line. It also includes HT29, DU145, PC3, MDAMB231, NCIH292, with IC50 values in the nanoscale.

Other Tubulin Colchicine Binding Site Inhibitors

ALB-109564

ALB-109564 is a vinblastine analogue with a similar structure. It causes metaphase arrest by interfering with microtubule polymerization [15,16].

TZT-1027

Tubulin polymerization inhibitor TZT-1027 has dual binding sites on tubulin, one highest-affinity and the other less affinity. When binds to tubulin, TZT-1027 can interact with vinblastine [17]. It exhibits significant cytotoxicity against in opposition to panel of humour tumour cell lines, causes cell cycle arrest at the G2/M phase, persuade apoptosis, and outperforms vincristine and CA-4 in terms of anti-vascular effects [18,19].

LY355703

It is a microtubule destabilizer that is structurally similar to the cryptophycin family of natural occurring cryptophycins separated from blue-green algae. It was found tobe effective on tumour with the MDR phenotype [20,21].

Microtubule Stabilizing Agents

With the discovery of paclitaxel in 1971, taxanes as microtubule stabilisers were thrust into the spotlight. Paclitaxel and docetaxel are approved to treat a variety of cancers, but they lack tumour specificity and are resistant to multiple drugs. The following are some of the choosen agents with proven clinical potency.

TPI-287

TPI - 287 latest taxane-family microtubule stabilising agents that causes cancer cell death by causing mitotic arrest.. TPI-287 is able to pass through the blood-brain barrier with ease.TPI-287 is made by modifying the side chains of naturally occurring taxanes to increase their lipophilicity, as well as bind to abnormal or mutant tubulin [22,23].

Cabazitaxel [XRP6258]

Cabazitaxel, a taxane of 2nd generation with a less affinity for P glycoprotein was recently approved by the FDA for metastatic castration resistant prostate cancer (mCRPC) resistant to docetaxel. It's a semi-synthetic 10-deacetylbaccatin III derivative. Cabazitaxel, unlike docetaxel, can pass the brain blood barrier due to presence of additional methoxy groups.

Larotaxel [XRP9881]

Larotaxel, like docetaxel and paclitaxel, is a synthetic artificial taxane that works in the same way. It can penetrate the blood-brain barrier and is active in taxane-resistant tumour cells [24].

Milataxel

Milataxel is a new docetaxel taxane analogue. It has the ability to overcome paclitaxel and docetaxel resistance caused by P-glycoprotein. It had a significant inhibitory effect on colon cancer.

Multiple Targeting Tubulin Inhibitors

KX2-391, AEZS-112 and MKC-1 are potential therapeutic effective on multiple targeting tubulin inhibitors. KX2-391,a dual inhibitor that inhibits both Srckinases and tubulin . KX2-391 showed high level of cytotoxicity against number of tumour cell lines [25,26]. AEZS-112 is a multi-targeted cytotoxic compound that inhibits tubulin polymerization, angiogenesis and topoisomerase II when taken orally. At low micromolar concentrations, it prevents tubulin polymerization. MKC-1, a tubulin and mTOR pathway inhibitor that is available as an orally administered small molecule, has shown potential in clinical trials tumour model's and is also useful against MDR cell lines.

CONCLUSION

Tubulin inhibitors are bright class of anticancer drugs that could help treat a wide range of cancers. Multiple targeting agents against proteins, enzymes and for receptors other than tubulin have recently passed through clinical observations, with some of the drugs demonstrating significant clinical potentials and thus progressing to the next stage of clinical research. Taxanes have been used to treat a variety of cancers with great success. Taxane anticancer drugs' therapeutic applications are expanding; primarily through amalgamation therapy and current taxanes design through side chain analysis are recently being investigated.

Statements and Declarations

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval and Consent to Participate

It is a review article. No ethics approval is required.

Consent to Publish

Not applicable.

Human and Animal Rights

It is a review article. No animals were used in the study.

Availability of Data and Materials

Not applicable.

Credit Authorship Contribution Statement

All the authors have substantial contribution for the preparation of the manuscript. Gagan Kumar Panigrahi and Akash Pradip Dash conceived the idea. Data curation and writing: Akash Pradip Dash, Annapurna Sahoo, Pradip Kumar Prusty, Shraban Kumar Sahoo, and Gagan Kumar Panigrahi. All the authors have read and approved the final manuscript before submission.

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RESEARCH ARTICLE

Screening through Computer Aided Approach to Evaluate Phytochemicals From *Elettaria cardamomum* Targeting COVID-19 Virus

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ABSTRACT

The new corona virus illness 2019 (COVID-19) was widely viewed as posing a huge threat to humanity owing to an unanticipated, impending pandemic. The infectivity, mortality, and latency of this novel virus are all high. Microbial infections, pneumonia, gastrointestinal infection, septic shock, and acute multiple organ failure could all be induced by SARS-immunological CoV-2 virus. Because of the virus's devastating impact on the world's livelihood and economy, researchers are looking into a variety of approaches to prevent its effects, including traditional methods. Flavonoids, alkaloids, and polyphenolic chemicals found in indigenous medicinal plants have antiseptic, disinfecting, and antibacterial properties. Plant extracts were utilised as potent antiseptics and disinfectants in the past to get rid of microorganisms. The goal of this study is to find phytochemicals that can inhibit COVID-19 in plant *Elettaria cardamomum* extracts. The Dassault system's BIOVIA Discovery Studio module was used to performe the molecular docking. The –CDOCKER energy and CDOCKER interaction energy were used to analyse and interpret the results. The strong positive value of the –CDOCKER energy and –CDOCKER interaction energy in this study indicates that the phytochemical acetic acid has a high affinity for the Crystal structure of the HR2 domain, effectively inhibiting its enzymatic metabolic activity.

Keywords: Phytochemical, BIOVIA, Discovery studio, *Elettaria cardamomum*, COVID-19, Healthy lives

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a devastating viral disease that was first detected in Wuhan, China's Hubei province, in December 2019. This virus, which affects the immune system, and which mostly affects the human

respiratory system, was named severe acute respiratory syndrome by the International Committee on Virus Taxonomy in February 2020 (SARS-CoV-2) [1]. Regrettably, the epidemic condition was declared a pandemic by the World Health Organization (WHO), and it is the first pandemic caused by the corona virus, according to WHO [2].Every medical profession, on the other hand, claims to have resources to help prevent, treat, or cure potential contagious viral infections.

The etiological agent i.e Corona viruses are enveloped positive sense, single-stranded RNA viruses that belong to the corona viridae family and have diameters ranging from 60 to 140 nm. They get their name from the Latin word "corona" or crown, which describes their crown-like morphology when viewed under an electron microscope [3]. The first Corona virus-based sickness was identified in 1931, and the first HCoV-229E Coronavirus was isolated from humans in 1965. However, SARS-CoV-1 (a member of the subgenus Sarbecovirus) was initially diagnosed in China in 2002 as a potentially lethal respiratory infection [4]. Because Covid-19 has an identical nucleotide with SARS-CoV, bat SARS-CoV, and MERS-CoV, phylogenetic evolutionary analyses have revealed similarities between Covid-19 and other already accessible coronavirus strains [5]. SARS-CoV-2 is a newly identified Coronavirus that encodes a glycosylated spike protein that is primarily responsible for binding to the ACE-2 receptor [6]. SARS-genetic CoV-2's material (RNA) is protected by a lipid bilayer envelope [7]. The fecal-oral route, contact with an infected individual, and respiratory droplets are all common modes of infection [8].

As it is a pandemic disease that spreads from person to person via aerosol transmission, posing a hazard to a large number of people. COVID-19 is reported to have a wide spectrum of clinical manifestations, ranging from asymptomatic to acute respiratory distress syndrome. The three most prevalent symptoms of COVID-19, according to the data gathered, are dry cough, fever, and difficulty breathing, with other symptoms including hypoxemia, a lung lesion, weariness, conjunctivitis, pigmentation of toes or fingers, and diarrhea [8].There are several chemical medications for therapy, such as flavipiravir and remdesivir, as well as vaccinations like covaxin and plasma treatments, however this virus can cause serious illness in the elderly and people who already have other medical problems, such as sensitivities to chemical compounds. Since ancient times, naturally occurring herbal botanicals and other herbal medications have been widely used to treat respiratory infections. Because of their low toxicity and ability to reduce the effects of SARS-CoV-2 infection by functioning as immunity boosters, herbal medications are deemed excellent [9].

And plants have long been a significant source of medication for humans. A total of at least 35,000 plant species are commonly utilised for medical purposes, according to published data. The demand for traditional medicinal herbs is fast rising, owing to a combination of factors. Traditional medicine, according to the World Health Organization (WHO), contributes significantly to the achievement of the organization's health goals. As evidenced by Ayurveda, India has a long history of herbal medicine. The two most prominent Ayurvedic treatises, Charak Samhita and Sushruta Samhita, detail the usage of 700 herbal medications. Antiviral action has been demonstrated in some of them. As viral illnesses, which include both chronic and new viruses, are a fast-growing global health concern, there is an urgent need for innovative and more effective antiviral medications due to the global illness load generated by such infections. Medicinal herbs and their bioactive elements are of particular interest because they may offer viable therapeutic choices for the people of poor nations, where the bulk of the population cannot afford expensive chemical medications used in western countries [9].

Plants are well-known for containing bioactive chemicals that have been converted into patent medications [10].Because of their accessibility and cost, phytomedicines are used by more than 80% of the African population. Plant compounds have been shown in the lab to be effective against other enveloped viruses such as HIV-1 and HIV-2, and they may also be effective against the COVID-19 virus. Many newspaper and social media publications have advocated numerous herbal remedies as therapies for COVID-19 since the outbreak. To avoid undesired side effects, these must be assessed for safety and efficacy. Because most herbal medicines have been used by the community in an apparently safe manner for many years, the path to the manufacture of improved traditional medicines is much shorter than that of allopathic medicines [11].

Plant extract compounds are a traditional and reliable technique for the prevention and treatment of infectious illnesses. *Elettaria cardamomum*, which belongs to the *Zingiberaceae* family, is considered as an extremely effective spice among herbs, earning it the nickname "queen of spices" [12]. Its potential health benefits have been discovered in a range of infections and health issues. Cardamom's health benefits can also be discovered in NAFLD patients (nonalcoholic fatty liver disease) [13]. The botanical name for black/large cardamom is *Amomum subulatum* [14]. Because of its color, green cardamom is also called as *Elettaria Cardamomum* [15]. The current research focuses on the efficacy of a specific phytochemical from *Elettaria cardamomum* to protect against SARS-CO V-2 virus symptoms by suppressing a protein pathway that can lead to viral growth control.

Pathophysiology of COVID-19

The histological architecture of a sick patient with Covid-19 exhibits diffuse alveolar damage, comparable to other viral respiratory illnesses as SARSCoV and MERS-CoV. SARS-CoV-2 infection, it can be differentiated by endothelial damage of varying degree, blood clots or thrombosis, microangiopathy, and angiogenesis. The pathophysiology of COVID-19 is thought to include the SARS-CoV-2 virus invading alveolar epithelial cells via the coronavirus spike (S) protein attaching to the angiotensin-converting enzyme-2 (ACE2) receptor. The invasion of epithelial cells is likely to increase direct toxicity and intensify the immune response, potentially resulting in considerable cytokine activation and mobilisation, which might result in lung injury, respiratory failure, and death in extreme symptoms [16]. Interleukins (IL-6, IL-7, IL-10), interferon gamma-induced protein 10, monocyte chemoattractant protein-1, macrophage inflammatory protein 1a, and tumor necrosis factor (TNF-) are reported to be highly expressed in severe COVID-19 cases, and excessive activation of these factors may be linked to poor prognosis as it could be an indication of the progression from mild to severe COVID-19 [17].

Efficacy of Phytopharmaceuticals in Viral Diseases

Virus infections have become a part of human civilization as the estimated incidence, morbidity, and mortality has increased in recent years. The influenza virus, AIDS (acquired immunodeficiency syndrome), dengue fever, Ebola, and SARS (severe acute respiratory syndrome) are just a few of the deadly viral diseases that infect and kill tens of millions of people each year. Many viral infections have no licensed medicines, and just a handful have vaccines, such as hepatitis A and B, mumps, and varicella [18, 19]. Polyphenols, steroids, terpinoids, polysaccharides among other chemical constituents, may have antiviral activities.

MATERIALS AND METHODS

Software Used

The Discovery studio module, which is a component of BIOVIA software, was utilised in this work to analyse the interaction between the phytochemical and the protein molecule. Using a machine learning algorithm, the software analyses of the molecular interaction between the phytochemical and the protein molecule was carried out.

List of Phytochemicals

Non-nutritive compounds found in plants that have the ability to fight disease or have disease-preventive characteristics are known as phytochemicals. These are non-essential nutrients that plants make to protect themselves from infective bacteria. Cardamom is the most researched chemical with antibacterial properties. Typically, it contains essential oil extracts as well as fruit and seed extracts. According to this study, cardamom has the ability to heal a variety of bacteria. Phytochemicals such as phenols, terpenoids, tannins, flavonoids, and others have been found in the herb *Elettaria cardamomum*, as is evidenced by studies [20].

Enzymes found in SARS-CoV-2

Different enzymatic pathways are responsible for survival of the microorganisms. If those pathways get obstructed then survival chance gets lowered. Acute respiratory distress syndrome (SARDS) is a severe form of acute respiratory distress, Coronavirus is a newly emerged virus that has been linked to a recent atypical pneumonia

outbreak. The coronavirus spike protein, an enveloped glycoprotein required for viral entry, is classified as a class I fusion protein and contains two heptad repeat (HR) sections, HR1 and HR2. RCSB database was used to download the crystal structure of HR2 having code 6LVN.

Molecular Docking

The interaction between phytochemicals derived from plants and viral proteins was investigated using molecular docking methods. To effectively suppress the microbe, the phytochemical serves as a ligand molecule, forming a strong covalent bond with the viral protein. The BIOVIA software's Discovery studio module was used to detect chemical contacts and perform molecular docking to determine the intensity of the interaction or the binding affinity between the ligand and the receptor molecule. The structure data file (SDF) of the phytochemicals of the plant *Elettaria cardamomum* was downloaded from PUB CHEM, and the PDB files of enzymes were retrieved from RCSB, in order to carry out this method. The activation of the enzyme's binding site was done using the "receptor cavity" item in the receptor ligand interaction menu. Under the "receptor-ligand interaction" category, the BIOVIA software's CDOCKER protocol was utilised to perform molecular docking. The phytochemical was used as a ligand, while the enzyme was used as a receptor. As quality indicators for molecular docking, the "-CDOCKER ENERGY" and "-CDOCKER INTERACTION ENERGY" parameters were used. These markers exhibited a high positive value, indicating that the ligand and receptor had a good contact. As a consequence, high-value interactions reveal a critical phytochemical implicated in the suppression of disease-associated protein.

RESULTS AND DISCUSSION

CDOCKER is a molecular dynamics (MD) technique based on simulated annealing. It's a grid-based molecular docking technique that's been fine-tuned for accuracy. The active site of the enzyme, shown in Fig. 1, enhances the ability of the ligand molecule's attachment point to provide more precise binding strength. The conformations of the ligands were obtained using molecular dynamic methods. After the molecular contact process was completed, the CDOCKER energy was calculated using the internal ligand strain energy and the receptor-ligand interaction energy. The –CDOCKER energy is the energy of the nonbonded interaction between the ligand and the protein. A high rate of positive value of-CDOCKER energy and a small difference between-CDOCKER energy and -CDOCKER interaction energy were used to establish the ideal interaction settings.

Table 1 conferms that the interaction of Acetic acid with the Crystal structure of the HR2 domain has the highest positive value of-CDOCKER energy, 11.43, and has the smallest difference of 2.41 between-C DOCKER interaction energy and-C DOCKER energy, followed by the interaction of Cinnamaldehyde with the Crystal structure of the HR2 domain. According to the findings, acetic acid can effectively disrupt Crystal structure of HR2 domain protein, preventing the virus's pathogenicity process and so inhibiting the virus's proliferation. The likelihood of the phytochemical having an influence on the viral enzyme for deactivation increases as the positive value rises. And the phytochemical's negative result indicates that it has a minimal influence on the viral enzyme during the deactivation process.

CONCLUSION

There are currently no viable therapies for Covid-19. In the foreseeable future, there may or may not be one. Many communities avoid using medications for Covid-19 in favour of natural therapy, believing that home-made therapies are far safer, have fewer side effects, and can also be used to prevent disease. From this current research work it is found that *Elettaria cardamomum* is a plant that has been found to impede the Crystal structure of the HR2 domain in the SARS-COV-2 virus. The purpose of this research was to identify the phytochemical responsible for the plant's therapeutic properties. A molecular docking strategy was employed with the BIOVIA Discovery Studio module to determine the phytochemical acetic acid, which has the capability to interfere with a key enzyme Crystal structure of the HR2 domain. The molecular research revealed that acetic acid has a substantial binding affinity or contact with

the viral enzyme, followed by Cinnamaldehyde, which successfully inhibits the virus's replication process. Thus the outcome of this study will be helpful further screening of better and effective antiviral drugs for treatment of COVID-19, creating a sustainable health environment and promoting good health and wellbeing of people by satisfying the Sustainable Development Goal 3.

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Table:1 Result of CDOCKING of the phytochemical with Crystal structure of the HR2 domain

SL NO	LIGAND	- C DOCKER ENERGY	- C DOCKER INTERACTION ENERGY	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Acetic acid	11.43	9.02	2.41
2	Cinnamaldehyde	9.53	13.42	3.89

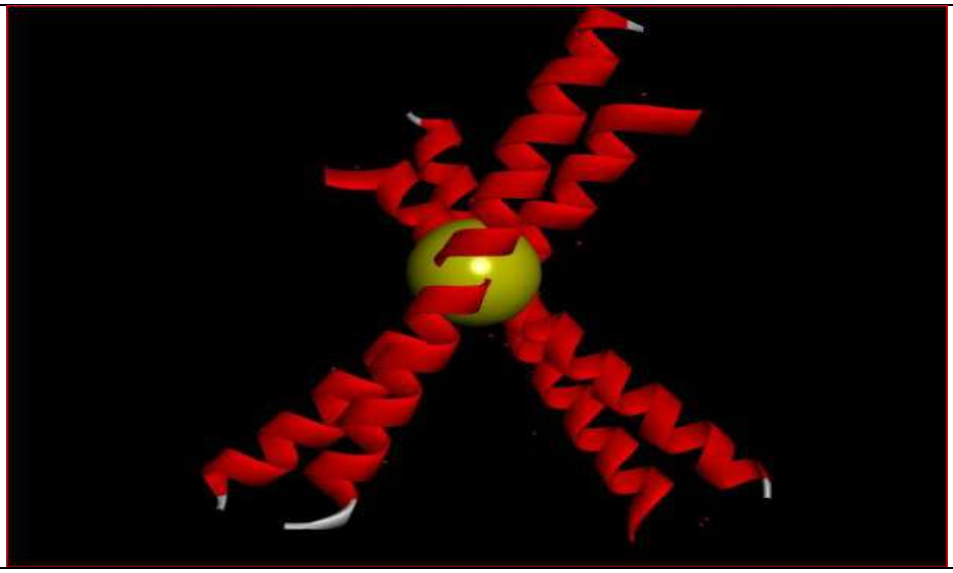

Fig:1 Active site of Crystal structure of HR2 domain

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RESEARCH ARTICLE

Silence that Speaks Eloquently: An Indian Context Presentation through Shashi Deshpande's 'That Long Silence

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ABSTRACT

The depiction of Indian women lives with their existing problems in the Indian context has been of prime interest of discussion in the contemporary Indian Women Writing in English. Shashi Deshpande is one of the notable figures in this area especially with her award-winning novel, 'That Long Silence'. The novel bearing the true Indian colours and pictures is an outstanding revelation of woman psychology in Indian cultural and social settings.

Keywords: Indian Women Writers, Empowering women, Gender Inequality, Feminism

INTRODUCTION

Trials and tribulations, convulsions, frustration, endurance have been the deciding characteristics of Indian middle class women in the present scenario. Silence is the imposed identity for them. But their existing silences speak eloquently the bitter truth, their untold stories of pains and sufferings. And Shashi Deshpande's 'That Long Silence ' authentically portrays that language of silence through the character-portrayal of Jaya, a middle class woman. In the story, Jaya is a successful columnist and an aspiring novelist. She meets her listeners through her writing, shares her mental state experienced in her day to day journey of life and thus tries to go beyond her silence. This article is basically an attempt to promote feminism through discussions of a novel written by a Indian woman writer. After going through this article the reader will clearly understand the philosophical importance of gender equality from the view point of a women writer who is also a feminist. It is significant for our society that people will understand and respect gender parity.

DISCUSSION

In the story line, Jaya, the woman protagonist makes her sincere effort to erase her long time process of 'that long silence' which has been started in her childhood in her material uncle. In her many encounters, she attempts to speak but fails to utter her voice. When Jaya's maternal uncle Ramukaka shows Jaya the family tree, he explains: "Look, Jaya, this is our branch. This is our grandfather- your great grandfather- and here's father, and then us- Laxman,

Vasu, and me. And here are the boys- Sridhar, Jannu, Dinkar, Ravi...'
Here Jaya is astonished and questions: 'But Ramukaka', 'i'm not here!'
And surprisingly, she gets shocked by the reply of Ramukaka and realises her in-between situations, gender inequality and her rootlessness in the existing and living society.

'You!' He had looked up, irritated by the interruption, impatient at my stupidity. 'How can you be here? You don't belong to this family! You're married, you're now part of Mohan's family. You have no place here." (p.143)

With such unexpected remarks, Jaya for a moment wants to break her silence. She wants to question Ramukaka: "Okay, i'd wanted to ask Ramukaka, if i don't belong to this family, what about the Kakis and Ai? They married into family, didn't they, why are they not here? And about ajji, who single-handedly kept the family together, why isn't she here? But i had said nothing- neither to Ramukaka, nor to Mohan, Ajji should be pleased with me. I had learnt it at last- no questions, no retorts. Only silence." (p.143)

The above conversation between Jaya and her maternal uncle Ramukaka highlights the gender biased ideology of our society and how women are prohibited to think and to ask even if at the cost of their survives. Most interestingly, after the marriage, woman is asked to be converted completely leaving all the traces related to her maternal family even her maternal name, the identity which she gets at the time of her birth. Jaya after her marriage is converted into Suhasini with the get up of a crisp cotton saru, with huge dark glasses, shaped eyebrows and short hair. She has been instructed to believe in the guidelines of Sparrow: " Close the doors, stay inside and you are safe." (p.124)

Eva Figes (1986) says: "Dominance is...is the keynote in an analysis of the man-woman relationship where the male attributes are ones associated with mental thought and positive activity, whilst the woman is regarded as essentially passive, her role to be respectable of male sexual drive for the subsequent reproduction of the species."

In India, marriage and motherhood are the pre-requisite conditions for women. Women is said to be born to fulfill these two conditions to provide fulfillment and happens to her husband, her family as well as the society. On the other hand, man is free of any condition and obligation. Jaya is the representative of this unequal status of women in our society. In the words of TapanBasu, "...Jaya who has input, a life time in surrender of her will to social modes and customs that had relegated women to a second class status."

In her deguised role of Suhasini, Jaya lives a long period of seventeen years with her husband Mohan and her two children. She adopts silence as her constant company. Her husband Mohan once warns her: " My mother never raised her voice against my father however badly he behaved to her."(p.83)

CONCLUSION

Jaya has been taught that a woman can never be angry; she can be neurotic, hysterical, frustrated. A hundred is a sheltering tree. Getting stuck with such patriarchal and gender biased ideologies, Jaya at last breaks the long silence lived in her seventeen years of married life, attempts to cross the barriers and goes beyond the silence. Now she is out of panic. Rajeshwari nicely points out here: "She chooses to operate within the self-imposed limits of the family,

resolving to change her life by renegotiating the power-relations and improving the interpersonal relationships within it rather than through the instrumentality of her writing. (p.22).

Silence of Indian middle class women really speaks eloquently. Though being instructed to be silent since their childhood times in their maternal families, but at times when these women try to open their hearts, the real and bitter truths of life unfolds. The true colour and picture of Indian society has been shown. The gap between words and actions ha been well-pronounced. Like Jaya, other women characters such as, Jeeja, Mukta, Vanitamami, Vimala, Mohan's mother, Kusum are the victims of male-dominated society. And their silences tell their protests against the system. ShakuntalaBharvani aptly comments: "The woman of today, therefore, speaking in the language of psychology, has a near schizophrenic personality; one side steadily "accepts" while the other craves to speak, to think and express the life of the mind."

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REVIEW ARTICLE

Biology, Epidemiology, Pathogenicity of *Candida* species: an Overview

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ABSTRACT

Candida species are members of the microbial community of the oral cavity, gastrointestinal tract, and genital tract, and are important for a range of clinical symptoms ranging from infections of the skin overgrowth to bloodstream infectious diseases. *Candida glabrata*, once thought to be non-pathogenic, was quickly faulted for human diseases. Year after year, these degenerative diseases become more usual and hard to treat, particularly when people with the disease consume any level of immunosuppressive drugs. These problems arise from *C. glabrata* capacity to establish biofilms as well as its better resistance to traditional antifungal forms of treatment. As a consequence, the aim of this review article is to present the biology, epidemiology, and pathologene city of *Candida* species including the mechanisms of resistance.

Keywords: Epidemiology, Virulence factors, *Candida* species, Antifungal resistance

INTRODUCTION

Fungal infection in human being is mostly caused by Candida species. Among them, *Candida albicans* is the common *Candida* species causing skin or mucous membrane infections. Other species, viz. *C.glabrata*, *C. krusei*, *C. parapsilosis*, *C.kefyr*, and *C.tropicalis* species may sometimes involve in vaginal infections. *Saccharomyces cerevisiae* has been linked to *Candida* infections. These yeasts differ from one another in their ability to formation of their colony and invade the epithelial cells of the host. *C. albicans* has the most epidermal sites of virulence. Resistance of the host to yeast intrusion is lowered at obstructed or dehydrated epidermal sites, as well as in patients with impaired cellular immunity. This enables mutualistic yeasts to pass through the ocular surface layer. Patients with deficient responses to T-lymphocyte, penetration beyond the epithelium is uncommon. The phenomenon of *Candida* virulence is now properly understood at both molecular and cellular level. Superficial infections by *Candida* species may be influenced by the host and yeast factors in pathogenesis process. The overall study will focus on different species of *Candida*,

pathogenic aspects including infection and host defense mechanism sensuring the awareness about human health and wellbeing.

Defense action of the host against *Candida* sp.

A variety of factors protect epidermal and external epithelial surfaces from microbial infection, two factors such as immune functions of T lymphocyte and proliferation of epidermal cells is significant in anti-candida defenses. The simple observation that *Candida* infections in cutaneous and mucosa more likely to occur in people with defects in their T-cells chronic and also the people having decreased CD_4 cell counts due to HIV infection which provides evidence for the importance of cellular immunity. Chronic muco-cutaneous *Candida* infection in skin, nails, vagina and mouth in womenmay be noticed in HIV-negative patients. The mouth and oesophagus are the primary sites of infection in HIV-infected patients, with little or without any evidence of nail and skin infection (Maibach and Kligman, 1962).

T-lymphocytes play an important role in the defense strategy for both outermost layer of epithelial and epidermal surfaces against *Candida*, as evidenced by these clinical results.These clinical findings highlight the significance of T-lymphocytes in the defensive strategy of both external epithelial and epidermal surfaces against *Candida*. Defect in two types of T-lymphocyte is associated with the interaction between yeast pathogen and host leukocytes. Langerhans cells may be involved in the responses of T-lymphocyte to epidermal infectionby *Candida*. Epidermal proliferation in candidiasis can occur in the form of horrific cutaneous crusts known as "granulomas" in traditional persistent mucocutaneous (Braathe *et al*., 1983). Clinical and pathological study of the infected sites reveals that the fungus continues to remain restricted to the corneal layer, implying that the rate of huge hyperkeratosis is equivalent or better than the fungal penetration rate in the epidermis. Sohnle and Kirkpatrick discovered an increase rate inepithelial tissue and thickening of epithelial cells in *C. albican s*infected mice. Epithelial cells proliferation was noticed in vagina and mouth as a reaction to the infection induced by *Candida* indicating clear response of the infection. Defense against *Candida* also include occurrence of natural microbial flora which competes with the *Candida*to colonize in epithelial site. In addition, cells of epidermis and epithelium are regularly covered with a liquid film containing efficient inhibitors of *Candida*to colonize, which is unspecified viz., numerous lipids and acids ended up finding in intestinal mucosa or specific secretory IgA molecules. Keratinocytes have the ability to phagocytoze*C. albicans* cells. Of course, the surface level lesions caused by *Candida* species vary. Cysts that form on occluded skin are typically swollen and red with pustules. This may result insterilised subcutaneous skin infections, supposedly caused by dissolved fungi constituents that cause adaptive immunity and an invasion of leucocytes. White "plaques" distinctive feature of infection by *Candida* species in oral and vaginal ulcers shows to have both fungal mycelia and materials of the host resultingin proliferation of epidermal cells Agatensi *et al*., 1991; Antley, 1988). The inflammation in the lesions is dependent on leukocyte influx of mononuclear cells, which is similarly observed in cutaneous *Candida* intertriginous dermititis.*C. albicans* characteristic that may be virulence factors in the colonial expansion and incursion of epidermal and mucous membranes sites. Flocculation, first and most important step in colonial expansion inthe epidermis site depends on components of microbial cell surface with a certain affinity for the receptors of epidermis. Membrane proteins of *Candida* are classified into three types. A protein molecule of surface glycoprotein binds to arginine glycine-aspartate (RGD) provides insight in fibronectin, vitronectin, collagen type, membrane protein including proteoglycans and other extracellular matrix in one type.The protein molecule of a surface glycoprotein adheres to the sugar part of host membrane proteins in a lectin-like without any time gap. The carbohydrate part of surface mannoprotein of *Candida* binds to unidentified receptors of the host in the third and least well-characterized mode. Calderone and Braun have thoroughly examined these various types of adhesions.(Borg and Ruchel, 1988; Claderone and Brau, 1991)

It is suspected that *C. albicans* produce a secretory as partyl proteinase, which is thought to be a causative agent in this particular species. Other investigation reported that this enzyme plays a role in the colonial expansion in the oral squamous epithelium. It was reported that *C. albicans* yeast cells created pits in corneocytes of mouse in *ex vivo*,

but the process was stopped in availability of pepstatin as it inhibits the enzyme aspartyl proteinase, suggested a direct action with the proteinase in early invasion of the corneal layer.

Initial attachment of *C. albicans* to corneocytes is not inhibited by pepstatin, only penetration, implying that adhesion and colony formation of the epidermal cells is not intervened by the enzyme proteinase. It was also worth noting that the proteinase-dependent penetration of corneocytes did not necessitate the *Candida* yeast cells morphologic transformation to hyphae.Even though very little firm evidence exists for the conventional dogma that *C. albicans* hyphae are the sale respondents in invasive mechanisms, whereas yeast forms are connected with mutualistic colonization, hypha formation has traditionally been recognized an act of virulence and tissue penetration in *C. albicans*(Sobel *et al.,* 1993; Sherwood *et al.,* 1992; Rippon, 1988; Ray and Wuepper, 1976) It is well known that hyphal forms of *Candida* adhere more easily and quickly to buccal epithelia than yeast forms, but this feature could possess on hyphae the importance of a steady, attached colonist from which infectious agent propagules (budding yeast cells) are produced.

This principle varies from traditional role of Candidias is hyphal forms in penetration. The most common *Candida* infections is penetration of the hyphae into epidermal, vaginal and buccal epithelial cell surfaces, but Ray and Paynel's experiments show that hypha formation is not required for *C. albicans* to invade epidermal cells (Ray and Paynel, 1988).Recent in vitro investigations have demonstrated that *C. albicans* mycelium is capable of contact signaling, also known as thigmotropism. The hyphae in clinical and pathological sections of *C. albicans* infected tissues have seemed to be randomly dispersed. In epithelial cells of keratinocytes, however, the hyphae seems to be divided into patterns that are either primarily along with the keratinocyte strata or parallel with the strata, even though these patterns are never as accurate or definitive as in some plant pathogenic fungal species that grow correctly oriented perpendicular to cell periphery.

The semi-regular configurations of *C. albicans* mycelium could possibly be due to a potential to expand in the way of freely accessible nutrient content, but it is possible in theory that such type of arrangements of hyphae are due to their thigmotropic reactions to the micro surfaces present in the keratinocytes layer. Hydrophobicity of the surface is a generalized factor that, through Vander Waals forces, can govern cell type adhesion. *C. almeans* have shown varying degrees of hydrophobicity depending on their growth temperature, and the differences correlate to disparities in surface adhesion of epithelial cells and virulence in response with mouse mortality rate. Fluctuations in hydrophobicity may thus take a part in the progression of superficial *Candida* infections, though this has not been investigated. *Candida* cells are unlikely to express all of the potential virulence factors described for *C. albicans* in all possible microhabitats. There is now indication that *C.albicans* has high advantages of fast swapping of its expressed phenotype, most likely via transcription factors during gene expression regulation(Sohnle and Kirkpatrick, 1978; Soli, 1992; Soli *et al.,* 1993). This incident may boost the capacity *of C. albicans* to adjust quickly to the latest micro niches, such as when yeast cells are transmitted from anus to vagina. This ability to adapt could be a factor in controlling the suitable virulence expression characteristics during different colonization and tissue penetration phases to establish a pathophysiologic inflammation.

Pathogenicity of *Candida sp.* Inepithelial Infection

Infectious diseases caused by *C.albicans* (and other *Candida* species) progress through stages in which various host and fungal factors play important roles (Klotz *et al.,* 1985; Mackenzie *et al.,* 1990). The exterior adhesion components of the fungus will decide whether it achieves in constructing itself during formation of biofilm of an endothelial or epidermal site. Other trying to compete the microbes and substances at the location inactivating *Candida* growth are the host defenses against colonial expansion besides from physical factors such as filtration methods (Csato *et al.,* 1987; Hazen *et al.,* 1991).

Once fungal cells entered in the surfaces of epitheliuml or epidermis, the process is obstructed by the mechanical resistance of keratinized surfaces but by the action of proteolytic enzymes of the fungus they may grow to form hyphae, and penetrate into the deeper of epithelia by sensing contact. At this phase, the host activates a number of

defensive mechanisms, such as proliferation of epidermal and epithelial cells, inflammatory reaction and instantaneous phagocytosis of *Candida* by keratinocytes. T-lymphocytes could be implicated for particular defense action against any or all the three pathogenesis stages.

CONCLUSION

The phenomenon of *Candida* virulence is described at both molecular and cellular level. Superficial infections by *Candida* species may be influenced by the host and yeast factors in the process of pathogenesis. The overall study revealed the pathogenic aspects of *Candida* species and provides a way to create awareness about human health and wellbeing.

Conflict of Interest: No conflict of interest is there.

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RESEARCH ARTICLE

Thermodynamic Parameters and their Excess Values for Binary Mixtures of Cyclohexane and Substituted Benzenes at Different Frequencies

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ABSTRACT

The ultrasonic velocity (U), density (ϱ) and viscosity (η) have been measured for the binary mixture of benzene, chlorobenzene, nitrobenzene and pyridine successively with cyclohexane at different frequencies and at temperature 318 K for different concentrations of component liquids. The experimental data of velocity, density and viscosity have been used for a comparative study of the molecular interaction in the different mixtures using the calculated thermodynamic parameter and their excess values, such as excess adiabatic compressibility (β^E), excess free length (L_f^E), excess free volume (V_f^E) and excess Gibb's free energy (ΔG^E). Variation in the above parameters for the different mixtures is indicative of the nature of the interaction between them.

Keywords: Ultrasonic velocity, Gibb's free energy, free length, and free volume.

INTRODUCTION

Ultrasonic investigations of liquid mixtures, consisting of polar and non-polar components are of considerable importance in understanding the intermolecular interactions between the component molecules, which find applications in several industrial and technological processes [1-10]. In the present paper, we have studied the various thermodynamic parameters along with their excess values from the study of variation in ultrasonic velocity at different frequencies for the following binary mixtures.
Mixture - I: Cyclohexane + Benzene
Mixture - II: Cyclohexane + Chlorobenzene
Mixture - III: Cyclohexane + Nitrobenzene
Mixture - IV: Cyclohexane + Pyridine

The temperature has been maintained at a constant value (318K). Cyclohexane belongs to the group of alicyclic hydrocarbons. It is a non-polar, un-associated, inert hydrocarbon and has a globular structure. It is highly inert toward an electrophile or nucleophille at ordinary temperature. Due to the above properties, dispersive types of interactions are possible between cyclohexane and other components. Benzene is a non-polar solvent. It is a cyclic hydrocarbon with a continuous pi bond. Chlorobenzene is a poor electron donor to the electron-seeking proton of any group. It has a low dielectric constant and dipole moment. The chlorine atom being an electron-withdrawing atom attracts the πelectron of benzene ring and thus a decrease of the electron density of the ring takes place. This makes the benzene ring a relatively poor electron donor to the Cyclohexane molecules. Nitrobenzene is a polar solvent with high dielectric constant and dipole moment. Hence intermolecular interaction, in this case, is large. Pyridine is a basic heterocyclic organic compound with a lower dielectric constant and dipole moment. Pyridine molecules are spherical in shape and tightly packed. Finding the basic physical foundation contributing to sustainable development is significantly useful in seeking ways to build an enduring human future.

Experimental Technique

The liquid mixtures of fixed concentration (6:4) in mole fraction were prepared by taking analytical reagent grade and spectroscopic reagent grade chemicals with the minimum assay of 99.9% and obtained from E.Merck Ltd (India). The density, viscosity, and ultrasonic velocity of all liquid mixtures were measured at temperature 318K and for different frequencies 2 MHz, 4 MHz, 6 MHz,8 MHz. Ultrasonic velocity measurements were made using an ultrasonic interferometer (Model M-84, supplied by M/S Mittal Enterprises, New Delhi), at different temperatures and different frequencies with the accuracy of ±0.1m·s^{-1}. The measuring cell of the interferometer is a specially designed double-walled vessel with provision for temperature constancy. An electronically operated digital constant temperature bath (Model SSI-03 Spl, supplied by M/S Mittal Enterprises, New Delhi), operating in the temperature range of−10°C to 85°C with an accuracy of ±0.1°C has been used to circulate water through the outer jacket of the double-walled measuring cell containing the experimental liquid. The densities of the mixture were measured using a 10-ml specific gravity bottle by relative measurement method with an accuracy of ±0.01 kg·m^{-3}. The specific gravity bottle with the experimental mixture was immersed in the temperature-controlled water bath. The weight of the sample was measured using an electronic digital balance with an accuracy of ±0.1 mg (Model: SHIMADZU AX-200, Kyoto, Japan). An Oswald viscometer (10 ml) with an accuracy of ± 0.001 Ns·m^{-2} was used for the viscosity measurement. The flow time was determined using a digital racer stopwatch with an accuracy of ±0.1s.

Theory

Adiabatic Compressibility (β_{ad})

Adiabatic compressibility the parameter which represents the ability to change the volume of a liquid sample is [11]

$\beta_{ad} = (\rho\, U^2)^{-1}$ …….. (1)

Intermolecular Free Length (L_f)

The formula for outer to outer distance between the interacting molecules

$L_f = K\sqrt{\beta_{ad}}$ ……..……(2)

Free Volume (V_f)

The free volumes of the binary mixtures have been computed using its relationship with the ultrasonic velocity and viscosity as given below

$V_f = \left(\frac{MU}{K\eta}\right)^{\frac{3}{2}}$ …….(3)

Where k is a constant, which is independent of temperature and its value is 4.28 X 10^9 for all liquids.

Gibb's Free Energy (ΔG):

The variation of „τ" with temperature can be expressed in the form of Eyring salt process theory [17].

$\frac{1}{\tau} = \left(\frac{KT}{h}\right).exp\left(\frac{-\Delta G}{KT}\right)$

The above equation can be rearranged as

$\Delta G = 2.30KT\log\left(\frac{KT\tau}{h}\right)$…….. (4)

Where, '$\boldsymbol{\tau}$' is the viscous relaxation time, T' is the absolute temperature, K is the Boltzmann"s constant and h is the Planck"s constant.

Excess Thermodynamic Parameters

With the help of excess parameters, the extent of deviation from the ideal behaviour of binary mixture can be estimated. The difference between the thermodynamic function of mixing for a real system and the value corresponding to a perfect solution at the same temperature, pressure and composition is called the thermodynamic excess function, denoted by Y^E.

Excess value Y^E for each parameter can compute by using the general formula

$Y^E = Y - (Y_1 X_1 + Y_2 X_2)$ …… (5)

Where Y is the parameter under consideration, X_1 and X_2 are mole fractions of two liquids.

Excess Adiabatic Compressibility (β^E)

The difference of the adiabatic compressibility of the mixture and the sum of the fractional contributory adiabatic compressibility of the two liquids individually is the deviation in adiabatic compressibility. At a given mole fraction it is given by

$\Delta\beta_{ad} = \beta_{ad} - (\beta_{ad1} X_1 + \beta_{ad2} X_2)$ …….. (6)

Excess Free Length (L_f^E)

The excess free length can be calculated with formula

$L_f^E = L_f - (L_{f1} X_1 + L_{f2} X_2)$ …….....…… (7)

RESULT AND DISCUSSION

The experimental values of density, viscosity and velocity are presented in table-1. Calculated values of acoustic and thermodynamic parameters are presented in table-2 and 3. Excess values of the parameters are shown in table-4 and 5. Ultrasonic velocity increases in the following order. It is maximum for mixture-I and increases from mixture-II to mixture-III and finally to mixture-IV. Since benzene and cyclohexane both are non-polar, their intermolecular interaction is weak; hence ultrasonic velocities in such mixtures are minimum. In the cyclohexane chlorobenzene mixture, the intermolecular interaction is also weak as mentioned before; hence velocity is less than that in the mixtures III and IV. Nitrobenzene has a larger dipole moment compared to pyridine but the intermolecular interaction is weaker in mixture-III compared to mixture-IV because of steric hindrance in nitrobenzene (Nitrobenzene being a complex and big molecule). When frequency increases, velocity in each case decreases indicating weakening of intermolecular interaction. Intermolecular free length (L_f) is maximum for mixture-I. This is obvious as the molecular interaction in this case is weakest. For the mixture-III, L_f is the next as the interaction in this case is next as expected due to steric hindrance. L_f for mixture-IV comes the next. L_f is minimum for mixture-II. Although intermolecular interaction in this case (mixture-II) is small, the molecules in the mixture fit in to each other yielding minimum intermolecular space. Excess free length (L_f^E) is positive for system-I, III and IV and decreases in the same order. Positive L_f^E indicates weak interaction.This may be due to the non-polar nature of molecules or steric hindrance or expansion in volume from additivity. However, because of comparatively stronger interaction in mixture-IV, L_f^E is positive but small. In mixture-II, L_f^E is negative. This may be due to the fact that the molecules fit well into each other and L_f decreases in the mixture. L_f^E does not vary with frequency in all the cases.

Adiabatic compressibility (β) decreases in the following order of the mixture-I, III, IV, and II. It changes in the same way as free length changes. At low frequencies, L_f and β are small for mixture-IV compared to mixture-II but is just the opposite when frequency increases. Excess adiabatic compressibility (β^E) is positive for mixture-I, III and IV and decreases in the same order. β^E is negative for mixture-II. β^E changes in the same way as L_f^E . Free volume (V_f) at any

frequency is maximum for mixture-II and decreases successively from mixture-I o III to IV. Since Lf decreases in the order mixture-I. III. IV and II, V_f should change accordingly but for system-II it is maximum. When chlorobenzene and cyclohexane are mixed, L_f is minimum. The molecules, in this case, are close to each other and the vibrations are transmitted through the molecules to a large distance increasing the apparent free volume. Free volume decreases very slowly with an increase in frequency. Excess-free volume (V_f^E) is positive for mixture-I, III and IV and decreases in that order. In case of mixture-I, positive V_f^E is due to expansion in volume because of additivity. V_f^E decreases with an increase in frequency. In mixture-III, V_f^E is less than that in mixture-I. The interaction in system-III being stronger, the expansion is less. However, V_f^E is less in mixture-IV than system-III as the interaction in mixture-III is less compared to mixture-IV because of steric hindrance in nitrobenzene solution. In mixture-II, V_f^E is negative and becomes more and more negative as frequency increases. When molecules are subjected to larger frequencies they vibrate rapidly, increasing the interaction between the molecules, which is of dispersive type. This reduces the free volume and hence the above observation. Internal pressure is maximum for mixture-IV and then decreases in the order mixture-I, II and III at any frequency. Pyridine molecules are spherical in shape, closely packed and have a finite dipole moment. Hence the intra-molecular as well as intermolecular interaction is maximum in case of mixture-IV. In case of system-III, it is the minimum. Nitrobenzene has a high dipole moment, but the complex structure of nitrobenzene molecules leads to less intermolecular forces and for the same reason also gives a less force of cohesion. Mixture-I and II show more internal pressure compared to mixture-III because of the molecular arrangement even though benzene is non-polar and dipole moment of chlorobenzene is low. Internal pressure increases very slowly with increase in frequency for mixture-I, II and III, but comparatively more in mixture-IV. This is because, when frequency increases molecular motion increases and the molecular interaction increases.

Gibb's free energy (ΔG) is maximum for mixture-III and then for mixture-IV, II & I in that order. In all the cases, ΔG increases slowly with increase in frequency. Increase in ΔG suggests shorter time for rearrangement of molecules in the mixture. This may be due to the fact that, when frequency increases, the energy imparted to the molecules expedites the rearrangement procedure. Excess Gibb's free energy (ΔG^E) is negative for mixture-I & II and is positive for mixture-III & IV. In mixture-I & II ΔG decreases in the mixture indicating longer time for rearrangement of molecules, as the intermolecular interaction in both of them are comparatively small. In mixture-III and IV, ΔG was large and hence ΔGE is positive. In the above two mixtures, the interaction being stronger, a shorter time is required for the rearrangement of molecules in the mixture. ΔGE changes rapidly with frequency for mixture-IV.

CONCLUSION

Variation of ultrasonic velocity with frequency in the binary mixture of cyclohexane and benzene group of liquids enabled us to study the thermodynamic parameters and their excess values. These indicate the nature of the interaction between the components of the mixture. Although cyclohexane is nonpolar the intermolecular interaction is evident through the excess values of the thermodynamic parameters. It has been observed that, the change in velocity with change in frequency is conspicuous in mixture-IV. This leads to large variation in the parameters and their excess values with change in frequency compared to the other mixtures.

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Table – 1: Values of Density (ϱ), Viscosity (η) and velocity (U) in binary mixtures for different frequencies.

Binary mixture	Density (ϱ)(Kg.m^{-3})	Viscosity ηx10^{-3} (N.s.m^{-2})	Velocity (U) m.s^{-2}			
			2 MHz	4 MHz	6 MHz	8 MHz
M-I: Ben+C.H	818.23	0.455	1168.6	1167.2	1165.1	1164.3
M-II: C.Ben+C.H	975.25	0.549	1172.1	1169.1	1166.4	1165.5
M-III: N.Ben+C.H	856.69	0.646	1170.2	1168.4	1165.1	1164.2
M-IV: Pyridine +C.H	869.56	0.571	1247.2	1238.1	1225.3	1209.4

Table – 2: Calculated values of β, and L_f in binary mixtures for different frequencies.

Binary mixture	Adiabatic compressibility (β x 10^{-10}) (N^{-1} .m^2)				Free length (L_f x 10^{-10}) (m)			
	2 MHz	4 MHz	8 MHz	8 MHz	2 MHz	4 MHz	6 MHz	8 MHz
M-I: Ben + C.H	8.949	8.971	9.003	9.014	0.608	0.608	0.609	0.610
M-II: C. Ben + C.H	7.462	7.501	7.537	7.543	0.555	0.556	0.558	0.558
M-III: N.Ben + C.H	8.524	8.549	8.584	8.608	0.593	0.594	0.595	0.596
M-IV: Pyr. + C.H	7.393	7.499	7.669	7.859	0.552	0.556	0.562	0.569

Table – 3: Calculated values of V_f and ΔGin binary mixtures for different frequencies.

Binary mixture	Free volume(V_fx 10^{-7}) (m^3 .mol^{-1})				Gibb's free energy (ΔG x 10^{-20} ($k.J.mol^{-1}$)			
	2 MHz	4 MHz	6 MHz	8 MHz	2 MHz	4 MHz	6 MHz	8 MHz
M-I: Ben + C.H	3.364	3.358	3.349	3.346	0.562	0.563	0.564	0.565
M-II: C. Ben + C.H	3.590	3.576	3.563	3.561	0.564	0.567	0.569	0.569
M-III: N. Ben + C.H	3.069	3.062	3.053	3.046	0.695	0.696	0.698	0.699
M-IV: Pyr. + C.H	2.663	2.635	2.591	2.544	0.578	0.584	0.594	0.605

Table–4: Excess values β^E and L_f^E in binary mixtures for different frequencies.

Binary mixture	Excess Adiabatic comp. (β^Ex 10^{-10}) (N^{-1} .m^2)				Excess Free length (L_f^Ex 10^{-10}) (m)			
	2 MHz	4 MHz	8 MHz	8 MHz	2 MHz	4 MHz	6 MHz	8 MHz
M-I: Ben + C.H	0.3138	0.3119	0.3238	0.3127	0.012	0.011	0.012	0.011
M-II: C. Ben + C.H	-0.31	-0.291	-0.274	-0.287	-0.08	-0.08	-0.07	-0.08
M-III: N. Ben + C.H	1.965	1.975	1.999	2.009	0.083	0.083	0.084	0.084
M-IV: Pyr. + C.H	0.03	0.115	0.265	0.422	0.006	0.009	0.014	0.020

Table – 5: Excess values V_f^E and ΔG^E in binary mixtures for different frequencies

Binary mixture	Excess Free volume (V_f^Ex 10^{-7}) (m^3 .mol^{-1})				Excess Gibb's free energy (ΔG^E x 10^{-20})($k.J.mol^{-1}$)			
	2 MHz	4 MHz	6 MHz	8 MHz	2 MHz	4 MHz	6 MHz	8 MHz
M-I: Ben + C.H	0.944	0.943	0.938	0.94	-0.092	-0.092	-0.091	-0.092
M-II: C. Ben + C.H	0.266	0.260	0.253	0.257	-0.031	-0.031	-0.030	-0.030
M-III: N. Ben + C.H	0.391	0.388	0.382	0.379	0.072	0.073	0.074	0.074
M-IV: Pyr. + C.H	-0.451	-0.471	-0.508	-0.544	0.056	0.061	0.069	0.078

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REVIEW ARTICLE

Efficacy and Pharmacological Activities of *Bacopa monnieri* : A Review

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ABSTRACT

Plants have been used as medicines for a long-time due to their involvement and social remedies. Continue to attract widespread attention for their role in treating minor and chronic illnesses. In recent times, worldwide interest in plant research has grown. A large body of evidence has been gathered to demonstrate medicinal plants' tremendous potential in many medical systems. One of the most helpful therapeutic plants in Ayurvedic medicine is *Bacopa monnieri*. *Bacopa monnieri* is a creeping perennial herb native to wetlands in southern and eastern India, Australia, Europe, Asia, and Northern and Southern America. Brahmi has a strong herbal flavour with a bitter aftertaste that is unique. Brahmi (*Bacopa monnieri*) is becoming increasingly popular as a nutritional supplement of its memory and intellect enhancing properties. There has been little data to show whether saponins are constantly present throughout the plant's growth phases or whether the seasons change the compounds. Saponin amount and distribution were also examined as a function of plant growth stages. Plant ages with varied plant components were used as treatments in a factorial, randomized design with three replications each season. *Bacopa monnieri* was found in the world's warmer and wetlands regions. Medicine was commonly used to cure various ailments. According to pharmacological research, it has multiple pharmacological properties, including memory improvement, anti-depressants, antioxidants, gastrointestinal, endocrine, and antibacterial. Brahmi is gaining popularity as a traditional medicine for treating various ailments. The current review focuses on *Bacopa monneiri* therapeutic potential in treating disorders. This plant has the potential to treat a variety of harmful conditions. *B. monnieri* includes bioactive chemicals that should be investigated further to isolate and purify new molecules.

Keywords: Brahmi, Medicine, Pharmacological, Nutritional Supplement, Saponin

INTRODUCTION

Bacopa monnieri is a family of Scrophulariaceae, a creeping herb with many branches, small elliptical leaves, and violet flowers (1). Phytochemical characteristics in *Bacopa monnieri* are moraine-type triterpenoid saponins called bacoside, with pseudjujubogenin moieties as aglycone units (2). It is a succulent herb, small and creeping. They are 10-30 cm long and arise from creeping stems that form roots at the nodes. The growth habit of Bacopa is like that of peppermint. They are straightforward, obovate, with the opposite narrower end at the base. The length of the leaves is approximately 2 cm × 1 cm, with entire margins. The flowers are blue or white. Pedicels in the leaf axils are solitary. They have five-lobed petals, white or pinkish. Size is up to 5 mm, developing in the persistent calyx. The plant is fresh and succulent, but when it is drying, it becomes wrinkled, and the taste is bitter. It is about 6-7 mm in diameter, longitudinally wrinkled, and brown. Pieces of the stem are cylindrical, glabrous, nodes prominent, attached with vertically growing branches and ventrally to a cluster of tortuous, brittle roots, internodes about 1-1.5 cm in length 3-4 mm in diameter, pale yellowish-green and with a purplish tinge (3). It is simple, opposite, decussate, somewhat sessile, glabrous, obovate-oblong to spatulate in shape, 0.6-2.5 cm in length and 3-8 mm in width, entire, the lower surface dotted with minute specks, obscurely 1-3 nerved, faint colour green. The flower is Pale blue or pinkish-white, nearly regular, solitary, axillary, usually longer than the leaves with two linear bracteoles (3).

Location

It is located all over India. It is found in Andaman and Nicobar Islands. It is found in all districts of Kerala, the southernmost state of India (4).It is Native to India, Sri Lanka, and Indochina. Genus consists of 56 species in tropical and subtropical regions (5).*Bacopa monnieri* is generally growing on the side of lakes and rivers, an essential constituent of medical purposes, and is traditionally used in India.

Season

Bacopa monnieri is highly produced in June and September. However, November is a good farming time for better growthof bacoside-A. In September, through March and in June, Bacoside A content was high (6, 7). It was the highest in the rainy season, while the weight yield of Brahmi was the highest in the summer season, in a succession of BM1 and BM7. In the summer season, the Bacoside-A level is also increased with BM1. Winter season record, the Bacoside-A level is low in the series of BM14(8).

Climatic Condition

Bacopa monnieri adapted to marine areas. It is distributed throughout tropical and subtropical parts of the world. It is an important medicinal herb. It is found throughout the Indian moist climate with a temperature range of 30 to 40 °C and relative humidity of 60 to 80 percent with a good sunshine duration. The pH ranges from 7 to 8 in the sandy soils. *Bacopa monnieri* has adapted to the pH content from 6 to 7 in water (11).

Origin

More than 3000 years ago, *Bacopa monnieri* originated. It is used for mental disorders like improving memory, sense, mood, etc. (13).A new variety of *Bacopa monnieri* is obtained (19). In Argentina, a comprehensive creeping plant has the Mercantile value of *Bacopamonnieri.* or 48 hours of polyploidization was earned submerging nodal segments. Events were detected, and two tetraploid plants were obtained (14). It is used as a nerve tonic in the medical system.

Distribution

Bacopa monnieri is likely a tropical Asian species that has spread across the tropics and subtropics. Africa, the Arabian Peninsula, Australia, the Iberian Peninsula, the Americas, and the Caribbean are all home to this species (16). Singapore, Spain, Portugal, and the Caiman Islands are among the countries where it has been introduced(17). *Bacopa monnieri* can be found in the world's tropics and subtropics, including Sri Lanka, India, Nepal, China, Taiwan, Vietnam, and Pakistan. It can also be found in Florida, Hawaii, the southern states of the United States, and the Mediterranean Basin. Nicobar Islands, Andhra Pradesh, Assam, Bihar, Delhi, Goa, Gujarat, Kerala, Karnataka,

Manipur, Orissa, Punjab, Rajasthan, Tamil Nadu, and West Bengal are among the Indian states where it is found. It has been seen in Bahrain, Kuwait, Northern and Southern Oman, the United Arab Emirates, Saudi Arabia, and Yemen, including Socotra. It can be found all over the south and western peninsulas and the plurinational State of Brazil; Cambodia; Chile; China; Costa Rica; Cuba; Dominican Republic; Ecuador; El Salvador; French Guiana; Grenada; Guadeloupe; Guatemala; Haiti; Honduras; India, Indonesia; Jamaica; Kuwait; Madagascar; Malaysia; Martinique; Mexico; Mozambique; Nicaragua; Nigeria; Oman; Pakistan; Panama; Peru; Philippines; Puerto Rico; Saint Lucia; Saudi Arabia; Somalia; South Africa; Sri Lanka; Swaziland; Taiwan, Province of China (North Yemen, Socotra, South Yemen) (18).

Varieties

A new variety of *Bacopa monnieri* was obtained from In-vitro polyploidization. In *in vitro* polyploidization, nodal segments of *Bacopa monnieri* were submerged for 24 or 48 hours in colchicine solution, 0.001 and P/V1 in DMSO. An aqueous solution was used as a control. *In-vitro* polyploidization, two tetraploid plants originated from independent events were detected (19). Compared to the control, they differ in leaf area, flower diameter, stem diameter, and many internodes in the recovered tetraploid plants. More robust plants(flowers and leaves), thicker and more rigid foliage, resistance to disease and pests, and a discernible increase in the tolerance to different stresses are associated with chromosome doubling. Doubling is accepted as a source of the evolution of flowering plants. The strategy was extensively used during the last 30 years. It was widely demonstrated that the *in vitro* colchicine treatment is a powerful tool.

Chemical Contents

Several groups of scientists have carried out ordered chemical inspections of this plant in the traditional system of medicine. Alkaloids, saponins, glycosides, flavonoids, and significant compounds including bacosides, bacosides, and bacopa saponins are some of the chemical constituents found to its beneficial effects. Bacopaside X, bacopaside II, bacoside A3, and bacopasaponin C are also found (9, 20). *B. monnieri* contains brahmine, herpestone, nicotine alanine, aspartic acid, glutamic saponins A, B, and C, bacosides A and B, triterpenoid, saponins, stigmastanol, betulinic acid, D-mannitol, stigmasterol as well as serine and pseudojujubogen(21). Bacoside A is a bacosides combination isolated from *Bacopa monnieri*. Bacosides A3, bacopaside II, Jujubogenin isomer of bacopasappnin C, and bacopasappnin C are among its most important ingredients (23).

Chemical Composition of Brahmi

Brahmi *(Bacopa monnieri)* is high in carbs, lipids, protein, and minerals, with an 88.4 percent moisture content. The herb's principal chemical makeup is listed (7).

Cultivation

For the cultivation of Brahmi,vegetative propagation (cutting of plant) is significant (10, 26).
Sowing Temperature: 25-30°C
Temperature:33-40°C
Altitude:1300-1400m
Rainfall:50-100cm
Harvesting Temperature:20-25°C.

Soil Condition

It is best grown in well-drained soil but will grow well in wet areas. It will even put up with a clogged drain. In alluvial marshes, it produces the most pleasing effects. It thrives in wetlands, canals, and other bodies of water. For optimal growth, it demands acidic soil (27). This creeping herb can grow around canals and water bodies throughout India, and in poorly drained soils, the plant flourishes. For congenial growth, the plant prefers acidic soil (28).

Sowing Time

The best time to plant is in the middle of June or July. They are cut into small pieces and roots, which provides ideal transplanting material, and seedlings are transplanted at a spacing of 20×20 cm. It is a moist-loving, marshy plant; it needs plenty of water (30).

Field Landing

Preparation of Land

To prepare the field well, first, the weeds should be removed. The land should be ploughed 2-3 times as it attains a smooth texture. In the preparation, farmyard manure of 5 tonnes per hectare should be applied along with the soil. It should be about 10×10 cm dug.

Irrigation Methods

It is essentialto supply the field irrigation after the rainy season. It is necessary to rinse the area in the winter for twenty days.

Intercultural Methods

Weeding

Weeding should be done everyday. It should bed one after planting every 15-20 days. Hand weeding is preferred for the crop, but it is more critical.

Intercropping System

Brahmi may fit well in the Kharif season and the rice-based cropping system in North India's plains with the following cropping sequence. Brahmi and rice-wheat, Brahmi and rice pea -wheat, Brahmi and rice Berseem-Maize, Brahmi and rice winter vegetables –Maize grows well under shaded conditions. It can also be grown as intercropping under coconut, area nut, and other perennial crops.

Fertilizer

At the time of the land preparation, it is necessary to apply farmyard manure (five tonnes per hectare) along with the soil. It should be supplied with Nitrogen (100 kg), Phosphorus pentoxide (60 kilograms), and Potassium oxide (60 kg) per hectare of land. *Bacopa monnieri* is planted in the ground or a container, and then fertilizer is applied. This helps in healthy and rapid growth. Zinc Sulphate ($ZnSo_4$)of 20 kg/hectares is often needed in areas showing deficiency, such as the plains of Punjab and Uttar Pradesh(31).

Ethnomedicinal Value of Medicinal Plants

Ethnobiology is one of the most well-developed fields of science, dating back to the Vedic civilization and encompassing a wide range of data on medicinal plants and animal species. Species, which were employed in the past, have high therapeutic potency and are regularly used by individuals from various groups and communities. Multiple studies have been conducted to document the ethnomedicinal properties of different medicinal plants in many parts of India. There are still many areas, particularly in Odisha, where documentation of traditionally used plants and animal species has yet to be studied (44).As a result, the current study is being conducted to document such plant species in various locations within the Udala Block of Odisha's Mayurbhanj district and assess their bioprospecting potential using phytochemical analysis. The survey was done in the four regions of Kundabai, Radho, Sridamchandrapur, and Adapal in the Udala block of Mayurbhanj, Odisha, as part of the current investigation. Plant species were processed for phytochemical research based on the results of a survey. According to the study, phytochemicals were found in the selected plant species. It could be a substitute for developing effective medications to combat the emergence of resistant microorganisms and their adverse effects, as the creation of new pharmaceuticals and antibiotics is a current strategy in Bio-medical science(24, 32, 38).

Ethnobotanical Uses *Bacopa monnieri*(Brahmi)

a) Brahmi leaf juice promotes blood flow and improves the nervous system (22).

b) Brahmi is a potent antioxidant used to treat oxidative damage. Mental diseases, epilepsy, and irritability are all relieved (36).
c) Brahmi leaf powder mixed with milk is used to cure gonorrhoea and sexually transmitted diseases.
d) Brahmi root ointment is used to treat elephantiasis.
e) Brahmi leaf extract treats jaundice and fever and isa neurological tonic with neuroprotective qualities.
f) It is utilized to cure dyspepsia, leprosy, anaemia, spleen disorders, and skin conditions.
g) It nourishes hair with nourishment and helps it grow longer and thicker (39).
h) It is also used to treat ulcers, dementia, and tumours.
i) Brahmi is used to treat mental sickness, cholera, piles, and amenorrhea (40, 41).
j) Brahmi improves nail, hair, and skin growth when combined with tulsi, neem, and amla.

Pharmacological Activities of *Bacopa monnieri*

In rats, ethanol extract(10mg/kg) of Brahmi improved motor learning. Ethanolic extract and the active component saponin have calming properties. The ingredient also decreased noradrenaline and 5-hydroxytryptamine levels in the brain. Ethanol extract and saponin were found to have an antianxiety effect. It has been reported to have anti-depressant properties (25). In diabetic rats, ethanol extract (50 mg/kg) was reported to exhibit antigastric ulcer action andant *Helicobacter pylori* activity in vitro. It shows antioxidant, anticonvulsant, analgesic, antiallergic, antifungal, cardiac depressant, and cardio-tonic activities by crude extract (42, 43).

Examples of Pharmacological Activities of *Bacopa monnieri*

Antioxidant Activity

Bacopa monnieri has shown antioxidant and antistress activity. Brahmi has a high antioxidant capacity, preventing oxidative damage (29, 46). Free radicals cause cellular damage, boosting antioxidant activity in other organs, primarily in the brain (33, 47). According to animal study findings, they have antioxidant activity in the hippocampus, frontal brain, and striatum (48). The expression of several enzymes involved in the production and scavenging of reactive oxygen species in the brain is modulated by BMEs. Because it showed the potential to be successful in stress, it was hypothesized that the herb's adaptogenic qualities would help manage stress-related disorders(45, 49). To stress alone and with doses of BME, the activity of the CYP 450-dependent enzymes 7-pentoxyresorufin-odealkkylase and 7-ethoxyresorufin-demethylase increased in all brain areas. It was suggested as a possible adaptive response to stress, but more research is needed. According to the findings, BME can control the activities of Hsp70, CYP 450, and SOD, allowing the brain to be better prepared to respond to stressful situations (35, 50).

Anti-Depressant Activity

Depression is a frequent life-threatening disorder that affects many people. It has lower levels of brain neurotransmitters such dopamine, serotonin, and norepinephrine (34). Substances influence the body's hormonal balance as well as the stress hormone. Its leaf raises serotonin levels in the brain, reducing anxiety and uneasiness and allowing the mind to relax(40, 51). It was found to have intense anti-depressant activity in the most regularly used behaviour paradigms in animal models of depression, namely the forced swim and learned helplessness tests. It was found to have anti-depressant efficacy in rodents comparable to that of the standard anti-depressant drug imipramine. The participation of serotonin and gamma-aminobutyric acid (GABA) in the mechanism of action is attributed to its anti-depressant and anxiolyticpotential(53).

Endocrine Effects

In mice, BME raised T4 by 41%. It is not stimulated, implying that the extract stimulates T4 synthesis and release at the epithelial level without influencing T4 to T3 conversion. Spermatogenesis and fertility were suppressed reversibly by BMEs. In mice, the therapy reduced sperm motility and viability and the number of spermatozoa in the cauda epididymis and testis, as well as causing changes in the somniferous tubules (55).

Free Radical Scavenging Effects

BM is an ayurvedic drug that has been utilized in therapeutic settings for memory enhancement, epilepsy, insomnia, and moderate sedation. The capacity of BM may explain, at least in part, the antistress, immunological modulatory, cognitive and enhancing, anti-inflammatory, and antiaging actions documented in experimental animals and clinical circumstances. It may justify additional research into its other therapeutic qualities (15, 37). Based on its antioxidant activity, this ayurvedic medication may effectively treat human disorders in which free radical generation is a factor (56). It has been linked to the development of cardiovascular and cerebrovascular illnesses, and creatine kinase (CK) and its isoforms have been suggested as sensitive markers for assessing cardiac and brain damage(57).

Memory Enhancer

The study found that improving several aspects of intelligence, such as immediate memory, arithmetic skill, and linguistic characteristics, had positive benefits by using Brahmi(58, 66).

Anti-Microbial Activity

Ethanol, Methanol, and chloroform were used to screen *Bacopa monnieri* antibacterial efficacy against several bacterial strains. *Streptococcus pyogens, Bacillus pumilus, Bacillus amayloliquefaciens, Salmonella typhi, Vulgarica, Micrococusluteus, Aspergillusniger, Bacillus megaterium, Bacillus subtilis* were all evaluated using chloroform, methanol and ethanol extracts. Based onthe growth inhibition zone, the bacteria's response to crude extracts differed depending on the solvent and the microorganisms (52, 59).

Hair Growth-Promoting Activity

Herbal hair oil is made from alcoholic extracts of *Emblica officinalis, Bacopa monnieri, Cyperus rotundus*, or the entire medication. The hair oil was made separately in varying concentrations of all three herbs and a constant percentage, using coconut oil as the foundation. In a primary skin irritation test, the hair growth was compared to a typical minoxidil 2 percent ethanolic solution using healthy albino rats and a hair length test. Hair oil formulations outperformed the others regarding follicular size expansion and anagen phase prolongation (60-62).

Gastrointestinal Effects

The effects of BME on the gastrointestinal tract have been studied in vitro in animals and humans. BME may benefit from irritable bowel syndrome and other disorders characterized by intestinal spasms (54, 63). Based on the findings, BME's spasmolytic effect on smooth muscles is primarily due to calcium influx inhibition, which applies to electrical impulse-mediated and receptor-mediated calcium channels in the cell membrane. In vitro and animal research have revealed that BM may have a protective effect. It has a preventive and curative impact on gastric ulcers (64-65).

CONCLUSION

There is little to no clinical evidence that *Bacopa monnieri* improves memory in healthy adults or adults with age-related memory problems. Furthermore, clinical evidence for treating Alzheimer's disease and depression with *Bacopa monnieri* is limited, as few studies have looked at Alzheimer's disease with a single herb formulation of *B. monnieri*, and none have looked at depression patients. Furthermore, more extensive, long-term studies comparing *B. monnieri* to current standard drugs are needed to see if it is a viable alternative medicine for earlier diseases. It should be standardized, and the same set of neuropsychological tests should be used in future meta-analysis investigations. The health benefits and nutritional content of *Bacopa* contributes to the medicinal world. The medical and food applications for this plant are possible, and it also contributes to the sustainable development goal (SDG) of promoting good health and well-being.

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Table 1: Morphological Character of *Bacopa monnieri*

Plant parts	Characters
Root	White in colour, cylindrical, 5 mm in diameter, longitudinally.
Stem	Glanton, branches are growing vertically, and nodes and internodes are present. They are about 1-1.5 cm long and 3-4mm in diameter, pale yellowish-green.
Leaf	Simple, opposite, and decussate, sessile, spatulate in shape, 0.6-2.5cm in length and3-8 in width, entire.
Flower	Pale blue or pinkish-white, solitary, axillary 0.6-3 cmin length., Corolla gamopetalous, stamens 4,didynamous, anthers two-celled, syncarpous ovary, two-chambered with many ovules, stigma bilobed.
Fruit	Glabrous capsule, 5 mm long, persistent calyx, ped1-3 CM long,purplish when fresh.
Seed	Numerous, minute, <1cm wide, elliptical, or irregular.

Table 2: Common Name of *Bacopa monnieri*(12)

Language	Common name
Bengali	Brahmisaka
Gujrati	Baam, jalanevari, kadaviluni
Hindi	Jalbuti, baam, jalnim, nirbrahmi
Kanada	Jalabrahmi, Nirubrahmi
Manipuri	Brahmisak
Marathi	Brahmi, Jalabrahmi, nirbrahmi
Oriya	Brahmi, prusniparnni

Assamese	Brahmi
Sanskrit	Brahmi, Tiktalonika
Tamil	Nir-P-Pirami, Piramiyam
Telegu	Sambrani Oku

Table 3: Chemical Composition of Brahmi

Component	Amount (/100gm)
Protein	2.1gm
Fat	0.6gm
Calcium	202.0mg
Moisture	88.4gm
Phosphorus	16.0gm
Nicotinic Acid	0.3
Energy	38 cal
Carbohydrates	5.9gm
Iron	7.8gm
Ash	1.9gm
Crude fibre	1.05gm
Ascorbic acid	63.0

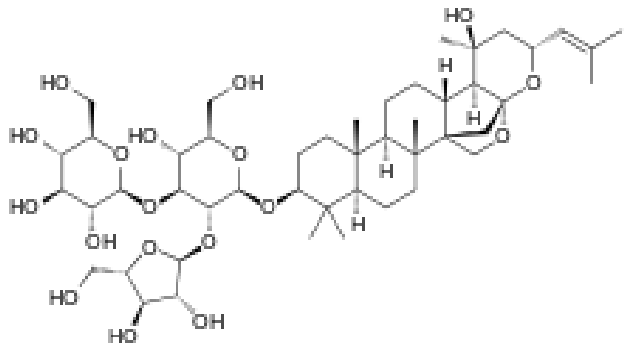

Fig 1: Chemical structure of bacoside A3, a principal constituent of bacoside A

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RESEARCH ARTICLE

Process Optimization of Biodiesel Production through Response Surface Methodology

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ABSTRACT

Biodiesel is fatty acid methyl ester produced through alkali or acid catalysed transesterification reaction of vegetable oils with methanol. The yield of the biodiesel conversion depends upon free fatty acid (FFA) content of vegetable oils used as feed stock. Other than FFA content, there are various reaction parameters affect the yield with respect to temperature, catalyst doses, reaction time, mixing rate and alcohol to oil molar ratio. the objective of this study was to study the RSM based optimization of biodiesel synthesis from non-edible simarouba oil by transesterification reaction in presence of methanol and calcium oxide based heterogenous catalyst derived from natural resources. A second order quadratic model was obtained by Design of Experiment statistical tool to predict the effect of reaction variables and their interaction effects on the percent biodiesel yield within experimental range. Based on the analysis of variance (ANOVA) data and the agreement of the experimental and predicted results on percent yield of biodiesel. Based on the experimental analysis and response surface methodology study, the optimum biodiesel yield of 96.55% was achieved at 95 minutes reaction time, 8.84% catalyst doses 11.75 methanol to oil molar ratio and 65℃ reaction temperature. The predicted yield was found in good agreement with the experimental value, with R^2= 0.9665 and it is proved the model adequacy for this study. The biodiesel produced at optimum reaction condition was confirmed by proton nuclear magnetic resonance (1H NMR) and its properties meets the standard biodiesel specification of IS15607:2016and enegry sustainbility.

Keywords: FAME, biodiesel, response surface methodology, ccd, catalyst, transesterification, sustainability.

INTRODUCTION

Biodiesel is fatty acid methyl ester (FAME), which is usually produced by the transesterification of virgin vegetable oils. Researchers have used various types of homogeneous or heterogeneous catalysed transesterification reactions for biodiesel production [1-5]. However, the homogenous catalyst uses for biodiesel production process is relatively fast with high biodiesel yields and minimal side reactions, it is still not cost competitive with petro-diesel. Since the catalyst cannot be recovered or reused, the washing step is a must for neutralization of biodiesel and removal of unreacted glycerides and catalyst, which, consequently, generate large amounts of wastewater causing waste management problems [6]. Heterogeneous solid catalysts are more beneficial over homogeneous catalyst with respect to low cost, low methanol solubility, non-corrosive, environmentally friendly and able to be reused for several times. Many researchers prepared biodiesel from plant seed oils by using heterogeneous catalyst derived from waste natural resources such as mud crab, egg shells, snail shells, oyster shells etc with biodiesel yield of 90-95% [1-5].

There are various reaction parameters affect the yield of biodiesel such as catalyst doses, oil to methanol molar ratio, reaction temperature, reaction time, and mixing rate. This method involves many parameters that affect the reaction and that require a set of experiments to optimize so many reaction variables, which would be laborious, time consuming and economically non-viable. The Central Composite Design (CCD) with Response Surface Methodology (RSM) is a valuable statistical technique for optimizing complex processes as it decreases the number of experiments needed to obtain enough data for a statistically valid result. Optimization of process parameters for the reaction process is the main step in surface response methods to achieve high quality without cost inflation [8]. In this paper, the synthesis of biodiesel from simarouba glauca oil was carried out using heterogeneous catalyst of natural resources. The process was developed and optimized by applying Design-Expert® 12 Software for design of experiments and response surface methodology. The effects of reaction variables such as reaction time, molar ratio of methanol to oil and catalyst concentration and their interaction effects on methyl ester yield was investigated.

MATERIALS AND METHODS

Materials

Non-edible oil from simarouba glauca seeds and heterogeneous catalyst from waste natural resources are utilized as feed stocks for biodiesel by transesterification reaction with methanol as solvent. The simarouba oil contains about 40% saturated fatty acids and 60% unsaturated fatty acid. The catalyst from natural resources contains calcium oxide of 95% with traces of other metal oxides.

Methods

Transesterification Reaction

Transesterification reaction was conducted with different doses of prepared catalyst, molar ratios of alcohol to oil (methanol: oil) and reaction time. The reaction was carried out in a 500ml flask with fitted water-cooled condenser on a heating source with magnetic stirrer. All the reaction carried out at constant temperature of 65±5℃ water bath and mixing rate of 600rpm magnetic stirrer. After completion of reaction, the whole content was centrifuged to separate the solid catalyst at bottom and the liquid parts get transferred to a separating funnel for separation of biodiesel and glycerol components. The glycerol discarded from the lower part of separating funnel and upper biodiesel layer collected and purified for removal of excess methanol and moistures. This purified biodiesel or fatty acid methyl ester stored in air tight glass container for detail analysis. Yield of fatty acid methyl ester (%) was calculated by dividing methyl ester yield with weight of the oil taken multiplied by 100 [11].

Statistical Design of Experiment

The transesterification reaction of simarouba oil and optimization of methyl ester was studied using Design of Experiment (DOE) version 12 (Stat-Ease, USA). Response Surface Methodogy (RSM) and Central Composite Design

(CCD) were used to find the interactions between the three variables and to predict the optimum condition for biodiesel yield [9-10]. These three reaction parameters selected as per the literature study and experiments conducted by various researchers. These parameters were reaction time (A), catalyst doses (B) and molar ratios of methanol to oil (C). Other two factors such as reaction temperature of 65℃ remains constant with the boiling temperature of methanol and mixing rate of 600 rpm for proper mixing of solid catalyst with oil. Biodiesel yield was used as the response variable. Table-1 shows the levels of the variables used and the ranges. A three-level-three-factors CCD (15 experiments) was adopted, consisting of 8 factorials, 6 axial points and 1 at centre point design. The yield of methyl ester was analyzed and optimized using the second order equation as follows,

$$y = \beta_0 + \sum_{i=1}^{k} \beta_i x_i + \sum_{i=1}^{k} \sum_{j=1}^{k} \beta_{ij} x_i x_j + \sum_{i=1}^{k} \beta_{ii} x_i^2 + \varepsilon$$

where Y is the yield of the reaction (% production of biodiesel), n is the number of factors, βo is the intercept term, βi, βij, and βii are the linear, interactive, and quadratic coefficients, respectively. Further, xi's are the independent variables (factors) under study.

Design-Expert® 12 Software was employed for regression analysis of the experimental data to fit the equation. The quality of the developed model was determined from the correlation coefficient (R^2) value and analysis of variance (ANOVA) was applied to establish their statistical significance at a confidence level of 95%. The statistical significance of the second-order model is determined by F value. When- ever the calculated F value is greater than the tabulated F value, the P value will be much smaller; it indicates the significance of the statistical model [8].

RESULTS AND DISCUSSIONS

Regression Model and Its Validation

Response Surface Methodology (RSM) was used to optimise the transesterification reaction and the experimental results were presented in table-2. Experimental yields were analyzed to get a regression model and compared with the experimental values. The estimated coefficient of regression model is given in table-3. Based on the CCD design and experimental results, regression analysis generated the following quadratic equation in terms of coded factors for the yield of biodiesel as shown as:

$Y = 95.56 + 3.21A + 2.57B + 3.40C – AB + 1AC + 0.25BC – 2.75\ A^2 - 7B^2 – 3.46C^2$

Where Y is the FAME yield whereas the coded terms A, B and C represent reaction time, catalyst loading and methanol to oil molar ratio respectively. Positive (+) signs in front of each terms indicates the synergic effect while negative (-) sign indicates antagonistic effect. Therefore, A,B,C, AC, BC terms play an important role in increasing the FAME yield where as A^2, B^2, C^2 and AC had a negative effect that decreases the FAME yield. To test the fit of the model, the determination coefficient R^2 was evaluated. In this case, the value of $R^2 = 0.9665$, indicates that the model could explain 96.65% of the variability in the biodiesel yield. The closer the R^2 value to the unity, better the model fit in reasonable agreement of experimental and predicted results. The relationship is illustrated in Fig1 as a linearity. A linear line was obtained, indicated that this model provided a good approximation to the experimental yields.

Response Surface Analysis

RSM has been applied successfully for optimization of biodiesel preparation from simraouba oil using heterogeneous biocatalyst. The interactive effects of the process variables on the transesterification efficiency were studied by plotting three-dimensional surface curves against any two independent variables, while keeping other variable at their central (0) level. It is visualized by the yield of biodiesel in relation to the reaction time, catalyst doses and methanol to oil molar ratio in figure-2

The elliptical shape of the curves indicates a good interaction of the two variables and circular shape indicates no interaction between the variables. The curves obtained in this study showed that there is a relative significant interaction between all the variables. The stationary point or central point is the point at which the slope of the contour is zero in all directions. The coordinates of the central point within the highest contour levels in each of the plots will correspond to the optimum values of the respective variables. The maximum predicted yield is indicated by the surface confined in the smallest curve of the contour diagram.

The optimal condition for this study was 8.84 wt% of catalyst, 11.75 methanol/oil molar ratio and reaction time of 95 minutes. To evaluate the accuracy of the developed model, The transesterification reaction was carried out with these optimum parameters at 65°C with constant mixing rate of 600rpm. The experimental biodiesel yield was 95.55%, which is in good agreement with the predicted yield 96.62%, with relatively small percentage error (1.10 %). This indicated that the proposed statistical model was suitable for prediction of optimized biodiesel yield and for optimization of transesterification process. In addition, investigation on residuals to validate the adequacy of the model was performed. Residual is the difference between the observed response and predicted response. This analysis was examined using the normal probability plot of residuals as shown in Fig1(a). The normal probability plot of the residuals shows that the errors are distributed normally in a straight line and insignificant.

CONCLUSION

In this work, a study was carried out on the optimization of simarouba glauca seed oil transesterification reaction by response surface methodology (RSM). The process parameters for transesterification reaction such as: reaction time, catalyst doses and methanol/oil molar ratio were investigated. The reaction temperature of 65C and mixing rate of 600rpm kept constant for all reactions. The analysis of variance (ANOVA) showed that a satisfactory result was obtained. The statistical model developed for predicting biodiesel yield showed a good agreement between the experimental and calculated values (> 0.96) demonstrating the usefulness of regression analysis as a tool for optimization purposes. Hence, the experimental results suggested the optimal condition of 95 minutes reaction period, 11.7:1 methanol/oil molar ratio and 8.84wt% catalyst doses. This optimized condition was validated with the actual biodiesel yield of 96%. The biodiesel produced at optimum reaction condition was confirmed by proton nuclear magnetic resonance (1H NMR) and its properties meet the standard biodiesel specification of IS15607:2016and can be effective measures for affodable and clean energy

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Table 1: Level Of Reaction Variables

Factors	Unit	symbol	Range and level		
			-1	0	+1
Reaction Time	Min.	A	60	65	70
Catalyst doses	wt. %	B	4	8	12
Molar ratio of Methanol to Oil (M:O)	M	C	6	9	12

Table 2: Experimental Design Matrix with Experimental and Predicted Values of Biodiesel Yield

Run	A: Reaction Time (minute)	B: Catalyst (%wt.)	C: Methanol to oil ratio (mol/mol)	Experimental BD Yield (%)	Predicted BD Yield (%)	Residual
1	60	4	6	77.50	73.72	3.78
2	40	8	9	72.00	81.04	-9.04
3	90	1.3	9	69.00	71.81	-2.81
4	90	8	14	88.00	91.24	-3.24
5	90	8	9	96.00	94.69	1.31
6	120	12	12	94.00	92.39	1.61
7	60	12	12	90.00	85.87	4.13
8	140	8	9	93.00	91.58	1.42
9	120	12	6	82.00	81.78	0.22
10	120	4	6	81.00	79.74	1.26
11	60	4	12	80.00	74.83	5.17
12	90	8	3.95	77.00	81.38	-4.38
13	60	12	6	90.00	83.51	6.49
14	120	4	12	88.00	89.10	-1.10
15	90	14.73	9	78.00	82.81	-4.81

Table 3: ANOVA Table For Response Surface Quadratic Model

Source	Sum of Squares	df	Mean Square	F-value	p-value	Remarks
Model	728.45	9	80.94	16.01	0.0035	Significant
A-Time	140.88	1	140.88	27.86	0.0032	Significant
B-Catalyst	90.40	1	90.40	17.88	0.0083	Significant
C-Molar ratio	158.33	1	158.33	31.31	0.0025	Significant
AB	8.00	1	8.00	1.58	0.2640	Slightly Significant
AC	8.00	1	8.00	1.58	0.2640	Slightly Significant
BC	0.5000	1	0.5000	0.0989	0.7659	slightly Significant
A^2	45.92	1	45.92	9.08	0.0296	Significant

B^2	296.34	1	296.34	58.61	0.0006	Significant
C^2	72.53	1	72.53	14.34	0.0128	Significant
Residual	25.28	5	5.06			
Cor Total	753.73	14				

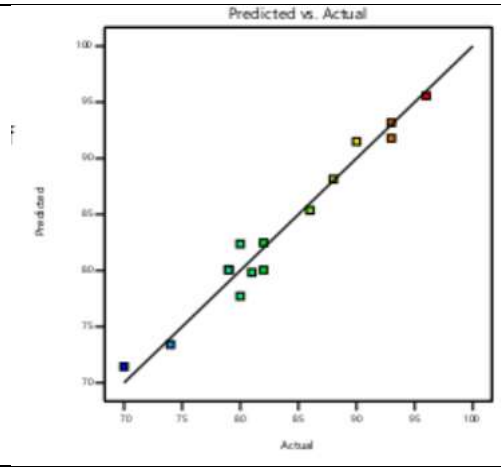

Fig 1: (a) Predicted versus actual response.

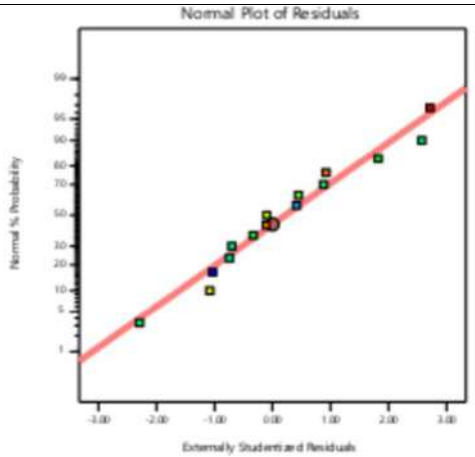

Fig 1: (b) Normality probability plot of the residual

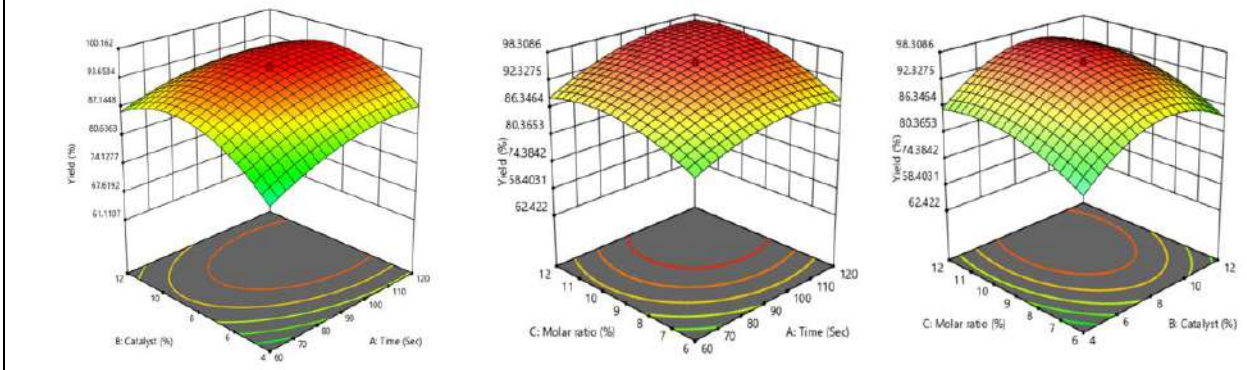

Fig 2: Three-Dimensional RSM plots between yield and reaction variables.

REVIEW ARTICLE

The Different Aspects of DNA Methylation In Mammalian Disease and Development: A Review

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ABSTRACT

The importance of DNA methylation in the development of mammalian embryos cannot be ignored. DNA methylation serves a variety of purposes: it is linked to the suppression of transposons and genes, as well as gene bodies that are actively transcribed and, in certain situations, activates genes. Sensitive approaches for studying DNA methylation mechanisms in a minimal number of cells have emerged in recent years. Because of the application of these technologies, we now have a better grasp of the dynamics and heterogeneity of DNA methylation in embryos and particular organs. When combined with genetic investigations, it is becoming clear that the control of both the elimination and reinstatement of DNA methylation differs significantly between phases of development. The processes and roles of DNA methylation and demethylation, which include promoters, gene bodies, and transposable elements with high CpG content in mice and humans, are inevitable. In embryonic, germline, and somatic cell development, the progressive elimination and reinstatement of methylation are also equally significant. Further studies to unravel the underlying epigenomic principles and mechanisms in various patho-physiological disorders will pave way forward in developing pharmaceutical strategies.

Keywords: DNA methylation, demethylation, epigenomics, patho-physiology, pharmaceutical.

INTRODUCTION

The methylation of cytosine's fifth carbon was first observed in bacteria before being detected in the first eukaryote. [1]. Because eukaryotic 5mC is commonly observed in the presence of complementary CpG dinucleotides [1-3] ,

which has long been thought to exist as a method for detecting DNA replication, where the hemimethylated CpG site is consistently methylated, and the daughter strand is also methylated simultaneously [4], Dignified tests later confirmed this notion [5]. Earlier in vitro and in vivo investigations indicated that 5mC was linked to transcription suppression. [6-8]. As a result, classic epigenetic processes such as imprinting on the genome [9–12] and X-chromosome disruption have been related to DNA methylation (XCI) [13,14]. Many eukaryotic lineages, including many mammals, have lost DNA cytosine methylation [15,16]; model organisms like Caenorhabditis elegans, Drosophila melanogaster, baker's yeasts, and fission yeasts, contain almost no 5mC. In actuality, 5mC comes at a price: because of its capacity to spontaneously deaminate, 5mC is innately mutagenic, resulting in C-T conversions [17]. CpG methylation results in reduced CpG content in organisms [18, 19]. For example, mammals have around 5-fold fewer CpG dinucleotides, which is totally based on the nucleotide makeup of their genome. It has also been demonstrated that DNA methyltransferases (DNMTs) induce damage to 3-meC lesions in DNA [20]. Because of the constant founder of DNMTs with a specific alkylation and the maintenance enzyme (ALKBH2), eukaryotes are able to tolerate DNA methylation. Interestingly, despite tissue-specific differences, mammalian genomes have relatively high CpG methylation levels, and about 70–80% of the CpGs in mammalian genomes are methylated [21]. DNMT-deficient mice also have significant developmental defects that lead to early embryonic death [22,23]. The genetic prerequisites for these epigenome reprogramming pathways have lately undergone significant development. Precision epigenome editing methods are being developed and employed to evaluate the role of DNA methylation at the locus level, while genome-wide approaches with base-pair precision have been created to unravel the complexity of DNA methylation dynamics throughout embryonic development. This review addresses recent major breakthroughs in our knowledge of the activities of DNA methylation during mammalian development, including its creation, maintenance, and erasure. The current study emphasizes the importance of critical proteins in maintaining human cell physiology and thus aligns with the objectives of one of the United Nations formulated Sustainable Development Goals (SDGs); SDG3 which ensures healthy lives and promotes well-being for all at all stages.

DNA Methylation's Cellular Roles

Methylation's Scribes And Erasers

The three primary steps of DNA methylation are formation (de novo DNA methylation), maintenance, and demethylation. The two main de novo methylating enzymes are DNMT3A and DNMT3B [32,33] and beyond that, ATRX DNMT3- DNMT3L (ADD) and PWWP, have a conserved DNMT domain or MTase domain in the c terminal and two chromatin accessing motifs. DNMT3L is an inactive DNMT catalyst that enhances the activity of DNMT3A and DNMT3B [34,35] , especially in the germline. In CpG-rich portions of routinely active genes, where the trimethylated histone H3 Lys4 (H3K4me3) [36] is generally high, DNA methylation is typically avoided. The ADD domain, which connects to the K4 residue of the H3 tails, is repelled by an increasing ratio of methyl moieties at K4, with H3K4me3 being the most resensitizing of the ADD domains [34,37,38]. When not connected to H3K4, ADD binds to the MTase domain, inhibiting the action of the DNMT3 enzyme; however, connecting the ADD pattern to unmethylated H3K4 frees the MTase domain, enabling DNA methylation to continue [39]. Highly transcribed gene bodies, in contrast to active promoters, have a lot of DNA methylation [1,2,29]. At replication forks, UHRF1 preferentially interacts with hemimethylated CpG dinucleotides, along with the TUDOR-PHD [47-50] tandem area, SET and SRA domains [45,46], as well as H3K9me2 and H3K9me3, because the Replication Focus Targeting Sequence (RFTS) domain is incorporated into the active MTase area, which corresponds to the ADD domains of the DNMT3 enzymes[51-53], whereas DNMT1 is auto-inhibitory. Through its ubiquitin-like (UBL) domain, UHRF1 binds to DNMT1, liberating it from auto-inhibition and allowing RFTS to link to ubiquitylated histone H3 tails via UHRF1's RING finger region [54,55]. The daughter DNA strand is then methylated by DNMT1. As a result, mouse ESCs with a mutant UHRF1 resemble the Dnmt1 mutant's DNA methylation phenotype [45,46].

Inhibition of Transcription by DNA Methylation

The association between DNA methylation and increased gene silencing having a high concentration of CpG dinucleotides at regulators has long been known as an inhibitory effect of DNA methylation in transcription [47-65].

However, its progression towards transcriptional repression has not been fully resolved, as the methyl marker itself is not present to induce silencing. The accessible chromatin regions are often weakly methylated or not methylated, indicating that transcription factors and the processes of DNA methylation are collectively unique [66]. DNA methylation could also make a contribution to heterochromatin formation by recruiting chromatin-to-chromatin modulators and remodelling by DNMT proteins: de novo DNMT proteins acting in association with lymphocyte regenerating chromatin helicase (LSH), H3K9 methyltransferase, and histone deacetylases [68–75]. Protein enrollment can also take place via the 5mC and read heads, as well as the protein's methyl CpG binding domain (MBD)[76,77]. MBD1-MBD4 and methyl-CpG binding protein 2 are the five MBD proteins found in mammals (MeCP2). Four MBD proteins demonstrated a linear association between increased CpG binding and enhanced CpG [78] methylation, whereas MBD3 does not prefer methylated cells [79]. All MBDs coordinate with changes in the nucleosome and the histone deacetylase complex in order to silence genes [80,81].

Inactivation of the X Chromosome

In female animals, the cis activity of the X inactive-specific non-coding RNA (XIST) transcription silences each cell having one X chromosome at random. Methylated X-linked CGIs appear to be common, preferably late during this XCI process and work as the last key inserted after gene silencing [82–90]. Silencing of the X-linked CGI promoter in mice is primarily dependent on DNMT3B—thus other DNMT3s are also required [91], and in a domain of X-linked CGI it also needs preservation of the structure of the hinge domain adaptability of chromosomes comprising the SMCHD1 gene [91–93]. SMCHD1 is also implicated in XCI in humans, although its relationship with DNA methylation has yet to be discovered. The precise method of DNMT3B activation during XCI is unknown, as why does SMCHD1 acquire such a critical XCI-specific role? Perhaps the highly controlled and hierarchical heterochromia of the X chromosome generates a unique chromatin environment that promotes X-linked CGI DNA methylation.

Genes have a Germline Specificity

Upon the commencement of somatic differentiation following embryo implantation, DNMT3B-mediated DNA methylation prevents the CGI regulator of germline-specific genes [27,116]. The parent genes are particularly susceptible to DNA methylation loss and are not expressed in DNMT1 [117] of ESCs of triple knockout mice. Human fibroblasts depleted of DNMT1 [118], embryos of mutant mice with DNMT3B [27,119], and humans with DNMT3B [27,119] can be related to diseases caused by DNMT3B [120] mutations. What causes the germline CGI promoters, of which CGIs are represented by only 5%, to depend on DNA methylation while the maximum of germ cells are CpG-rich promoter genes that are leftover as unmethylated? The cause might be the PRC1.6 non-conical Polycomb 1 (PRC1) repressor complex, which is a germline repressor promotor in mouse ESCs [121,122]. MAX [121,124], MGA [121,122], and E2F6 are among the DNA123-binding proteins in the group that enables sequence-specific targeting (ref.125). PRC1.6 also binds to L3MBTL2, which connects to H3K9 G9A methyltransferase (also known as EHMT2). G9A mutant mouse embryos are deficient in a large number of germline-specific genes [119]. Participation of elements of PRC1.6 in germline-specified gene repression is still unknown, such as how germline gene CGI is addressed by DNMT3B but not by DNMT3A. Unlike many other CGI promoters, which are immune to de novo DNA methylation, they are being transferred as germline CGIs that have acquired specific sequenced mechanisms for imposing processes of DNA methylation to guarantee lifelong somatic silencing.

The Biological Consequences of Rejecting Methylation Reprogramming

Regardless of the fact that embryonic and germline demethylation occur everywhere around the world, a considerable proportion of DNA methylation persists at the end of both phases. The prospect of intergenerational and maybe transgenerational epigenetic inheritance has piqued interest as a result of this discovery. Around 20% of CpGs in the inner cell mass of early embryonic conceptions in both mice [147-149] and humans maintain gamete-inherited methylation. They are linked to sequence-specific DNA demethylation, which is resistant via KRAB–ZFP. The recruitment of KAP1 is particularly aligned to ICRs, as expected, given the intergenerational nature of genomic imprinting [111, 113, 114].

On the other hand, ICRs make up a very small proportion of the genome. Hundreds of "transitory" methylation indentations, which are primarily obtained from the female gamete, maintain maternal-specific DNA methylation until the blastocyst stage, most likely through KRAB–ZFPdependent protection, and then lose it after implantation via DNA demethylation or remethylation, exist in contrast to these conventional ICRs. Not just before, but also after implantation, the maternal genome retains much more DNA methylation than the paternal genome, notably in placental tissues [130,151], suggesting that this process is more common in humans. According to research on the Zdbf2 locus, transient hypomethylation of the paternal allele can result in long-term imprinting via a sequence of epigenetic alterations that limit neonate size. It will take more research to see if other fleeting perceptions have a significant effect. Transposable elements, rather than single-copy sequences, are responsible for the majority of the surviving blastocyst gametic methylation. DNA hypomethylation persists in the developing placenta, which is mostly composed of ExE cells [144]. In the epiblast, hypomethylation is linked to reduced DNMT3 enzyme activity, and even retrotransposons are severely hypomethylated.

Epigenetic Consequences, Genetic Illnesses

Variations in the DNMT and TET genes have been linked to a number of illnesses. Its impacts on DNA methylation patterns are as diverse as its tissue and clinical features, which range from immune system disorders to developmental abnormalities, neurodegeneration, and malignancies of the blood. Many morphologically similar diseases have been related to genes that exhibit DNA methylation and demethylation features that have yet to be explained. The identification of genetic alterations in DNA methylation pathways has substantially increased our knowledge of the complexities and variations of DNA methylation-based gene regulation.

Immune Disorders and DNMT3B

The immune deficiency, centromeric disintegration, and aesthetic defects were the first to be connected to a lack of prenatal DNA methylation [154]. ICF patients have a rare antibody shortage, which leads to chronic and frequently life-threatening disorders. ICF is recognised by a chromosomal abnormality characterised by multiradiated chromosomes 1, 9, and 16, as well as particular demethylation of pericentromeric satellite repeats II and III. The majority of ICF fatalities are caused by recessive defects in the DNMT3B gene, which characterises ICF1. Many ICF1 alterations will be single amino acid changes or reductions, correlating to decreased rather than destroyed DNMT3B function, according to the established mortality of mouse models with Dnmt3B loss-of-function mutations [155]. ICF has been linked to germline mutations in three additional genes, zinc finger and BTB domain-containing protein 24 (ZBTB24; defines ICF2), cell division cycle-associated protein 7 (CDCA7; ICF3), and HELLS (which encodes LSH; ICF4), whose product lines are thought to aid DNA methylation [150-155].

DNMT3A, Cellular Expansion, and Cancer

Heterozygous genetic variants in DNMT3A are linked to early prenatal growth abnormalities, with different developmental patterns based upon the origin of the alterations. In people with anencephaly, Down syndrome, misspelling and gain-of-function alterations in the PWWP domain have been reported, a set of disorders characterised by a significant but proportional decrease in both body and head size. All of those are gain-of-function alterations that impair DNMT3A's interactions with H3K36me3 groups that change its nucleosome binding affinity. A PWWP gain-of-function mutation in mice mimicked the body shape and brain mass alterations seen in severely deformed Down's syndrome, as well as aberrant methylation phenotypes [156-161]. Tatton-Brown–Rahman syndrome is caused by heterozygous DNMT3A haplo insufficiency mutations, which result in macrocephalic overgrowth and mild cognitive impairment. The PWWP domain (upstream of the gain-of-function mutations), the ADD domain, and the MTase domain of the DNMT3A gene have all been shown to carry TBRS mutations. While the large genomic areas that are hypermethylated in DNMT3A gain-of-function mutants appear to be unaffected in TBRS [162-164] patients, the ramifications of these modifications on DNA methylation mechanisms are yet unknown. Given that DNMT3A deficiency promotes stem cell hyperproliferation in a variety of organs in mice [165].

Reflections and Outlooks for the Future

Since its discovery in the 1980s, the number of journals citing DNMT1 has increased dramatically, as has scholarly interest in DNA methylation, according to Timothy Bestor, one of the mammalian DNA methylation field's founding fathers. Much is unknown about DNA methylation processes and variations, despite significant advances. Like, why do embryos fail to survive at a young age when they are lacking DNA methylation? Deficiency of DNA methylation appears to be a given prediction, although it is exactly what causes prenatal failure: aberrant protein-coding gene expression; massive derepression of modifiable factors; genome fragility; a mix of all of these, perhaps less evident? Moreover, DNA methylation is typically unregulated in cancerous cells, and the genes DNMT3 and another one, TET, are commonly altered. So, which methylation alterations are important for cancer development and which ones will be merely coincidental? Now, we are approaching an age of extraordinary genetic tools, precise and extremely accurate decoding technology, as well as the capacity to surgically modify DNA methylation. Massive challenges that had previously proven insurmountable suddenly became attainable. Nonetheless, obstacles persist. While analysing DNA methylation sequences linked with a specific cell type or chronological phase, for instance, we can only extrapolate relatively stable rates of methylation caused by the conflicting functions of the enzymes that create and eliminate DNA methylation. A series of measurements of DNA methylation cycles is required. Integrating theoretically and experimentally, techniques should allow us to simulate the concepts of local DNA methylation kinetics, allowing us to better grasp where and why instabilities emerge in the ageing process and cancer. Moreover, a key unanswered question is related to the biology of mammalian DNA methylation, which plays a major role in substantial demethylation in the developing embryo and germline, specifically if it is essential for the creation of pluripotency. At the moment, it seems difficult to halt this practise of evaluating the embryonic development impacts of DNA methylation.

Statements and Declarations

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval and Consent to Participate

It is a review article. No ethics approval is required.

Consent to Publish

Not applicable.

Human and Animal Rights

It is a review article. No animals were used in the study.

Availability of Data and Materials

Not applicable.

Credit Authorship Contribution Statement

All the authors have substantial contribution for the preparation of the manuscript. Gagan Kumar Panigrahi and Ankita Priyadarshani conceived the idea. Data curation and writing: Ankita Priyadarshani, Jyotishree Acharya, Annapurna Sahoo, Bishnupriya Patalsingh and Gagan Kumar Panigrahi. All the authors have read and approved the final manuscript before submission.

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RESEARCH ARTICLE

Effects of Hall Current and Rotation on Magneto Hydro Dynamic (MHD) Couette Flow of Class-II with Induced Magnetic Field

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ABSTRACT

An attempt has been made to study the effects of Hall current and rotation on MHD Couette flow of Class-II of a viscous, incompressible, and electrically conducting fluid in a rotating system in the presence of a uniform transverse magnetic field, applied parallel to the axis of rotation, considering induced magnetic field into account when both the plates of the channel are perfectly conducting. Governing equations, for the fluid flow problem, are solved analytically and exact solution in obtained in closed form. Expressions for shear stress at both the lower and upper plates due to primary and secondary flows and mass flow rates in the primary and secondary flow directions are derived. Using MATLAB software, the numerical values of velocity and induced magnetic field are computed and are displayed graphically versus channel width variable η for various values of pertinent flow parameters (Hall current parameter m, rotation parameter K^2 and magnetic parameter M^2) whereas numerical values of shear stress at the lower and upper plates due to primary and secondary flows and mass flow rates in the primary and secondary flow directions are presented in tabular form for various values of pertinent flow parameters.

Keywords: MHD, Couette flow,Hall current, Coriolis force.

INTRODUCTION

The idea of rotating fluids [1] is extremely important since it appears in a variety of natural phenomena and has implications in a variety of technical scenarios that are driven directly by the "*Coriolis force*." It is generally accepted that the fluid flow in Earth's liquid core is considerably influenced by Coriolis and magnetic forces. It is well known that a large number of astronomical bodies (i.e. "Sun, Earth, Jupiter, Magnetic Stars and Pulsars") possess fluid

interiors and (at least surface) magnetic field. In addition to it such studies may find application in fluid engineering (e.g. turbo-machines, rotating MHD generators, nuclear reactors etc). The study of unsteady MHD Couette flow in a rotating system is important because fluid transients might occur when MHD devices are turned on. Taking into account these facts, Jana *et al*. [2], Seth and Maiti [3], Seth *et al*. [4-12], Chandran*et al*. [13] Singh *et al*. [14], Singh [15], Hayat *et al*. [16, 17], Guria*et al*. [8], Das *et al*. [19], Jha and Apere [20, 21], Seth and Singh [22-24] and Guchchait et al. [25] investigated the MHD Couette flow in a rotating system considering several perspectives. Taking into account the investigations made above on MHD Couette flow in a rotating system, we are in an opinion that MHD Couette flow may be induced in two ways [Seth *et al*. [8, 11, 12], Seth and Singh [22-24]] and it may be recognized as (i) "MHD Couette flow of class-I" and (ii) "MHD Couette flow of class-II". The fluid flow induced due to movement of a plate, when the fluid is bounded by a stationary plate placed at a finite distance from the moving plate, may be regarded as "MHD Couette flow of class-I". This fluid flow is similar to the flow generated due to movement of a plate when the free stream is stationary. The fluid flow past a stationary plate, which is induced due to movement of a plate placed at a finite distance from the stationary plate, may be recognized as "MHD Couette flow of class-II". This fluid flow is similar to the flow past a stationary plate due to moving free stream. Investigations carried out by Jana *et al*. [2], Seth and Maiti [3], Seth *et al*. [4-7, 9, 10], Chandran *et al*. [13], Singh *et al*. [14], Guria*et al*. [18], Das *et al*. [19], Jha and Apere [20, 21] and Guchchait *et al*. [25] belong to "MHD Couette flow of class-I" whereas research studies made by Singh [15], Hayat *et al*. [16, 17], Seth and Singh [22-24] and Seth *et al*. [8, 11, 12] belong to "MHD Couette flow of class-II".

As Cowling [26] points out, the effects of "*Hall current*" become important in an ionised fluid where density is low and/or the magnetic field is considerably strong. "*Hall current*" is likely to be important in underground energy storage system, magnetometer, Hall effect sensors and spacecraft propulsion. Sherman and Sutton [27] considered the effects of "*Hall current*" on the efficiency of MHD power generator.Hall current and rotation are likely to be important in many sciences and engineering applications viz. MHD power generators, MHD pumps, MHD accelerators, geophysical and astrophysical problems of interest as well as in flows of plasmas in laboratory. Since Hall current as well as rotation induces secondary flow in the fluid, therefore, it seems to be important to compare and contrast the effects of these two agencies and also to study their combined effects. Keeping in view the importance of such study Jana and Datta [28], Mandal *et al*. [29], Mandal and Mandal [30], Seth and Ahmad [31], Ghosh [32] and Jha and Apere [20, 21] discussed MHD Couette flow of class-I in a rotating system with Hall effects considering different aspects of the problem. Seth *et al*. [11, 12] investigated the effects of Hall current on steady hydromagneticCouette flow of class-II of a viscous, incompressible and electrically conducting fluid in a rotating system in the presence of a uniform transverse magnetic field taking induced magnetic field into account. Seth et al. [12] considered both the plates of the channel as electrically not conducting in their study while one of the plates of the channel has been considered as perfectly conducting in the research study made by Seth *et al*. [11].

Motivated by the above mentioned investigations, the present study aims to analyze the effects of Hall current and rotation on MHD Couette flow of Class-II of a viscous, incompressible, and electrically conducting fluid in a rotating system in the presence of a uniform transverse magnetic field, applied parallel to the axis of rotation, considering induced magnetic field into account when both the plates of the channel are perfectly conducting. The beauty of this work is it fulfills the SDGs 4 (Quality education), 8 (Decent Work & Economic Growth), and 9 (Industry, Innovation and Infrastructure). Authors are confident enough that the present study will definitely enable the researcher to emphasize their understanding towards sustainable development goals like quality education; economic growth; industry, innovation and infrastructural developments.

Mathematical Model

Consider steady Couette flow of a viscous, incompressible, and electrically conducting fluid within a parallel plate channel (positions of the plates are at $z = 0$ and $z = L$), in the presence of a uniform transverse magnetic field B_0 applied in a direction parallel to z-axis. Fluid and channel rotate (in anti-clockwise direction) in unison with uniform angular velocity Ω about *z* - axis. Fluid flow within the channel is induced due to movement of upper plate $z = L$

in x - direction with uniform velocity U_0 whereas lower plate $z=0$ is kept fixed. Geometry of the problem is presented in figure 1. Since plates of the channel are of infinite length along x and z directions and fluid flow is steady so all the physical quantities, except pressure, are functions of $z$only. The fluid velocity $\vec{q}$ and magnetic induction vector $\vec{B}$ are assumed in the following form

$$\vec{q}=\left(u_x,u_y,0\right);\qquad \vec{B}=\left(B_x',B_y',B_0\right) \tag{1}$$

This assumption is in agreement with the fundamental equations of Magnetohydrodynamics in a rotating frame of reference.

Under the assumptions, made above, the governing equations describing the fluid flow and induced magnetic field in rotating frame of reference become,

$$-2\Omega u_y=-\frac{1}{\rho}\frac{\partial p}{\partial x}+\upsilon\frac{d^2u_x}{dz^2}+\frac{B_0}{\rho\mu_e}\frac{dB_x'}{dz} \tag{2}$$

$$2\Omega u_x=-\frac{1}{\rho}\frac{\partial p}{\partial y}+\upsilon\frac{d^2u_y}{dz^2}+\frac{B_0}{\rho\mu_e}\frac{dB_y'}{dz} \tag{3}$$

$$0=-\frac{1}{\rho}\frac{\partial p}{\partial z} \tag{4}$$

$$0=B_0\frac{du_x}{dz}+\upsilon_m\frac{d^2B_x'}{dz^2}+m\upsilon_m\frac{d^2B_y'}{dz^2} \tag{5}$$

$$0=B_0\frac{du_y}{dz}+\upsilon_m\frac{d^2B_y'}{dz^2}-m\upsilon_m\frac{d^2B_x'}{dz^2} \tag{6}$$

where $p=\left(p'+B^2/2\mu_e\right)$, σ, μ_e, ρ, υ, $\upsilon_m=\frac{1}{\sigma\mu_e}$, $m=\omega_e\tau_e$, ω_e and τ_e are modified pressure including fluid pressure, centrifugal force and magnetohydrodynamic pressure; electrical conductivity, magnetic permeability, density, kinematic coefficient of viscosity, magnetic viscosity, Hall current parameter, cyclotron frequency and electron collision time respectively.

Both the plates of the channel are considered as perfectly conducting. Thus the boundary conditions for fluid velocity and induced magnetic field are given by

$$u_x=0,\ u_y=0 \text{ at } z=0;\qquad \frac{dB_x'}{dz}=0,\ =\frac{dB_y'}{dz}=0 \text{ at } z=0 \tag{7}$$

$$u_x=U_0,\ u_y=0 \text{ at } z=L;\qquad \frac{dB_x'}{dz}=0,\ =\frac{dB_y'}{dz}=0 \text{ at } z=L \tag{8}$$

Equation (4) shows that the modified pressure p is constant along z-axis i.e. the axis of rotation. For MHD Couette flow of class-I, the pressure gradient terms $-\frac{1}{\rho}\frac{\partial p}{\partial x}$ and $-\frac{1}{\rho}\frac{\partial p}{\partial y}$, in equations (2) and (3) respectively, are not considered by researchers [Jana *et al*. [2], Seth and Maiti [3], Seth *et al*. [4, 6, 7], Chandran*et al*. [13], Singh *et al*. [14], Guria*et al*. [18], Das *et al*. [19], Jha and Apere [21] and Guchchait*et al*. [25]]. This assumption is valid in view of

conditions (7). For MHD Couette flow of class- II, values of the pressure gradient terms in equations (2) and (3) are obtained with the help of boundary conditions (8) which are given by

$$-\frac{1}{\rho}\frac{\partial p}{\partial x}=0\ ;\quad -\frac{1}{\rho}\frac{\partial p}{\partial y}=2\Omega U_0 \tag{9}$$

Using (9) in equations (2) and (3), we obtain

$$-2\Omega u_y=\upsilon\frac{\partial^2 u_x}{\partial z^2}+\frac{B_0}{\rho\mu_e}\frac{\partial B_x'}{\partial z} \tag{10}$$

$$2\Omega\left(u_x-U_0\right)=\upsilon\frac{\partial^2 u_y}{\partial z^2}+\frac{B_0}{\rho\mu_e}\frac{\partial B_y'}{\partial z} \tag{11}$$

Combining equation (5) and (10) with the equations (6) and (11) respectively and representing them in non-dimensional form, we obtain

$$0=\frac{dp}{d\eta}+\frac{d^2Q}{d\eta^2}-mi\frac{d^2Q}{d\eta^2} \tag{12}$$

$$2iK^2\left(P-1\right)=\frac{d^2P}{d\eta^2}+M^2\frac{dQ}{d\eta} \tag{13}$$

where,

$$\left.\begin{aligned}&P=u+iv,\ \ Q=b_x+ib_y,\ \ b_x=B_x/R_m,\ \ b_y=B_y/R_m,\\&\eta=z/L,\ \ u=u_x/U_0,\ \ v=u_y/U_0,\ \ B_x=B_x'/B_0,\ \ B_y=B_y'/B_0.\end{aligned}\right\} \tag{14}$$

In equations (12) and (13), $R_m=\sigma\mu_e U_0 L$ is magnetic Reynolds number, $K^2=\Omega L^2/\upsilon$ is rotation parameter which is reciprocal of Ekman number and $M^2=\sigma B_0^2L^2/\rho\upsilon$ is magnetic parameter which is square of Hartmann number.

Boundary conditions (7) and (8), in non-dimensional form, become

$$p=0,\ \ \frac{dQ}{d\eta}=0 \text{ at } \eta=0;\quad p=1,\ \ \frac{dQ}{d\eta}=0 \text{ at } \eta=1 \tag{15}$$

Solution of equations (12) and (13), with the help of the boundary conditions (15), are given by

$$P\left(\eta\right)=\left[\frac{1}{\sinh\lambda}\left(1+\frac{2iK^2}{\lambda^2}\cosh\lambda-\frac{2iK^2}{\lambda^2}\right)\right]\sinh\lambda\eta-\frac{2iK^2}{\lambda^2}\left(\cosh\lambda\eta-1\right) \tag{16}$$

$$\begin{aligned}Q\left(\eta\right)=&\frac{1}{M^2}\left[\frac{2iK^2}{\sinh\lambda}\cosh\lambda\eta+\frac{\left(2iK^2\right)^2}{\lambda^2}\cosh\lambda.\cosh\lambda\eta-\frac{\left(2iK^2\right)^2}{\lambda^2}\cosh\lambda\eta-\frac{\left(2iK^2\right)^2}{\lambda^2}\sinh\lambda\eta+\frac{\left(2iK^2\right)^2}{\lambda^2}\eta\right]\\&-\frac{1}{M^2}\left[2iK^2\eta+\frac{\lambda^2}{\sinh\lambda}\cosh\lambda\eta+\frac{2iK^2}{\lambda}\cosh\lambda.\cosh\lambda\eta-\frac{2iK^2}{\lambda}\cosh\lambda\eta-\frac{2iK^2}{\lambda}\sinh\lambda\eta\right]\end{aligned} \tag{17}$$

where,

$$\lambda=\alpha+i\beta \tag{18a}$$

$$\alpha,\beta=\frac{1}{\sqrt{2\left(1+m^2\right)}}\left[\left\{M^4+\left(2K^2\left(1+m^2\right)+mM^2\right)^2\right\}^{\frac{1}{2}}\pm M^2\right]^{\frac{1}{2}} \quad (18b)$$

Shear Stress at the plates

Non dimensional shear stress components τ_x and τ_y, due to primary and secondary flow respectively, at stationary and moving plates of the channel are given by

$$\tau_x+i\tau_y\big|_{\eta=0}=\lambda\left[\frac{1}{\sinh\lambda}+\frac{2iK^2}{\lambda^2}\frac{\cosh\lambda}{\sinh\lambda}-\frac{2iK^2}{\lambda^2\sinh\lambda}\right] \quad (19)$$

$$\tau_x+i\tau_y\big|_{\eta=1}=\lambda\left[\frac{\cosh\lambda}{\sinh\lambda}+\frac{2iK^2}{\lambda^2}\frac{\cosh\lambda}{\sinh\lambda}\cosh\lambda-\frac{2iK^2}{\lambda^2}\frac{\cosh\lambda}{\sinh\lambda}-\frac{2iK^2}{\lambda^2}\sinh\lambda\right] \quad (20)$$

Mass Flow Rates

Non dimensional mass flow rates Q_x and Q_y, in the primary and secondary flow directions respectively, are given by

$$Q_x+iQ_y=\frac{\cosh\lambda}{\sinh\lambda}+\frac{2iK^2}{\lambda^2}\frac{\cosh\lambda}{\sinh\lambda}\cosh\lambda-\frac{2iK^2}{\lambda^2}\cosh\lambda+\frac{2iK^2}{\lambda^2} \quad (21)$$

RESULTS AND DISCUSSION

To study the effect of Hall current, rotation and applied magnetic field on the fluid velocity and the induced magnetic field , numerical values of the fluid velocity and induced magnetic field are computed and are depicted graphically versus channel width variable η in figure 2 to 7 for various values of Hall current parameter *m*, rotation parameter K^2 and magnetic parameter M^2 .It is evident from figure 2 and 3 that primary velocity u increases on increasing *m* and K^2 throughout the channel, while secondary velocity *v* increases on increasing *m* except at the vicinity of the lower plate. It also increases on increasing K^2 except just near to the upper plate. This implies that both Hall current and rotation induces primary as well as secondary velocity.

It is noticed from figure 4 that primary velocity is getting decreased on increasing M^2. The secondary velocity is getting decreased the lower half of the channel whereas it is getting increased in the upper half of the channel. This implies that magnetic field reduces primary velocity throughout the channel and secondary velocity in the lower half of the channel where has it has reverse effect on secondary velocity in the upper half of the channel. It is revealed from figure 5 that on increasing *m*, primary induced magnetic field decreases throughout the channel whereas the secondary induced magnetic field decreases at the vicinity of the upper plate. This implies that Hall current reduces primary induced magnetic field throughout the channel where as it reduces secondary induced magnetic field near the upper plate of the channel.

It is observed from figure 6 that primary induce magnetic field increases on increasing K^2 throughout the channel, the secondary induced magnetic field also increases, near the upper plate of the channel on the increasing K^2. This implies that rotation enhances primary induced magnetic field throughout the channel. It enhances secondary induced magnetic field only near the upper plate of the channel.It is seen from figure 7 that both the primary and

secondary induced magnetic field are getting increased by an increment in M^2. This implies that the applied magnetic field has the tendency to enhance both primary as well as secondary induced magnetic field. The numerical value of the shear stress at both the plates due to primary and secondary flows are computed and are presented in tabular from in tables 1 to 6 whereas that of mass flow rates in primary and secondary flow directions are displayed in tables 7 to 9 for various values of Hall current parameter *m*, rotation parameter K^2 and magnetic parameter M^2.

It is noticed from table 2.1 to 2.3 that primary shear stress at the stationary plate i.e. $\tau_x|_{\eta=0}$ increases whereas secondary shear stress at the stationary plate i.e. $\tau_y\big|_{\eta=0}$ decreases on increasing m. $\tau_x|_{\eta=0}$ and $\tau_y|_{\eta=0}$ increases on increasing K^2 where as both $\tau_x|_{\eta=0}$ and $\tau_y|_{\eta=0}$ decreases on increasing M^2. This implies that Hall current tends to enhanced primary shear stress at the stationary plate where as it has reversed effect on secondary shear stress at the stationary plate. Rotation tends to enhanced both primary and secondary shear stress at the stationary plate whereas magnetic field has reverse effect on these.

It is found from tables 4 to 6 that on increasing *m*, primary shear stress at the moving plate i.e. $\tau_x\big|_{\eta=1}$ decreases and secondary shear stress on the moving plate i.e. $\tau_y\big|_{\eta=1}$ increases except for $M^2=10$. Both $\tau_x|_{\eta=1}$ and $\tau_y|_{\eta=1}$ decreases on increasing K^2 and increases on increasing M^2. This implies that Hall current tends to reduce primary shear stress at the moving plate where as it has reverse effect on secondary stress at the moving plates except for $M^2=10$. Rotation has a tendency to reduce both the primary as well as secondary shear stress on the moving plate whereas magnetic field has reverse effect on these.

It is noticed from tables 7 to 9 that primary mass flow rate Q_x increases on increasing *m* whereas secondary mass flow rate Q_y decreases on increasing *m*. Both Q_x and Q_y increases on increasing K^2. Q_x decreases on increasing M^2. Q_y also decreases on increasing M^2 except for $m=1.75$. This implies that Hall current tends to enhanced primary mass flow rate where as it has reverse effect on secondary mass flow rate. Rotation tends to enhance both the primary and secondary mass flow rates. Magnetic field has a tendency to reduce primary mass flow rate while it has a tendency to enhance secondary mass flow rate except for $m=1.75$.

CONCLUSIONS

Present investigation deals with the theoretical study of effects of Hall current and rotation on MHD Couette flow of Class-II in a rotating system in the presence of a uniform transverse magnetic field. Significant outcomes are summarized below.

1. Hall current and rotation induces primary as well as secondary velocity.
2. Hall current reduces primary induced magnetic field throughout the channel where as it reduces secondary induced magnetic field near the upper plate of the channel.
3. Rotation enhances primary induced magnetic field throughout the channel. It enhances secondary induced magnetic field only near the upper plate of the channel.
4. Magnetic field has the tendency to enhance both primary as well as secondary induced magnetic field.

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Table 1: Shear stress at the stationary plate when $M^2 = 15$.

$K^2 \downarrow m \rightarrow$	$\tau_x\big\|_{\eta=0}$			$\tau_y\big\|_{\eta=0}$		
	0.75	1.25	1.75	0.75	1.25	1.75
1	0.3060	0.3978	0.4969	0.3090	0.2352	0.1889
2	0.4681	0.5944	0.7087	0.7570	0.7072	0.6852
3	0.6576	0.8156	0.9462	1.1607	1.1199	1.1100

Table 2: Shear stress at the stationary plate when $m = 0.75$.

$K^2 \downarrow M^2 \rightarrow$	$\tau_x\big\|_{\eta=0}$			$\tau_y\big\|_{\eta=0}$		
	10	15	20	10	15	20
1	0.4373	0.3060	0.2278	0.3341	0.3090	0.2990
2	0.6104	0.4681	0.3796	0.8260	0.7570	0.7096
3	0.8210	0.6576	0.5523	1.2597	1.1607	1.0857

Table 3: Shear stress at the stationary plate when $K^2 = 1$.

$m \downarrow M^2 \rightarrow$	$\tau_x\big\|_{\eta=0}$			$\tau_y\big\|_{\eta=0}$		
	10	15	20	10	15	20
0.75	0.4373	0.3060	0.2278	0.3341	0.3090	0.2990
1.25	0.5491	0.3978	0.2986	0.2674	0.2352	0.2306
1.75	0.6560	0.4969	0.3804	0.2419	0.1889	0.1748

Table 4: Shear stress at the moving plate when $M^2 = 15$.

$K^2 \downarrow m \rightarrow$	$-\tau_x\big\|_{\eta=1}$			$-\tau_y\big\|_{\eta=1}$		
	0.75	1.25	1.75	0.75	1.25	1.75
1	3.2098	2.6521	2.2332	0.8395	1.0377	1.0410
2	3.1052	2.5266	2.0965	0.6294	0.8228	0.8187
3	2.9823	2.3871	1.9465	0.4571	0.6585	0.6581

Table 5: Shear stress at the moving plate when $m = 0.75$.

$K^2 \downarrow M^2 \rightarrow$	$-\tau_x\big\|_{\eta=1}$			$-\tau_y\big\|_{\eta=1}$		
	10	15	20	10	15	20
1	2.6134	3.2098	3.7207	0.5916	0.8395	1.0396
2	2.4943	3.1052	3.6272	0.3625	0.6294	0.8462
3	2.3498	2.9823	3.5201	0.1848	0.4571	0.6817

Table 6: Shear stress at the moving plate when $K^2 = 1$.

$m \downarrow M^2 \rightarrow$	$\tau_x \big\vert_{\eta=0}$			$\tau_y \big\vert_{\eta=0}$		
	10	15	20	10	15	20
0.75	2.6134	3.2098	3.7207	0.5916	0.8395	1.0396
1.25	2.1612	2.6521	3.0795	0.7338	1.0377	1.2817
1.75	1.8297	2.2332	2.5941	0.7173	1.0410	1.3007

Table 7: Mass flow rates when $M^2 = 15$.

$K^2 \downarrow m \rightarrow$	Q_x			Q_y		
	0.75	1.25	1.75	0.75	1.25	1.75
1	1.1063	1.1529	1.1918	0.1050	0.0885	0.0729
2	1.2092	1.2779	1.3332	0.1701	0.1321	0.1020
3	1.2996	1.3742	1.4328	0.2076	0.1520	0.1123

Table 8: Mass flow rates when $m = 0.75$.

$K^2 \downarrow M^2 \rightarrow$	Q_x			Q_y		
	10	15	20	10	15	20
1	1.1620	1.1063	1.0788	0.1363	0.1050	0.0842
2	1.3043	1.2092	1.1576	0.2006	0.1701	0.1437
3	1.4148	1.2996	1.2311	0.2246	0.2076	0.1842

Table 9: Mass flow rates when $K^2 = 1$.

$m \downarrow M^2 \rightarrow$	Q_x			Q_y		
	10	15	20	10	15	20
0.75	1.1620	1.1063	1.0788	0.1363	0.1050	0.0842
1.25	1.2189	1.1529	1.1176	0.1029	0.0885	0.0747
1.75	1.2640	1.1918	1.1513	0.0720	0.0729	0.0657

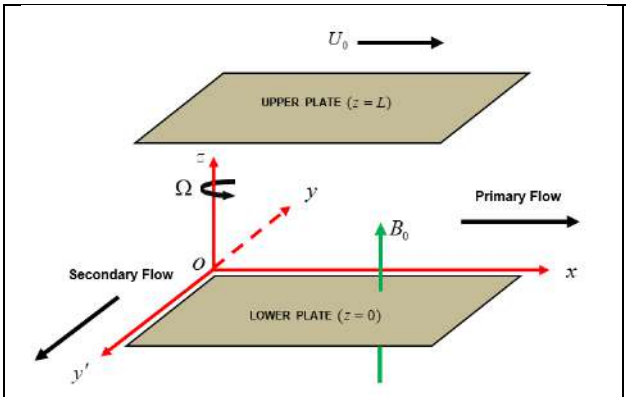

Figure 1: Geometry of the problem

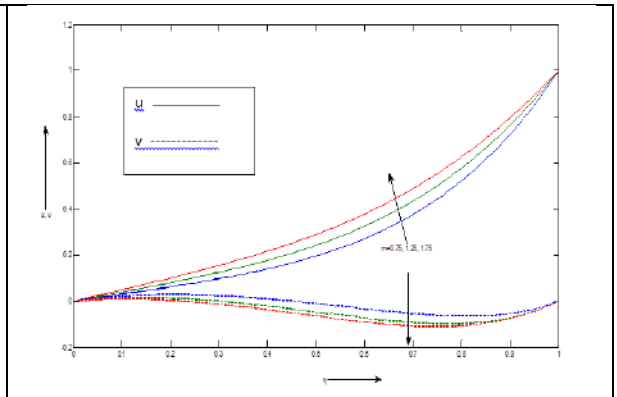

Fig. 2: Velocity profiles when $M^2 = 15$ and $K^2 = 1$.

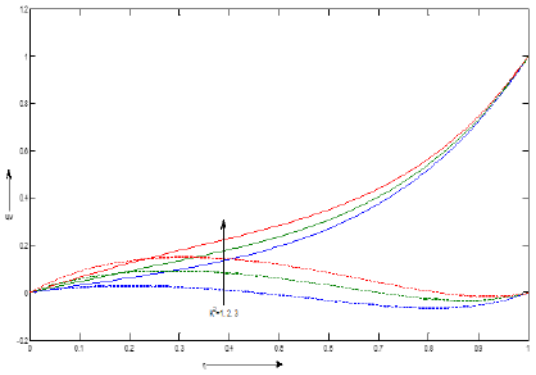

Fig. 3: Velocity profiles when $M^2 = 15$ and $m = 0.75$.

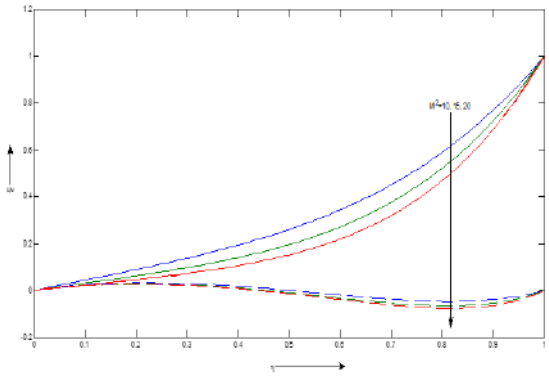

Fig. 4: Velocity profiles when $K^2 = 1$ *and* $m = 0.75$

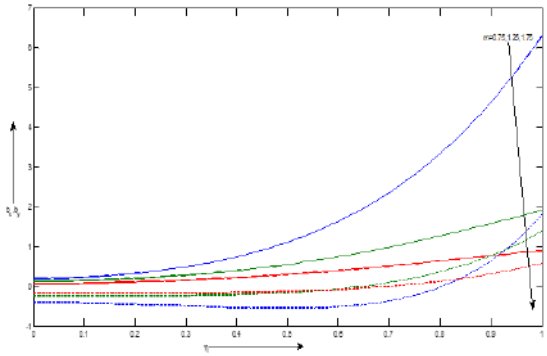

Fig. 5: Induced magnetic profiles when $M^2 = 15$ *and* $K^2 = 1$

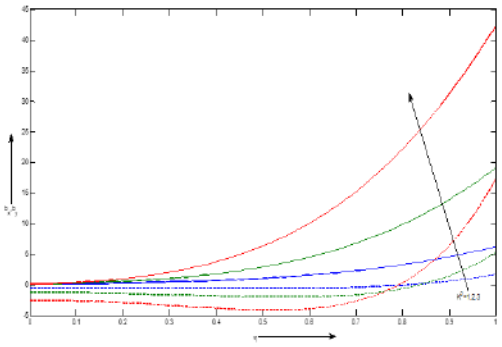

Fig. 6: Induced magnetic profiles when $M^2 = 15$ *and* $m = 0.75$

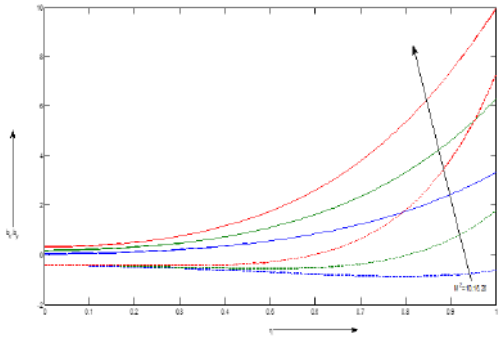

Fig. 7: Induced magnetic profiles when $K^2 = 1$ *and* $m = 0.75$

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RESEARCH ARTICLE

Study of Density, Viscosity and Ultrasonic Wave Propagation in a Power Transformer oil

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ABSTRACT

The power transformers is an important components of any power generation and transmission system. All over the world mineral oil immersed transformers play an important role in generation and transmission of electric power. Mineral based insulation oil is used for liquid insulations, stop arcing, and to dissipate the heat of the transformer (i.e. act as a coolant).for the past some decades. Which is free from fatty acids. This paper presents the experimental results of effect of aging of transformer and analysis the change in characteristics such as density, viscosity and ultrasonic velocity. The measurements of the density, viscosity and ultrasonic velocity were carried out at temperatures ranging from 30 °C to 60 °C.

Keywords: Density, viscosity, ultrasonic velocity, and mineral oil.

INTRODUCTION

Transformer is a very important component in the power system network. Mineral oils are widely used in transformers as an insulating agent and coolant because these oils are easily available in large quantities at low cost. The internal state of transformer gets degraded as a result of its subjection to thermal, mechanical, electrical and chemical stresses during their function. The lifetime of a transformer mainly controlled by the condition of the oil-paper insulation system, which is a universally accepted fact [1].

Standard tests for oil samples taken on regular basis are usually conducted for both power and distribution transformers. In this paper transformers are filled with naphtha based mineral insulating oil [2-3]. During the service time of transformer, transformer oils are exposed to electrical, mechanical and chemical stresses. Due to the jointed or distinct action of these stresses, aging phenomenon of transformer oil initiated which leads to slow and permanent changes in their properties [5-6]. As effect of the aging process transformer oil loses its strength slowly and start

decomposed and oxidized and ultimately starts to create mud. And this referred to the degradation phenomenon of the transformer oil[7]. The key aspects that increases transformer oil aging and degradation phenomenon are moisture, oxygen and other contaminants. And the presence of corrosive Sulphur in transformer oil also disturb the insulating characteristic of the oil-paper insulation [8-9].Inclusive and sustainable industrialization, together with innovation and infrastructure, can unleash dynamic and competitive economic forces that generate employment and income. They play a key role in introducing and promoting new technologies, facilitating international trade and enabling the efficient use of resources.

MATERIALS

In order to investigate and compare different characteristics property of pure and used mineral insulating oil, oil samples were collected from Gramtarang transformers laboratory, Centurion University of Technology and Management, Odisha. First oil sample was collected after filtration. The filtration of the oil was carried out at a temperature about 333K and this process removes dissolved moisture unwanted dust particles, sludge and dissolved gases from the oil. Second sample was collected from transformer which in service for one year. Third sample was collected from transformer which in service for 2 year. All the oil samples are collected from lower level of the tank.

Experimental Details

Measurement Of Density

The densities of the transformer oil were estimated using a 25 ml Pycnometer bottle. The Pycnometer bottle with the oil was submerged in a temperature-controlled water bathat30 °C.40 °C, 50 °C and 60 °C. The density was estimated using the equation

$$\varrho_2 = \frac{w_2}{w_1}\varrho_1 \text{ ---------- (1)}$$

Where, w_1 = weight of distilled water, w_2 = weight of transformer oil, ϱ_1 = Density of water, ϱ_2 = Density of transformer oil.

Measurement of Viscosity

The viscosities of the transformer oil were estimated using Ostwald's viscometer. The Ostwald's viscometer with the transformer oil was submerged in a temperature-governed water shower 30°C, 40°C, 50°C, and 60°C. The time of flow was estimated by using an advanced stopwatch with an accuracy of 0.01 s. The viscosity was calculated using the equation,

$$\eta_2 = \eta_1 \left(\frac{t_2}{t_1}\right)\left(\frac{\varrho_2}{\varrho_1}\right) \text{ ---------- (2)}$$

Where, η_1 = Viscosity of distilled water, η_2 = Viscosity of transformer oil, ϱ_1 = Density of distilled water, ϱ_2 = Density of transformer oil. t_1 = Time of flow of water, t_2 = Time of flow of transformer oil.

Measurement of velocity

The expression used to determine the ultrasonic velocity is

$$U = 2d/T \text{ (m/s)}$$

Or. $U = 2d \times v$

Or, $U = \lambda \times v$ ---------- (3)

(Here-$2d=\lambda$)

Where, v is the frequency of the generator which is used to excite the crystal; (In the present investigation, the frequency 4MHz interferometer was taken) d- Separation between the reflector and crystal; T. Travel time of the ultrasonic wave.

RESULTS AND DISCUSSIONS

The density of oil samples is given in Table 1 and variation of oil samples with density is represented in fig.1, and variation between density and temperature is shown in fig.2. The viscosity of the oil samples is listed in Table 2 and variation of viscosity with oil samples is shown in fig.3 and variation between viscosity and temperature is shown in fig.4. The velocity of oil samples is listed in the Table 3 and the comparison of ultrasonic velocity with oil samples is denoted in Fig.5,and variation between ultrasonic velocity and temperature is shown in fig.6. The variation in the surface area of molecules, their relative velocity and their inner closeness are responsible for variation of density and viscosity of pure and used oil samples i.e., the structure of the molecule, and all these perform an important role in determining these parameters.

From fig.1 it can be understood that the density of pure oil sample is less and increases with age of the transformer because oil density depends on its composition, and composition of oil changes with aging the molecules, shows structural readjustment of molecular packing taking place in the aging oils. According to fig.3. Viscosity of the oil samples drops by small amount with aging of transformer oil it is due to the dissociation of molecules between them. With increase in temperature, density and viscosity decrease (fig-2 and fig-4) which indicates that due to rise in thermal energy of the system their intermolecular forces decrease. As the inter molecular distance among molecules increases so that volume of the oil samples increases which leads to decrease in density and viscosity with rise in temperature[10].

Which conforms the dissociation of molecules among them as the temperature increases the velocity of transformer oil decreases (fig.5).It is observed that, Ultrasonic velocity decreases (fig.6) for filtered oil and then increases with aging of transformer oil at a particular temperature. This is due to the structural changes occurring in the oil. So it is concluded that molecules of pure oil has less intermolecular force of attraction among them, which is an indication of weak molecular association. But when the oils age increases the cohesive forces among them increases, this indicates existence of molecular association, which leads to increase in velocity with aging

CONCLUSION

It is observed that the aging is related to the magnitude of the variation of density, viscosity and velocity. A comparison of the samples used transformer oil, and fresh transformer oils confirms that, as the action time of a transformer rises, the fraction of aromatic hydrocarbons in transformer oil increases signifying oil degradation level. As ultrasonic interferometer measurement provides the clear results, which can be used as a device for studying the transformer oil for its weakening and ageing due to electrical and thermal stresses.

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Table-1: Values of density of oil samples in kg/m$^{3.}$

Temperature(K)	pure oil	used oil (1year)	used oil (2 year)
303 K	828.76	831.43	833.67
313 K	822.73	825.12	828.03
323 K	817.53	819.78	821.62
,323 K	814.03	815.77	818.37

Table-2: Values of viscosity of oil samples in N.s.m^{-2}

Temperature(K)	Pure oil	Used oil (1 year)	used oil (2 year)
303 K	15.510	14.677	14.293
313 K	12.466	11.814	11.513
323 K	10.999	10.408	9.789
333 K	9.521	8.837	8.356

Table-3: Values of ultrasonic velocity of oil samples in ms^{-1}

Temperature(K)	Pure oil	Used oil (1 year)	used oil (2 year)
303 K	1378.00	1355.00	1361.6
313 K	1353.00	1338.40	1345.2
323 K	1330.00	1314.67	1320.4
333 K	1305.00	1284.13	1296.4

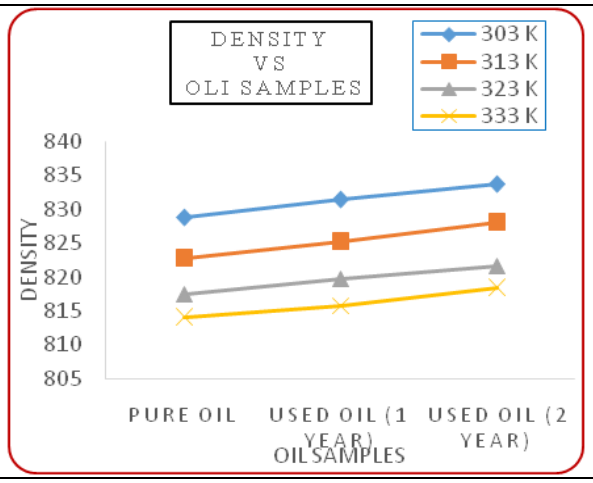

Fig-1 variation of density with oil samples

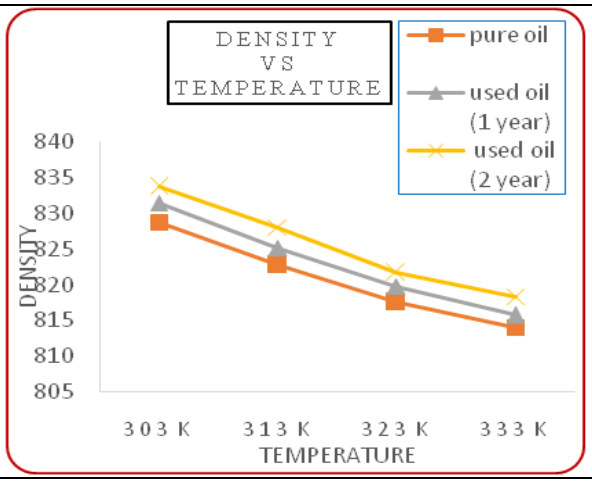

Fig-2 Variation of density with temperature

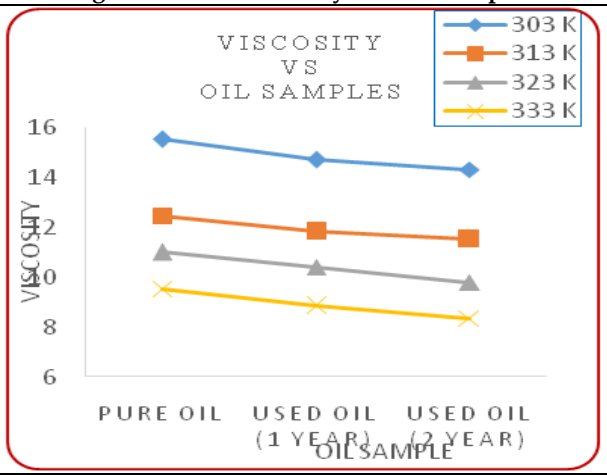

Fig-3 Variation of viscosity with oil samples

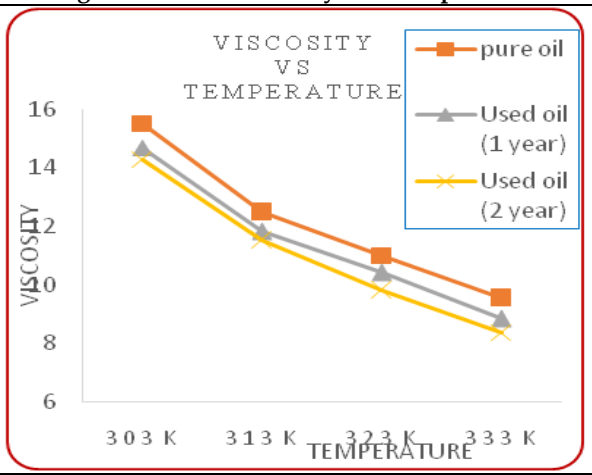

Fig-4 Variation of viscosity with temperature

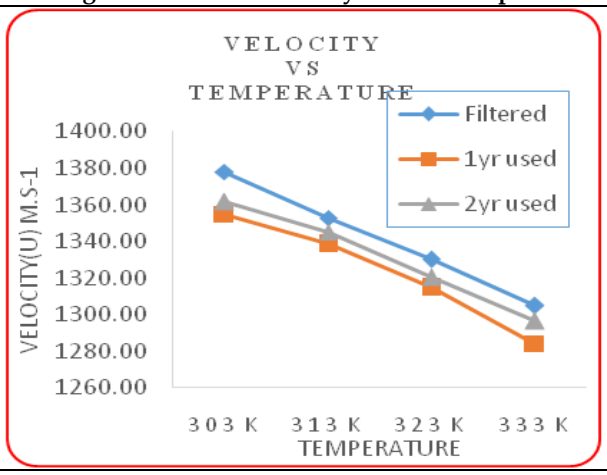

Fig-5 Variation of ultrasonic velocity with temperature

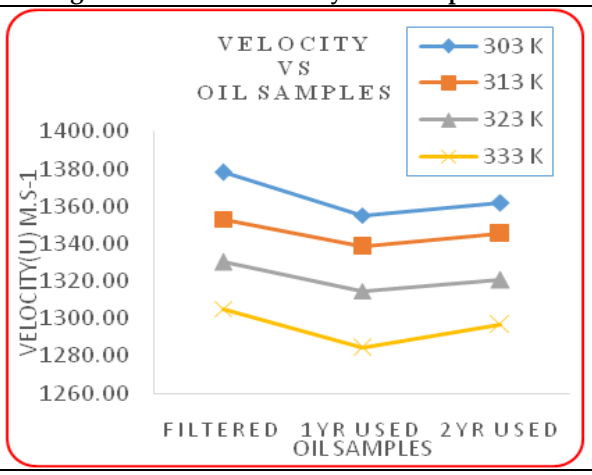

Fig-6 Variation of velocity with oil samples

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RESEARCH ARTICLE

Compare the Cost and Net Return of Organic and Conventional Red Gram Farming Practices in Dry Land Areas of Karnataka

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ABSTRACT

Organic farming is a method of farming which excludes the use of compound chemicals such as chemical fertilizers, pesticides and herbicides. Instead of that natural resources such as organic matters, mineral and microbes are used. The present study was conducted in Gulbarga district was selected purposively because it is the "pulse bowl" of the state with highest area i.e., 3,36,853 ha and production 1,53,285 tonnes and productivity of 0.46 tonnes/ha of red gram in the country and also it has maximum number of organic red gram growers (Ministry of Agriculture, Govt. of India 2014-15). A sample of 120 red gram farmers under organic farming and another 40 sample of farmers growing red gram under conventional farming were selected randomly for the present study. Based on the total returns obtained by the organic (n=120) and conventional (n=40) respondents were selected from the same 120 sample size the statistical test i.e., "Z" test was applied to find out the difference between the organic and conventional to know the differences in their returns. The average cost of cultivation per acre of red gram on organic farming was Rs. 8825 as against Rs.5400 on conventional farming. This difference in cost of cultivation was due to the higher cost incurred on biological fertilizers as well as on bio pesticides by organic red gram farmers. The net return on organic red gram farm wasRs.9550 and Rs.7450 on conventional farming.

Keywords: Organic farming, Conventional farming, Organic input, Net return and Enterprise.

INTRODUCTION

Red gram is an important pulse crop in India. It is also known as Pigeonpea, Arhar and Tur. Red gram is mainly cultivated and consumed in developing countries of the world. Red gram is a protein rich staple food. In addition to being an important source of human food and animal feed, Red gram also plays an important role in sustaining soil fertility by improving physical properties of soil and fixing atmospheric nitrogen. Being a drought resistant crop, it is suitable for dry land farming and predominantly used as an intercrop with other crops. Red gram ranks sixth among pulses production in the world and is a major legume crop. The area under cultivation (4.5 million hectares) is stagnant. It is largely grown in the northern parts of the state especially in Gulbarga, which is called "Pulse bowl of Karnataka". In this district, Red gram occupied an area of 3,36,853 ha and production of 1,53,285 tonnes. Most farmers in Karnataka State are pioneers in organic agriculture and have developed many different systems of cultivation through indigenous knowledge base. They have developed their own methods of using organic wastes and developed holistic pest control agents to control pests and diseases. Although, domestic market is at the early stage and unable to utilize the existing production potential, increased awareness towards healthy and safe organic foods have surged the demand for organic products especially in urban areas. It is witnessed that there is almost 20-25 per cent increased growth in organic sector per annum during the last 10 years. In spite of economic recession fears the growth of organic sector is unaffected.

MATERIALS AND METHODS

The present study was conducted in Gulbarga district was selected purposively because it is the "pulse bowl" of the state with highest area *i.e.*, 3,36,853 ha and production 1,53,285 tonnes and productivity of 0.46 tonnes/ha of red gram in the country and also it has maximum number of organic red gram growers and also it has maximum number of organic Red gram growers. (Ministry of Agriculture, Govt. of India 2014-15).Gulbarga district consists of ten mandals and Red gram is being grown in all ten mandals, out of ten mandals, three mandals were selected at random based on highest acreage and from each block, a list of villages with organic Red gram cultivation were prepared, from which two villages were selected at random to make a sample of six villages for the study. From the prepared list, 20 farmers were selected by simple random sampling procedure from each village. Thus, the total size of the sample selected for the study was 120 organic red gram growers and 40 conventional red gram growers.

RESULTS AND DISCUSSION

Cost of Cultivation

The cost of cultivation is operationally defined as the expenditures for different operation by the respondents due to the adoption of recommended package of practices of organic Red gram cultivation. Based on the total cost of cultivation obtained by the organic (n=120) and conventional (n=40) respondents were selected randomly from the same 120 sample size the statistical test *i.e.*, 'Z' test was applied to find out the difference between the organic and conventional to know the differences in their cost of cultivation.

It was evident from the table 2 that, calculated 'Z' Value (47.82) was greater than table 'Z' value at 0.05 level of probability. So the null hypothesis was rejected and hence it could be concluded that there exists a significant difference between cost of cultivation of organic and conventional farming. This might be due to the expenditure for inputs like FYM/manure, jeevamruth, NSKE, more price for bio-pesticides, bio-fertilizers, seed treatment bio-agent and the transportation charges for the input from other places and the cost of human labour was highest, therefore the cost of cultivation is more in organic Red gram compare to conventional farming Red gram. This is in conformity with *Trivedi et al. (2007) and* Uematsu and Mishra (2012).

It was operationally defined as the total returns gained by the respondents due to the adoption of recommended package of practices of organic Red gram cultivation. Based on the total returns obtained by the organic (n=120) and conventional (n=40) respondents were selected from the same 120 sample size the statistical test *i.e.*, 'Z' test was applied to find out the difference between the organic and conventional to know the differences in their returns.

It was evident from the Table 3that, calculated 'Z' Value (22.87) was greater than table 'Z' value at 0.05 level of probability. So the null hypothesis was rejected and hence it could be concluded that there exists a significant difference between returns of organic and conventional farming. This might be due to the quality, weightage of the organic Red gram and high demand from the consumers for organic produce or dal. Therefore the premium price for organic Red gram is more compare to conventional Red gram. This is in conformity with Kshirsagar (2008), Clark (2009), Dhandhalya *et al.* (2010) and Adhikari (2009).

CONCLUSION

The study shows that the cost and net returns of organic and conventional red gram in Gulbarga district, the main objective is to compare the cost and returns of organic and conventional red gram farming practices in dry land areas of Karnataka. The results revealing that majority of the respondents in my research study belonged to young age group. Due to their enthusiasm and interest, farmers might have driven them towards a new farming system *i.e.*, organic farming. The list of results obtained in this research study concludes that the investment on manures,bio-fertilizers and bio-agents followed by labour charges were higher in case of "organic red gram cultivation" as compared to conventional red gram cultivation and also the net return on organic red gram cultivation was higher as compared to conventional red gram cultivation. Organic inputs like green manure, FYM and compost, adds organic matter to the soil. This stimulates the activity of soil microorganisms and ultimately it leads to improve the soil fertility, yield and net returns of the organic red gram growers, more ecofriendly to the nature and consumption of organic food and fodder sustain the health condition of human and animal. Initial cost of cultivation to the organic farming is high as compare to the conventional farming but the "net return", demand and cost of the organic product is high in the market. Hence organic farming is a kind of "enterprise" to the rural youth to get maximum return.

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Table 1 Selection of Respondents from Gulbarga District of Karnataka

Sl. No	Mandals (n=3)	Village (n=6)	Respondents (n=120)
1	Gulbarga	Melakunda(b)	20
		Pattan	20
2	Sedam	Kottapalli	20
		Kadacharla	20
3	Aland	Gola	20
		Kadaganchi	20

*Significant at 0.05 per cent probability level

Table 2: Difference between organic and conventional respondents based on the cost of cultivation of Red gram farming

Sl. No	Category	Mean cost of cultivation(Rs/acre)	S.D	Z value
1	Organic respondents (n=120)	8825	328.28	47.82*
2	Conventional respondents(n=40)	5400	411.37	

*Significant at 0.05 per cent probability level

Table 3: Difference between organic and conventional respondents based on the returns of Red gram farming

Sl. No	Category	Returns (Rs/acre)	S.D	Z value
1	Organic respondents (n=120)	9550	503.83	22.87*
2	Conventional respondents (n=40)	7450	499.57	

*Significant at 0.05 per cent probability level

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RESEARCH ARTICLE

Legislative Regulation of Bio-Pesticides in Indian Subcontinent

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ABSTRACT

Biopesticides, consisting of two different words namely bio, stands for biome and pesticides, contain various types of pest management interventions through parasitic or more precisely endo and ectoparasitic and chemical relationships. The concept has traditionally been associated with one of the most significant features of Integrated Pest Management (IPM) namely biological control. Biopesticides often use pre-existing micro-organisms, living organisms' manipulation actions and plant-derived products. Globally, the environmentally friendly nature and target specificity of biopesticides are becoming increasingly common. However, use of biopesticides is still minuscule in developing countries like India compared to traditional chemical pesticides. Although the Indian government has promoted the use of biopesticides by including them in many of the agricultural schemes, biopesticides face many challenges at the grassroots level. The reduced adaptability and the declining interest of farmers in biopesticides has become a concern. The cost of registering biopesticides in India and the long-term procedure involved, further deter companies from engaging in biological pesticides research and development.

Keywords: Biopesticides, biological control, India, constraints, life on land, biodiversity, conservation.

INTRODUCTION

The Indian economy is primarily based on agriculture, with around 70 per cent of Indians participating in agricultural-related activities. But agriculture has always faced the destructive activities of various plagues such as insects, fungi and weeds. The introduction of chemical pesticides effectively resolved this problem. But the over-

reliance on and subsequent uninhibited use of chemical pesticides has posed environmental issues such as polluted soils and groundwater contamination, which has resulted in nutritionally imbalanced and unproductive lands. Pesticide residues also raise concerns about food safety among domestic consumers, and pose trade barriers to export crops. Developing plant breeds that are immune to, or more resistant to, pathogens is an eco-friendly option, but it takes a long time to develop, research, authorize and commercialise new varieties.

Therefore, an ecofriendly substitute became the need of the hour. Bio-pesticides or biological pesticides based on pathogenic microorganisms specific to a target pest provide an environmentally safe and efficient alternative to pest problems. They pose less danger to human health and the climate. Several government agencies such as the Ministry of Agriculture and Farmers Welfare, Department of Biotechnology (DBT) and the Ministry of Science and Technology have been endorsing research, expansion and commercialisation of biopesticides. However, biopesticides in India are still largely to take off due to mixed constraints, considering their enormous market potential and the national and state initiatives to promote them as alternatives to chemicals. Despite strong government support in India, the North American Free Trade Agreement (NAFTA) countries (USA, Canada, and Mexico) are the world's largest user of biopesticides and use about 45% of all global biopesticides, the European Union uses 20%, and Asia (China and India) uses just 5% of world biopesticides (Bailey *et al*., 2010). Globally, biopesticides amount to only 4.5 % of the total pesticides produced, while in the USA it is 6 %, whereas in India, it is only 3 %. The annual growth rate of production of biopesticides is projected at 2.5 per cent in India (Padma, 2019). Despite Indian regulatory bodies making considerable efforts to promote the use of biopesticides, its slow permeation in agricultural applications remains a major challenge.

Regulation of Bio-Pesticides in India

The Indian government has different rules and regulations for promoting large scale biopesticides registration and production. The National Agricultural Technology Project (NATP) led the Integrated Pest Management (IPM) project (1998-2005) and also encouraged the use of biopesticides in agriculture through the National Farmer Policy (2007). By simplifying the biopesticides registration and regulation process, the Insecticide Act (1968) stimulated greater development and application of biopesticides. The Central Insecticides Board (CIB) and the Registration Committee (RC) is interested in this act and both are extremely important regulatory bodies for biopesticides (Kabaluk *et al*., 2010). CIB is the apex advisory committee with experts from all disciplines and has standardized guidelines and data criteria for not only registration but also minimum infrastructure facilities for biopesticides development (NAAS, 2013). The RC grants human beings and animal's registrations, after scrutinizing and confirming statements about their bio-efficacy and protection. The National Framework of Agricultural Research plays a leading role in supporting biopesticides. This structure includes several Indian Council of Agricultural Research (ICAR) institutes, as well as numerous agricultural universities in the country (Rabindra, 2005).

Rising sale of spurious Bio-products in Indian markets

In India the selling of fake goods has recently spiked. A recent survey conducted by the National Level Pesticide Manufacturers Association found that numerous bio-products are being sold on the market that either have no registration certificate number given by CIRB & RC (Central Insecticide Board and Registration Committee) or do not have active ingredients, license number or address on the label. Many such spiky bio-products laced with chemical pesticides are developed and sold across the world. In the 12th financial year, the selling of dubious goods in India was estimated at 5000 crores. In monetary terms the harm incurred by using such fake goods is even higher. The spiked bio-products available on the market are made from pesticides that are smuggled / illegally procured from unregistered sources, which in recent years also contribute to the rejection of export consignments of grapes, chilies and rice. Most farmers who use these goods are gullible and do not know the ingredients that are being used, leading to contamination and export shipments being rejected. Market studies show that only 25-30 per cent of farmers are aware of pesticide use and thus most farmers are easily preyed to spurious goods. The problem is predominantly momentous in the states of Andhra Pradesh, Maharashtra, Tamil Nadu, Madhya Pradesh, Karnataka, Gujarat etc. where these bio products are not within the purview of Insecticides Act, 1968 or any other act. As an example, 298 companies in Andhra Pradesh (AP) were involved in unprincipled activities in 2010 and another 83 companies got

added to the list by the year 2011. The business of counterfeit products in AP alone was estimated at 500 crores in 2011 (Anonymous, 2013). The loss caused by sale of such products is not only regulatory but also in terms of loss of reliance of the customers on the products.

Constraints which prevent widespread use of biopesticides in India

Production of biopesticides is a high-risk venture that needs a high initial capital investment right from the screening stage to select suitable strains for sale, packaging, storage and distribution. However, the single greatest restriction to its production and growth is the widespread selling of under-standard or bogus biopesticides with chemical pesticides. Adding to the issue of fake, tainted or sub-standard biopesticides are unregulated organic products not authorised by the Central Insecticide Board and Registration Committee (CIBRC) and marketed under the name of organic bio-inputs certified by the Agricultural and Processed Food Products Export Development Authority (APEDA) under the Indian Ministry of Commerce and Fertilisers. These 'organic' products are not subject to any bio-efficacy and bio-safety tests imposed by CIBRC, and account for an estimated 65 percent of the country's overall sales volume of biopesticides.

Biopesticides consist primarily of living microbes; variations in temperatures, humidity and ultraviolet radiation exposure dampen their effectiveness. Additionally, any pollution significantly decreases its efficacy in field environments. Also, a big problem for farmers is their short shelf life. Biopesticides are extremely dose-dependent, and they vary from environment to environment. Unlike synthetic pesticides that can be manufactured in desired purity and yield, pure botanical pesticides are often difficult to produce due to large variations in the active and associated ingredients of the parent plants in different agro-climatic zones. This leads to differences in their physical and chemical properties, as well as that associated toxicology and other. Often complicated by their physical, chemical or microbial contamination.

Meanwhile, the increase in demand for biopesticides due to national and state initiatives has ended up stimulating the marketing of spurious biopesticides that undermine the respectability of the biotechnology industry, in a worrying trend. One of India's major constraints is the restricted production of biopesticides, with only 14 bio pesticidal formulations listed under the 1968 Insecticide Act, which primarily catalogues the requirements for bio-safety determination of pesticides (Padma, 2019). CIBRC registers a total of 970 biopesticides companies which screen potential bio-security biopesticides. Currently the number of units for bioproduction has risen to 410, of which 130 are in the private sector (Desai *et al.,* 2016). In addition, since 2010 about 35 commercial companies and 32 IPM centers have been supported by the Ministry of Agriculture and Farmers Welfare in developing biopesticides (Keswani *et al*., 2016a). The cost of biopesticide registration in India, and the involvement of long-drawn-out procedure, further discourages companies from engaging in biological pesticides research and development. Another constraint is the need to check the bio-safety microorganism before the biopesticides are registered and propagated. Many universities and research institutions which conduct the initial research and develop biopesticides are incapable to abide the additional costs prerequisite for extensive safety and allergy tests.

CONCLUSION

India is still facing major challenges with regard to the growth of the agricultural sector, in order to meet its demographic challenges in the coming 20-50 years to provide food security. Biopesticides have been used for decades to deter pests and diseases from growing crops. Compared to traditional chemicals, however, their market and position among agrochemicals is still far behind. Scientific and technical approaches related to the production of biopesticides are also inadequate, as demonstrated by a lack of understanding of ground-level processes, a lack of reliability on bio-products and a lack of penetration in the pest control industry. The challenges in India 's widespread use of biopesticides are related to effectiveness, shelf-life, production methods, a limited range of host or target pests, poor field performance, and distribution system problems, economics and regulations. Besides these technical issues, the authorities need to press for the promotion of biopesticides for farmers' research, development

and awareness-raising. To create faith in biopesticides, both the private and government sectors will need to come together and work at the grassroots level with the farmers. Also, relevant will be the government's policy and support in providing better regulation-friendly research and development infrastructure and assuring farmers support for the use of biologics. Chemical pesticides have an immense effect on the atmosphere and soil fertility; hence it is high time that the change to biopesticides is achieved quickly to make our agro-ecosystems, conservation viable in future for food security.

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REVIEW ARTICLE

Applications of Lightweight Natural Hybrid Composites in Aircraft Industries: A Review

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ABSTRACT

In the manufacture of structural parts of aircraft, there was a revolution in the development of commercial aircraft to replace steel with raw materials. The most popular and elegant material available in this century is composites. Their degradation sensitivity depends on the nature of the environment and on each element 's numerous and specific reactions. During their service life, all of these systems and elements are exposed to many conditions. They are used today in the aerospace industry for private and new commercial aircraft. The awareness of the feasibility of product creation and development processes is one of the social and environmental components of the aircraft structure. Hybrid composites (compounds) are those materials that are processed in a simple matrix by incorporating two or more separate fibres. There are several descriptions given by various researchers of hybrid compounds. Hybrid compounds are more complex and have a wider potential for application than other fibre-backed compounds. Previous research on natural synthetic fibrous composites has concentrated on reduced use of synthetic fibers. The technological advantages of manufacturing, properties & applications in the aerospace trade of natural hybrid compounds(composites) are discussed in this chapter.

Keywords: Hybrid Composites, Aircraft Structure, Synthetic Fiber, Natural Fiber, Matrix

INTRODUCTION

In the manufacture of structural parts of aircraft, there was a revolution in the development of commercial aircraft to replace steel with raw materials. Many composites achieve higher strength properties than raw materials, decreasing

aircraft weight and thereby decreasing passenger transport costs[1]. During multiple takeoffs / landings, the composite is prone to metal fatigue, resulting in inspections that are less costly than the lifespan of the aircraft[1]. During multiple takeoffs / landings, the composite is prone to metal fatigue, resulting in inspections that are less costly than the lifespan of the aircraft[1]. The most popular and elegant material available in this century is composites. Their degradation sensitivity depends on the nature of the environment and on each element 's numerous and specific reactions. During their service life, all of these systems and elements are exposed to many conditions. Stability is becoming an important driver in the aerospace industry for the technical advancement of aircraft structures. In aircraft production, several components are widely used. For instance, in World War II, the compound was first used for military aircraft. They are used today in the aerospace industry for private and new commercial aircraft. It is important to remember that carbon fibre and fibreglass are replaced by the three most popular composites. The awareness of the feasibility of product creation and development processes is one of the social and environmental components of the aircraft structure. Sustainability includes exposure technology and functionality, that are related. With Gordon Erolite, which was discarded with phenolic resins, natural fibre composites were introduced into the airport industry. The high strength and lightness of Gordon Arololite make it ideal for use as an material for aircraft[2]. Researchers have developed a natural fiber-based heating and cooling agent for use in aircraft inside panels in another study.It has been found that the board has the necessary flame retardant and heat resistance are cheap and give substantial weight savings compared to traditional sandwich panels, allowing fast processing and disposal[3]. The technological advantages of manufacturing, mechanical properties & applications in the aerospace trade of natural hybrid compounds(composites) are discussed in this chapter.

Hybrid Composite Advantages

Hybrid composites(compounds) are those materials that are processed in a simple matrix by incorporating two or more separate fibres. There are several descriptions given by various researchers of hybrid compounds. Composites are characterised by Liao and Thwe[4] as reinforcing materials integrated in mixtures of different matrices. Fu *et al.*[5], on the other hand, demonstrated that these components are strengthening materials consisting of two or more fillers and fillers embedded in a matrix. Hybrid compounds are more complex and have a wider potential for application than other fibre-backed compounds. Previous research on natural synthetic fibrous composites has concentrated on reduced use of synthetic fibers[6-8]. Furthermore, previous studies have identified the potential benefits related to natural synthetic fibre hybridization[9]. A hybrid compound's efficacy is the amount of the individual components where there is a more desirable balance of benefits and disadvantages.The benefits of one type of fibre can complement the properties that the hybrid composition lacks in other ingredients. As a consequence, by effective material design[10], a compromise between cost and efficiency can be achieved. Kenafaramide with Kevlar[11], collar / glass weave[12], and polycarbonate composites with added carbon[13] are several examples of hybrid compounds. Hani *et al.*[14] Coconut woven composites were also investigated and found that coconuts could be used to replace some of the composite's synthetic fibres, which would increase the composite 's performance.

Resistance of the material to shock and penetration. Fiber orientation, fibre content and layer pattern length of both fibres, their mixing capacity, fibre-to-matrix interface, and single-fiber deformation can influence the properties of hybrid composites. The phenomenon of improving the compatibility of the properties of composites with two or more fibres may be described by positive or negative hybrid effects[9]. The main problem in the design and production of hybrid composites is the choice of the corresponding fibres and the degree of fibre properties[10].To get the best results from hybrid materials, two fibres have been mixed by several researchers to maximise the harmful benefits of both. Due to the high strength of sisal fibres and the tightness of coconut oil, sisal fibre and oil are a nice combination of ingredients. The desired properties of the respective ingredients[15-16] would therefore be indicated by any ingredient containing both cooking oil and coconut oil.In commercial structures, parks, space, marine and recreational environments, hybrid composites can be used for primary structures. It has a wide range of advantages in the industries of aerospace, such as high resistance to corrosion and fatigue and excellent resistances to

impact. Weight reduction, which can save between 20 percent and 50 percent, is the most important benefit. Furthermore, it is possible to adjust the mechanical properties to the "stop" design with a thin reinforcing fabric thickness and change direction.

Fibre Classification

Fiber Of Natural Origin

Natural fibres are distinguished from plants , animals or minerals on the basis of their origin. The composition of plant fibres is cellulose-based, whereas proteins are composed of animal fibres. Onions, leaves or hard fibres, seeds, vegetables, straw, cereals and other grass fibres are among the plant fibres. Figure: 1 illustrates along with examples the classification of these fibres. The composition of plant fibres consists of cellulose , hemicellulose, lentin, and wax. Cellulose is a natural homopolymer available in high modulus in plant fibres, also known as polysaccharide. D-glucopyranose bonds and glycosidic bonds bind this homopolymer to individual molecules. Elements like H, C and O_2 are plant fibreclusters[17] that contain between 65 and 70 percent cellulose. The non-cellular material is bound to the cell wall and the final features of the fibre are altered by its presence. They almost never extract non-cellular materials from these fibres because most of them are too costly to do so. The abilitiesof moisture absorption from the environment in large amounts because cellulose is hygroscopic [18] is an important feature of plant fibres.Due to moisture absorption, most polymer fibres swell. This absorption, as well as strength and rigidity, contributes to changes in weight and height. Cellulose , hemicellulose, and lentin are the chemical components of Lycopene fibres. In addition, small amount of wax, pectin& water-soluble substances are also present in these fibers[18]. While it is chemical-free, the chemical bond between hemicellulose and cellulose is strong and difficult to break down. In softwoods, the hemicellulose composition is based on xylan, whereas those in hardwoods are based on mannan. On average, hemicellulose accounts for about 22% of coniferous trees, 26% of hardwoods and 30 percent of other agricultural waste[19].Lentin is a natural polymer product. Where it is caused by the enzymatic polymerization of the first three precipitators: the cross-linking machine and the trans-p-coumaril [10]. The dissimilarity between the previous levels is the amount of methyl group (AOCH3) present in the aromatic ring. In addition, lentin fills the space in the cell between hemicelluloses, pectin and cellulose. It is also a high-branched, aromatic triangular polymer[10]. It is encapsulated in the wall of the cell and binds to hemicellulose partly. In addition, chemical hemicellulose replacements have been related to lentin, such as galactose, arabinose and 4-O-methylglucuronic acid. It does not decompose into a single unit due to its intolerance to water, ammonium properties and hydrophobic binding ability.

Fiber Synthetics

Synthetic fibres are manufactured from raw materiallike chemicals or petrochemicals-based oil[20]. These materials are made of polymerized material of various chemical compositions in a chemical linear and are used to manufacture various forms of fibres. Synthetic fibres account for around half of all fibre use, with fibre technology and textiles being used in all fields. As potential commercial goods, several groups of fibres based on synthetic polymers are assessed. There are several methods for synthetic fibres to be made, but the spinning process is the most common. This requires heating the fibre until it starts to melt, after which the burger must remove the fibre as quickly as possible from the melt. The next step is for the molecules to be prepared in parallel. This brings together the fibres and makes it possible for them to crystallise and orient themselves. Heating is another procedure used. Synthetic fibres last longer than most natural fibres and can absorb various colours quickly. Furthermore, many synthetic fibres give useful characteristics such as stress, water permeability and resistance to stain[20]. Moisture, Sunlight and human skin oil cause breakage and exhaustion of all the fibres. There are more sensitive natural fibres than blends. Heating is another procedure used. Synthetic fibres last longer than most natural fibres and can absorb various colours quickly. Furthermore, many synthetic fibres give useful characteristics such as stress, water permeability and resistance to stain[20]. Sunlight, moisture and human skin oil cause breakage and exhaustion of all the fibres. There are more sensitive natural fibres than blends. There are more sensitive natural fibres than blends. This is because natural products are interchangeable. Synthetic fibres are generally formed by the release of fibrous material through

the rotation of air and water to form a thread. Prior to the development of synthetic fibers, man-made fibres were made up off polymers derived from petrochemical.

Classification of Matrix

A matrix is a material that confines the structure and loads the material of reinforcing of a composite together. They are usually weaker than reinforcing materials[21]. Plastic matrices have strength, low density and rigidity. Fiber reinforcement has high strength and rigidity, but requires an environment that maintains the fibres and transfers load between them. In other words, to keep the reinforcing material in place, the matrix is used as a binder. Furthermore, as the load is applied, it often separates and transmits the outside load equally to the fibre. The matrix also provides diffusion resistance and tolerance for damage due to the flow of plastic into the crack key. Furthermore, the matrix also protects the surface of the fibre against environmental impact and wear, especially during the composite process[21].It also holds the reinforcing fibres in the correct position and orientation to allow them to support the expected load, to distribute the load between the fibres to provide resistance to spreading and damaging cracks, and to provide layer strength. The whole of the composite. To provide stable, solid bases for engineering purpose, the matrix is used to embed the requisite fibres. To balance the characteristics of the fibres, the properties of matrix are generally chosen. High strength and rigidity will lead to the combination of matrix and fibre. This is because it depends on the interaction between the two elements to propagate repression. As a plastic material, thermal resin is defined first as a liquid molybdenum or prepolymers[21]. They are unified by the use of heat or catalysts to become insoluble and soluble raw materials. There have three dimensions that link the polymer chains with covalent markings, thus providing a high modulus structure and improved wave resistance, preventing slippage of chains. During curing, the liquid resin is transformed into a solid body by chemical bonding with bonding or hardening and by heating so that a closely related three-dimensional network structures are formed from resin. The resin can't be melted, processed or heat treated. Hence, the process of heartburn is carried out before treatment. Thermal rubber has low cracking and brittleness at room temperature. In environments where water or moisture levels rise, micro-compounds will absorb maximum water than cracked compounds. As off this scenario, weight of the composite increases and as resin is attacked by moisture, hardness decreases which reduces the properties of the fibers. Improving the adhesion of the resin fibres is obtained from the resin and the effect of chemotherapy on the fibers.

Boundaries of Natural Fibres :

Natural fibres typically have the ability to absorb moisture and are hydrophilic. In the cell walls of plant fibres, a large amount of the hydrogen bonds (hydroxyl group OH) remaim present. As moisture is absorbed into the fibres, these hydrogen bonds form new hydrogen bonds with water molecules. This is because of poor bonding between fibres and the matrix, matrix suppression, geometrical instability and poor properties (mechanical) of the composite [22].Therefore, before preparing the composite, moisture has to be detached from the fibres. In addition, chemotherapy, such as alkali, xylene, acetic acid, benzoylation and peroxide, may reduce the absorption of moisture from natural fibers[23].

Processing Techniques

So many traditional processing methods for compounding, such as manual, resin (RTM), vacuum and compression are there. Such techniques are successful and well developed in the production of composites of special quality. Methods of processing are designed to fit a specific product design where the choice of method for a specific product depends on the raw material, the design and application of the product.

Laying Hands On:

Manual stopping is the old estand simplest method of opening moulds for making composites. Initially, dry fibres were hand-placed on the die in the form of woven, embroidered or glued fibres, and a brush was used to apply the resin matrix to the reinforcing material. To facilitate distribution of resin and to obtain required thickness, manual rolling is then used to roll over the wet composite to provide interaction among reinforcement and die. Lastly, under standard weather conditions, hardwood floors are allowed to harden. The method is divided into four phases:

preparation of the matrix, painting with gel, and curing. Curing is the method of curing, without external heat, a fiber-reinforced resin. Initially, to achieve a high quality surface of the product[24], the pigmented gel is added to the surface of the mould. There are some demerits of this particular method. Skills such as mixing of resin, resin content and laminate consistency are very important for lamination, reinforcement and matrix. Laminate is usually achieved by inserting too much cavity volume. The low molecular weight of hand-held resins means that they are potentially more dangerous than high molecular weight products. The low viscosity of resin also indicates that, they have an improved tendency to enter clothing. The resin must have a low viscosity to operate manually. This normally impairs their mechanical and thermal properties because of the high degree of weakness / kidney requirement, in addition the amount of fibre load largely depend on the processing methods. This is also affected by the fibrous cavity anatomical characteristics called Yeah, Fibrosis. The manual implementation method is used primarily in aerospace structures and marine [24].

Method of Vacuum:

This technique is a continuation of the manual application process in which pressure is applied to the floor after it has been applied to maximise its cohesion[24]. By sealing the plastic film on the floor and on the equipment, this is done. A vacuum pump collects the air under the vacuum sheet, which allows for friction before the atmosphere is added to the protective layer. For this form, the most appropriate resin forms are hypotonic and polyolonic. Due to the extraction of too much dinarine from the resin of the vacuum cleaner, equipment made of polystyrene and resin is unsuitable. This strategy has many benefits. It is typically possible to obtain laminates with higher fibre content and lower cavity content than conventional methods of hand placement. With excess thrown into the material of the bag, the resin will flood the structural fibres.The amount of volatile substances that are released during treatment is also decreased by the vacuum bag film. Additional processing, however, increases the price of both labour and packaging materials.

Move Moulding of Resin (RTM):

A method of producing composites made from fibrous composites is resin displacement (RTM). The reactive resin is poured into the semi-finished fibre parts in the RTM process and these parts are thus submerged in a closed vessel by heat. For high pressure applications , the following techniques are notable: vacuum injection, high pressure injection, differential pressure injection and double wall injection. Rouison *et al.*[25] Production by resin transfer process (RTM) of unsaturated hemp polyester composites to produce composites of up to 20.6 percent by volume with different fibre content[26].The robustness of the High-content fibre substrates suggest that the time of resin injection has been substantially increased. The temperature of the mould must be constant to achieve the hardness and uniformity of the solid composition. However, only slight differences are shown by comparisons between projected and experimental temperatures. Between the predicted hardening level and the hardening rate of the resin, similar results can be observed.

Compression of Mould

Due to its high reproducibility and low cycle time, compression compression is the most common technique for composite construction. There are two mainly utilised techniques: compression and compression of flow depending on form of semi-finished product used and its cutting, the process varies. Using vertical pressing, such as hot and cold pressing methods, these moulding techniques consist of a compressive material containing a heat transfer agent in a hot-rolled metal matrix. The fundamental method of this technique is similar to the method of hand-laying, which allows the compound to be closed by applying pressure before hardening.

Applications in the Aerospace Industry of Hybrid Composites

A image of a good aircraft has been developed by the aviation industry: it will be very light, will have variable geometric wings, will operate with renewable energy & will make less noise. Thus, because of the many factors that demonstrate their potential for use in aerospace industries, including performance, production functions, and eco-friendly excellence, natural synthetic hybrids are significant. The structural improvements of complex composite

structures are one of the key criteria for components used in the aerospace industry. In addition, at high temperatures, the composite structure exhibits stronger and more stable properties in wet environments. The aerospace industries have increased their interest in weight loss by substituting for steel with composites that are natural hybrids. Furthermore, hybrid composites have greater load, power, strain, and strength versatility and a higher strength ratios as compared to steel. Natural fibres in composites are cheaper, lighter and practically superior to the eco-friendly alternative to synthetic fibres. In the aerospace industry, the latest definition of "carefree structure" implies that ideal structures must be built for optimum efficiency at minimal expense, and this strategy is related to the many off-the-shelf choices of fabrics with polymers. The production of new aircrafts that will profit from hybrid materials will be motivated by environmental and safety issues. Recent work has shown that applying biologically modified clays to hard epoxy resins lead to a 60% decrease in water resistance, increased liquid oxygen compatibility, and increased corrosion resistance. [13], microcracking.

CONCLUSIONS

Natural lightweight hybrids show their potentials to be used in aerospace industries because of their low weight and high mechanical properties. This is because synthetic reinforcing compounds face difficulties related to recycling and non-perishability. Thus, natural compounds represent significant environmental advantages due to their resistance to biogas, low cost, and high specific mechanical properties. It still has issues such as low temperature resistance, low strength and high absorption of moisture. A decrease in the hardness of the composite under bending intensity and the effect at increased temperature were observed and showed that the softening matrix of the composite thus activates the interaction bonds between the napoli, the fibreglass and the hypothetical resin. Furthermore, because of the high moisture absorption, the resistance to bending and effect steadily decreases from the moment of absorption of the submerged sample in water. The poor matrix surface of the fibres can be induced to reduce the softness, bending and impact of the composite after immersion due to this absorption of water particles into the fibres. It also has been discovered that natural synthetic compounds increase strength, temperature resistance and decrease absorption rates of moisture. Thus, with more study and experimentation, natural synthetic compounds may be used on a wide range in the aerospace industries. The work satisfied the sustainability development goal Industry innovation and infrastructure.

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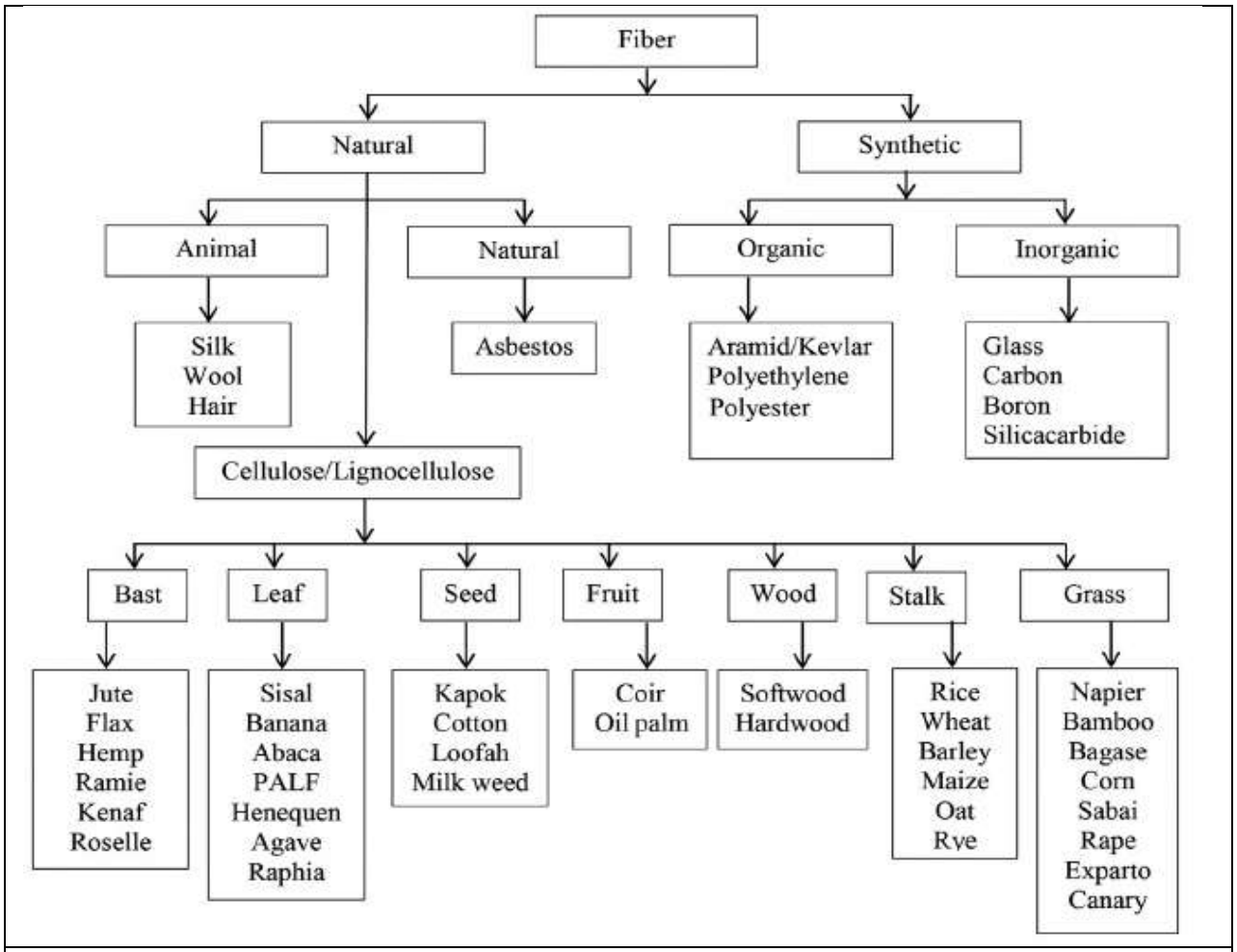

Figure.1: Classification of Synthetic And Natural Fibers.

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RESEARCH ARTICLE

A Survey through Python and Machine Learning approaches for predicting Early-Stage Diabetes

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ABSTRACT

Diabetes is a major chronic illness that has the potential to devastate the global health-care system. Age, obesity, a lack of exercise, a sedentary lifestyle, a poor diet, high blood pressure, and other variables all contribute to the risk of developing such a condition. Diabetes patients are at risk for a variety of ailments, including eye problems, heart disease, renal disease, stroke, and more. Hyperglycemia, or high blood sugar, is a typical side effect of untreated diabetes, and it, along with other health difficulties, can lead to serious health problems, particularly in the nerves and blood vessels. However, owing to the tremendous expansion of machine learning (ML) and Python classification algorithms in several fields, such as health science, detecting diabetes in its early stages has become easier than expected. We conducted a comparative examination of many ML and DL algorithms for early diabetic illness prediction in this investigation. According to our tests, the DT classifier outperformed the other algorithms by about 95%, whereas the other algorithms were significantly less accurate.

Keywords: Diabetes, machine learning, python, early-stage prediction, Healthy lives

INTRODUCTION

Diabetes is a rapidly spreading disease that affects both adults and children. To understand diabetes and how it develops, we must first understand what happens in the body without diabetes. Sugar (glucose) comes from the things we eat, especially carbohydrate foods. Carbohydrate meals are our bodies' principal source of energy; everyone, including diabetics, needs them. Bread, cereal, pasta, rice, fruit, dairy products, and vegetables are all carbohydrate foods. When we ingest these nutrients, our bodies convert them to glucose [1]. And when this glucose

level gets elevated from its normal range it is called as diabetes. This should not be overlooked; if left untreated, diabetes can lead to serious complications in humans, such as heart disease, renal disease, high blood pressure, and damage to other organs [2]. There are various different forms of diabetes. According to the etio pathology of the condition, there are two basic clinical types: type 1 diabetes (T1D) and type 2 diabetes (T2D). T2D appears to be the most frequent type of diabetes (90 percent of all diabetic patients), with insulin resistance being the primary symptom. T1D is supposed to be caused by auto immunological death of pancreatic cells in the Langerhans islets, whereas T2D is thought to be caused by lifestyle, physical activity, dietary choices, and hereditary [3]. In case of women suffering with gestational diabetes during their pregnancies, their children, have a higher chance of developing type 2 diabetes later in life. Hyperglycemia with a blood glucose level over normal but below the diabetes diagnostic criteria is characterized as gestational diabetes. Gestational diabetes is defined as hyperglycemia with a blood glucose level above normal but below the diabetes diagnostic level. Women with gestational diabetes are more vulnerable than ever before to problems that arise during and after pregnancy [4].

In any event, predicting diabetes early is a difficult task for medical professionals due to the complicated link between several variables. Diabetes has an impact on human organs such as the heart, nerves, foot, kidney, eye, and so on. Data mining is a technique for extracting useful information from massive datasets, such as those connected to diabetes in hospitals, which are incredibly large and broad. Computational process, Artificial Intelligence, Classification procedures, Statistical technique, Clustering, and pattern recognition are all part of this multifaceted discipline of information technology. In recent years, data mining techniques have been widely used in data forecasting, with different data mining algorithms being used to anticipate disease with more precision in order to save human lives and save treatment costs. The outcome of data mining techniques is also influenced by multidimensional data's potential properties [5].

Due to the difficulty of preventing diabetes, it can now be handled in a variety of methods. The first and most crucial step is to obtain an accurate diagnosis, which can assist to reduce the risk of further difficulties. Further, treatment of such lifestyle diseases are carried out focusing on least side effect caused by the medication [6, 7, 8] There are several techniques to early detection in medical science, however in this part, machine learning plays a key role in recognizing diabetes at an early stage. Diabetes-related tasks such as diabetes diagnosis, glucose control, and the evaluation of diabetes-related outcomes may now be predicted thanks to the rapid rise of deep learning techniques and the amount of data. Modern deep learning algorithms and frameworks are frequently used to assist in the identification of several diseases such as diabetes [9]. To improve classification precision, the study also generalizes the acquisition of ideal data set features. Our algorithm will assist us in predicting diabetes diseases based on medical data at an early stage. We want to be able to function with more information in the future. We also wanted to make dataset analysis more practical, accurate, and efficient. Polyuria, polydipsia, weariness, sudden weight loss, polyphagia, vision blurring, vaginal thrush, edema, delayed recovery, irritability, partial paresis, obesity, alopecia, and muscle stiffness are some of the indicators employed in this study's data collection.

METHODOLOGY

We'll learn about the various classifiers used in machine learning to predict diabetes in this part. We'll also go over our proposed methods for increasing accuracy. To begin, we gathered and pre-processed the diabetes dataset. There are numerous diabetic datasets accessible. As a result, machine learning and python is required for medical diagnostics. Python is a strong and easy-to-use programming language. It has high efficiency level data structures and a basic yet most effective high object-oriented programming style because it contains so many libraries. The goal of this study is to forecast a patient's probability of developing diabetes. Machine learning algorithms are used for this purpose [10]. The dataset was separated into train and test sets after pre-processing. Machine learning is a branch of science that studies how machines learn from their experiences. The phrases "machine learning" and "artificial intelligence" are used interchangeably by many scientists because the ability to learn is the most important quality of an entity that is deemed intelligent in the broadest sense of the term [11].

Dataset Collection

It entails gathering and analyzing data in order to uncover hidden patterns and trends that aid in forecasting and evaluating outcomes. In this study the dataset was collected from Kaggle.

Libraries Used

The python platform has a lot of library material, but we only looked at a handful of them in this study, such as pandas, numpy, matplotlib, and seaborn. These libraries have distinct functions that differ from one another, such as pandas lib's function to analyse a particular dataset and numpy lib's function to perform solely numerical computations.

Dataset Processing

This step of the model deals with erroneous data in order to get more accurate and precise results. For example, the Id in this dataset is erroneous, thus we removed the feature. The goal is to determine whether or not the patient is diabetic based on the measurements.

Distribution of Important Predictor Variables

Both displots and boxplots are employed in this distribution.

Verification of Missing Values

Although there is no missing value in the dataset in this study, it is critical to check the missing value in the prepared dataset in order to obtain the desired result.

Bar Plot for Outcome Class

The graphs below show how data is dispersed among many parameters in diabetics.

Plotting and Checking the Visualization Correlation

The correlation charting can be done using pair plots, joint plots, and so on, and then the visualisation checking of the dataset can be done in probability form.

Exploratory Data Analysis

It is critical to evaluate the variable in order to anticipate the outcome, and the correlation between the variables plays a significant part in obtaining the outcome.

Algorithims used for Classification

Once our dataset has been created, we use Machine Learning methods to classify it. Polyuria, polydipsia, weariness, sudden weight loss, polyphagia, vision blurring, vaginal thrush, edoema, delayed recovery, irritability, partial paresis, obesity, alopecia, and muscle stiffness were used in this study, as well as two more features collected from the dataset using the Explorative Data Analysis technique.

Support Vector Machine (SVM)

Supervised machine learning (SVM) is an acronym for supervised machine learning. The SVM is concerned with locating an optimal hyperplane that can isolate the instances of any class. This classifier defines the hyperplane that isolates the spots to put the most notable number of points of a comparable class on the same side while expanding the interval of each class to such a hyperplane. The support vectors are the hyperplane's nearest points. The distance between the points in a class is the smallest distance between them and a hyperplane. This approach, which uses nonlinear mapping as a guide, converts the original train data into higher-dimensional space. The accuracy level of this model is 0.93%.

K Nearest Neighbour (KNN):

KNN is a simple learner algorithm that is non-parameterized and instance-based. With the particular case of instance-based learning with zero cost during the learning process, instance-based models are defined by memorising the training dataset and selecting the best. The accuracy level of this model is 89.42%.

Decision Tree (DT)

DT is a well-known supervised learning algorithm that may be used to classify and predict data. It creates classification and regression models using a tree topology. In this way, the input features are represented as nodes, resulting in a tree. It selects the feature depending on the data gathered. The accuracy level of this model is 95.19%.

RESULTS

Machine learning algorithms demonstrate effective use of time and space. The machine's ability to adapt to the dataset is honed using these strategies. As shown in the preceding research, the DT model has a high accuracy of 95.0% when compared to SVM and KNN. Visualization and regression show that weight, polyuria, polyphagia, and polydipsia all have a direct impact on diabetics.

CONCLUSION

The principles of machine learning, such as multiple linear regressions, SVM, KNN, and DT model creation, have been discussed. We ran the code using the Python programming language and were able to achieve the intended outcome. Weight, polyuria, polyphagia, and polydipsia are more closely linked to Outcome, according to observation. We can also broaden the research by identifying whether a non-diabetic person is at risk of developing diabetes in the coming years. Thus, the objective of the current study is to create a sustainable health environment and also promoting the good health and wellbeing of people by satisfying the Sustainable Development Goal 3.

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```
In [34]: data.info()
<class 'pandas.core.frame.DataFrame'>
RangeIndex: 520 entries, 0 to 519
Data columns (total 17 columns):
 #   Column              Non-Null Count  Dtype
---  ------              --------------  -----
 0   Age                 520 non-null    int64
 1   Gender              520 non-null    object
 2   Polyuria            520 non-null    int64
 3   Polydipsia          520 non-null    int64
 4   sudden weight loss  520 non-null    int64
 5   weakness            520 non-null    int64
 6   Polyphagia          520 non-null    int64
 7   Genital thrush      520 non-null    int64
 8   visual blurring     520 non-null    int64
 9   Itching             520 non-null    int64
 10  Irritability        520 non-null    int64
 11  delayed healing     520 non-null    int64
 12  partial paresis     520 non-null    int64
 13  muscle stiffness    520 non-null    int64
 14  Alopecia            520 non-null    int64
 15  Obesity             520 non-null    int64
 16  class               520 non-null    object
dtypes: int64(15), object(2)
memory usage: 69.2+ KB
```

Fig: 1Dataset Info

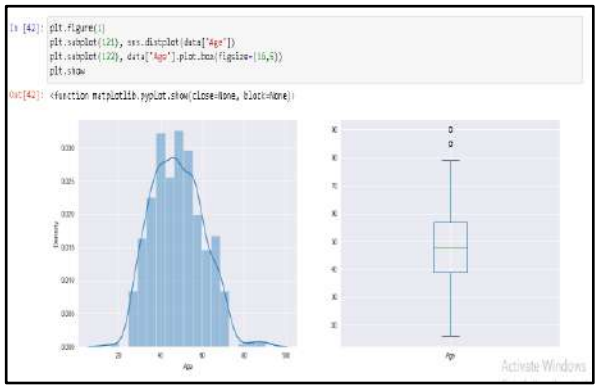

Fig: 2 Distribution of Age

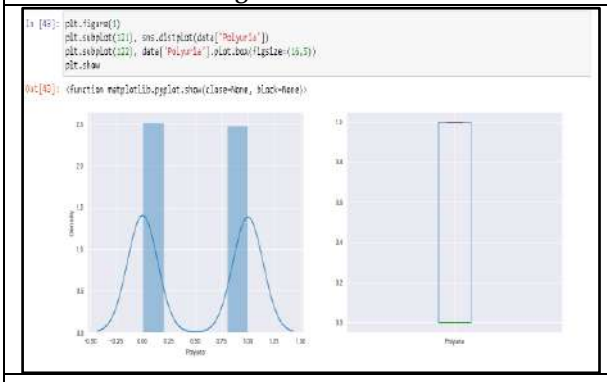

Fig: 3 Distribution of Polyuria

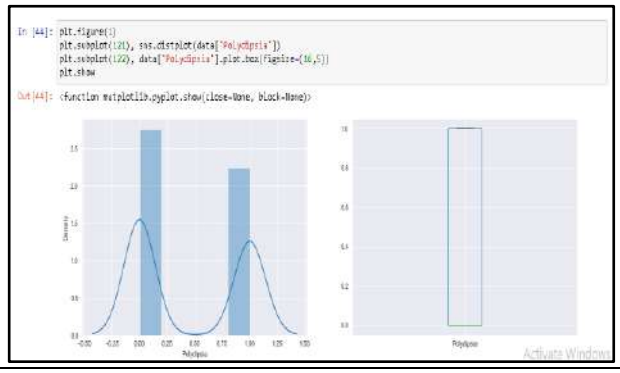

Fig: 4 Distribution of Polydipsia

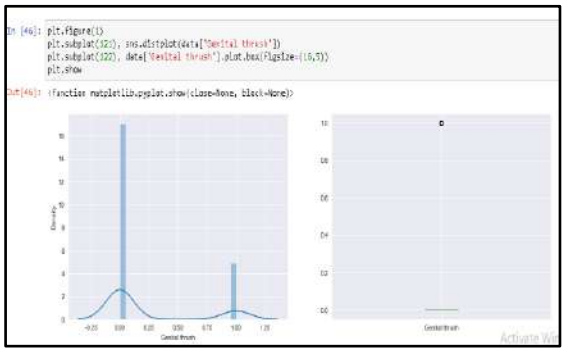

Fig: 5 Distribution of Genital Thrush

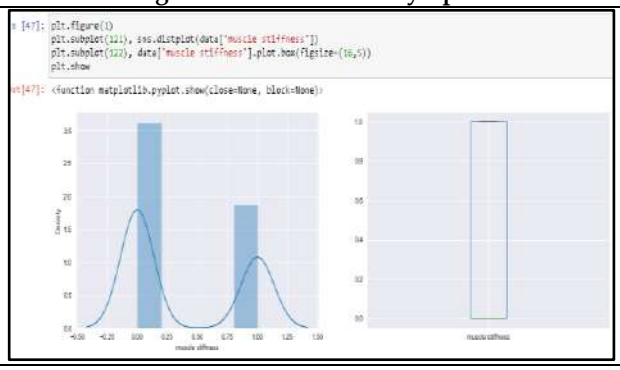

Fig: 6 Distribution of Muscle Stiffness

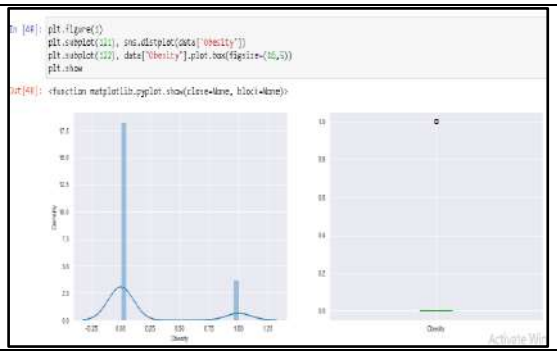

Fig: 7 Distribution of Obesity

```
In [49]: data.isnull().sum()
Out[49]: Age                 0
         Gender              0
         Polyuria            0
         Polydipsia          0
         sudden weight loss  0
         weakness            0
         Polyphagia          0
         Genital thrush      0
         visual blurring     0
         Itching             0
         Irritability        0
         delayed healing     0
         partial paresis     0
         muscle stiffness    0
         Alopecia            0
         Obesity             0
         class               0
         dtype: int64
```

Fig: 8 Value Verification

```
In [41]: sns.countplot(x ='sudden weight loss', data = data)
Out[41]: <AxesSubplot:xlabel='sudden weight loss', ylabel='count'>
```

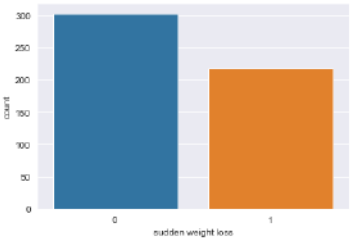

Fig: 9 Weight loss Data Info

```
In [38]: sns.countplot(x ='Polyphagia', data = data)
Out[38]: <AxesSubplot:xlabel='Polyphagia', ylabel='count'>
```

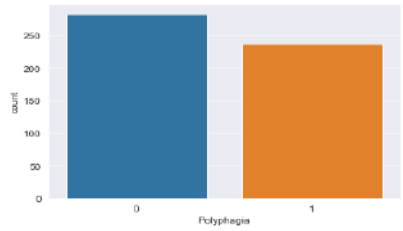

Fig: 10 Polyphagia Data Info

```
In [39]: sns.countplot(x ='Polydipsia', data = data)
Out[39]: <AxesSubplot:xlabel='Polydipsia', ylabel='count'>
```

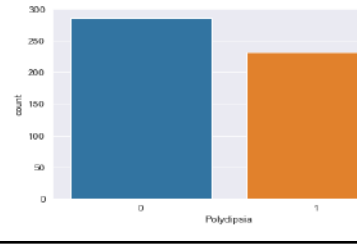

Fig: 11 Polydipsia Data Info

```
In [40]: sns.countplot(x ='Polyuria', data = data)
Out[40]: <AxesSubplot:xlabel='Polyuria', ylabel='count'>
```

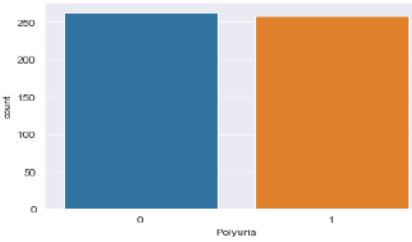

Fig: 12 Polyuria Data Info

```
In [51]: data.corr()
```

Out[51]:

	Age	Polyuria	Polydipsia	sudden weight loss	weakness	Polyphagia	Genital thrush	visual blurring	Itching	Irritability	delayed healing	partial paresis	muscle stiffness	Alop
Age	1.000000	0.199781	0.137382	0.064808	0.224596	0.315577	0.096519	0.402729	0.296559	0.201625	0.257501	0.232742	0.307703	0.32
Polyuria	0.199781	1.000000	0.598809	0.447207	0.263000	0.373873	0.087273	0.235095	0.088289	0.237740	0.149873	0.441664	0.152938	-0.14
Polydipsia	0.137382	0.598809	1.000000	0.405985	0.332463	0.316839	0.028081	0.331250	0.128716	0.203446	0.116691	0.442249	0.180723	-0.31
sudden weight loss	0.064808	0.447207	0.405985	1.000000	0.282884	0.243511	0.089858	0.060754	-0.004516	0.140340	0.088140	0.264014	0.109756	-0.20
weakness	0.224596	0.263000	0.332463	0.282884	1.000000	0.180266	0.027780	0.301043	0.309440	0.146698	0.335507	0.272982	0.263164	0.08
Polyphagia	0.315577	0.373873	0.316839	0.243511	0.180266	1.000000	-0.063712	0.293545	0.144390	0.239466	0.263980	0.373589	0.320031	-0.05
Genital thrush	0.096519	0.087273	0.028081	0.089858	0.027780	-0.063712	1.000000	-0.148408	0.125336	0.160551	0.136111	-0.195612	-0.100188	0.20
visual blurring	0.402729	0.235095	0.331250	0.060754	0.301043	0.293545	-0.148408	1.000000	0.291191	0.077095	0.177767	0.364156	0.412369	0.01
Itching	0.296559	0.088289	0.128716	-0.004516	0.309440	0.144390	0.125336	0.291191	1.000000	0.114006	0.453316	0.118669	0.215575	0.26
Irritability	0.201625	0.237740	0.203446	0.140340	0.146698	0.239466	0.160551	0.077095	0.114006	1.000000	0.126877	0.151571	0.201637	0.04
delayed healing	0.257501	0.149873	0.116691	0.088140	0.335507	0.263980	0.136111	0.177767	0.453316	0.126877	1.000000	0.187382	0.260078	0.20
partial paresis	0.232742	0.441664	0.442249	0.264014	0.272982	0.373589	-0.195612	0.364156	0.118669	0.151571	0.187382	1.000000	0.232634	-0.22

Fig: 13 Correlation Chart

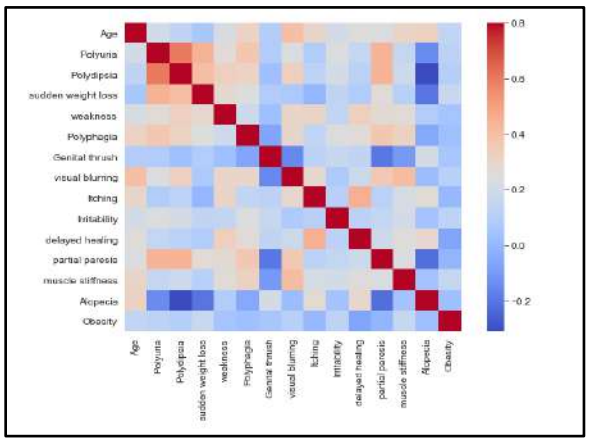

Fig: 14 Heat Map

```
In [37]: #Caluclate the accuracy of the model

         from sklearn.metrics import accuracy_score, confusion_matrix

         acc_svc=accuracy_score(y_test,y_pred1)
         print("Accuracy of SVM model: "+str(acc_svc))


         #get Confusion matrix
         cm1=confusion_matrix(y_test,y_pred1)

         print("Confusion Matrix is:")
         print(cm1)

         Accuracy of SVM model: 0.9326923076923077
         Confusion Matrix is:
         [[48  4]
          [ 3 57]]

In [38]: x_test.shape

Out[38]: (104, 15)
```

Fig: 15 Accuracy Value of SVM Model

IMPLEMENTATION OF KNN Model ¶

```
In [41]: from sklearn.neighbors import KNeighborsClassifier
         from sklearn.metrics import accuracy_score, confusion_matrix, classification_report

         #create the KNN model k=3
         clf3= KNeighborsClassifier(n_neighbors=3)

         #fit the model
         clf3.fit(x_train,y_train)

         #predict the model with test dataset or new dataset
         y_pred3=clf3.predict(x_test)

         ##get Confusion matrix
         cm3=confusion_matrix(y_test,y_pred3)

         print("Confusion Matrix is:")
         print(cm3)

         cr3=classification_report(y_test,y_pred3)
         print("Classification report of KNN model with DIABATIC PATIENT DATA data")
         print(cr3)

         Confusion Matrix is:
         [[48  4]

[44]:    #Calculate the accuracy of the model

         accuracy3=accuracy_score(y_test,y_pred3)*100
         print("Accuracy of the KNN model:", accuracy3)

         Accuracy of the KNN model: 89.42307692307693
```

Fig: 16 Accuracy Value of KNN Model

IMPLEMENTATION OF Decision Tree Model

```
In [39]: from sklearn.tree import DecisionTreeClassifier
         from sklearn.metrics import accuracy_score, confusion_matrix

         #create the Decision Tree model
         dst_clf=DecisionTreeClassifier()

         #train the model
         dst_clf=dst_clf.fit(x_train,y_train)

         #predict the model by using test dataset i.e. new dataset
         y_pred2=dst_clf.predict(x_test)

         #find the accuracy of the model
         acc_dst=accuracy_score(y_test,y_pred2)

         print("Accuracy of Decision Tree Model:"+str(acc_dst*100)+"%")


         ##get Confusion matrix
         cm2=confusion_matrix(y_test,y_pred2)

         print("Confusion Matrix is:")
         print(cm2)

         Accuracy of Decision Tree Model:95.19230769230771%
```

Fig: 17 Accuracy Value of DT Model

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RESEARCH ARTICLE

Product Recommendation Techniques-Past and Present

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ABSTRACT

In the advance world, the rapid growth of Internet takes an important role in our life & the world is moving towards online world where utmost of the effects is digitized and available on a mouse click. Now utmost of the deals are done on Internet with the help of on- line shopping and other digital conditioning. Always huge amounts of data are used by the users in performing on-line task. So, the using of huge amount of data puts extra overload on server that's why Product recommendation ways are being used extensively to reduce this redundant load and recommend the scanned product to the guests. In past how this recommender system works & how it useful in that time & now how present is different from than past that written in this paper & we try to give a proper overview of this recommendation ways with suitable exemplifications.

Keywords: Product Recommendation system, traditional commerce, E-commerce, datamining.

INTRODUCTION

A huge quantum of data present by filtering the important data handed by a stoner and other coffers that make the stoner's preference and interest is known as Recommendation system. It learns the match between the stoner and the item and makes recommendations based on the data. Recommender structures are the structures which might be designed to advocate items to the stoner rested on sever a one-of-a-kind factor. These structures prognosticate the maximum in all likelihood product that the addicts are maximum in all likelihood to shop for and are of hobby to. Companies like Netflix, Amazon, YouTube etc. use recommender structures to assist their addicts to discover the perfect product, vids, track or cinema for them. For illustration, as we know Netflix is used for filmland or web series. So, as per recommendation it uses a recommendation system like if we handpick a movie also from that movie's order or order the system recommends or suggests that type of filmland & web series to user. There are multitudinous different goods that can be recommended by the system like filmland, books, news, papers, jobs, adverts etc.

Suggestion System use intended for to make the existence easier as well as smoother way this saves our period of looking the desired or interested gizmos in every conventional trade plus virtual trade, reduce work as well as overhead. After using this particular device order cost or promoting cost of products plus different offerings faster common medium. This is utilized intended for really a couple of regions like YouTube. com advice device, item advice device, foods advice device, and so on. With typically commemorated exemplifications taking the particular condition of playlist creators for videotape and song choices, recommends meals since in step along with we desired, item recommenders for across the internet stores, or subject material recommenders for social media marketing systems and open up net content materials recommenders.

These buildings are able in order to do using a good unmarried input, such as song, film or even more than one particular input inside plus throughout systems such as news, books, work opportunities and seek inquiries. There are furthermore famous recommender buildings for precise motifs like cafes, fit, dealing homes plus on-line courting. Recommender structures have moreover been advanced in order to find out pursuit papers and professionals, collaborators, sightseer areas, quotations, new reading through, tale harkening Fahrenheit. M. and economic offerings. The evolving of springing upward technology as properly as the rapid-hearth place boom of Web will increase within excessive cost which usually influences us since well as the particular arena is moving in the direction of e-international simply by which utmost associated with the consequences is definitely digitalized and end up being had on the particular mouse.

From the various areas of recommendation system, product recommendation system is one of the best of them. Product recommends the item related item which we choose or selected. Before digitalization Product recommendation system is known as Traditional commerce & after digitalization it is known as electronic commerce or digital commerce or E-commerce. Now, in modern age after digitalization also traditional commerce is used as like shops & malls & most of the transactions are performed through Internet with the help of on-line shopping and other digital activities that makes e-commerce to become more popular and famous. Popular E-commerce websites are like amazon.com, flipkart.com, meesho.com, etc.

Literature Review

Recommender systems generally appoint each or every collaborative filtering and content material predicated filtering (moreover called the persona predicated approach), further to distinctive systems analogous as expertise predicated systems. Cooperative filtering techniques make a model from a character`s formerly behaviour (information previously presented or named and/ or numerical conditions given to those information) further to similar critiques made thru distinctive stoners. (1) This model is also used to are anticipating information (or conditions for information) that the character may additionally have an interest in. (2) Content predicated filtering techniques use a chain of separate, pretagged developments of an item a very good manner to recommend smooth information with similar parcels. (1) (3) (4) (5)

The basics of recommender systems were primarily based totally with the resource of the use of inquiries into cognition wisdom (1) and data recovery (2), and its first manifestation have become the Usenet conversation machine created with the resource of the use of Duke University with inside the change half of the 1970s (3), wherein stoners were suitable to partake textual content with each other. These had been disbursed via way of means of newsgroups and organizations to lessen the issue of searching, however they're now not straight away responding to or centering on Stoner`s potential. The first comparable end result identified became the pc librarian Grundy. He first investigated Stoner's alternatives after which advocated analysing an e-book in this statistic. Based at the data collected, the tool gave clients the proper to apply opportunity primitive devices, so we advocated the identical e-book to all women and men withinside the identical organization. See Rich's 1979 composition (1) for special data on Grundy's profits and the effect of the cut up among Stoners.

This approach might also additionally appear a chunk early, however it is while it is a paradigm shift in computerized offerings due to the fact it is personalized. It`s essential to note that this corner has now not been reached with the resource of the use of all net stores, simply now. Still, Grundy`s cease end result snappily obtained masses of critics withinside the scientific world. Nisbett and Wilson nation that "people are truly prone withinside the look at and description of their private cognitive processes"(4). According to their studies, people constantly take away darkness from their attributes which motive them to face happy with the rest of a selected organization, making stereotyping sweats more delicate. Of course, it could be that we surely want to. As Heli Vaiano, the director of 1 in each of Northern Europe`s largest shopping for stores expressions a hint sort of in her earlier interview "People respond to questionnaires in a way that makes them look better. I don`t watch about lies. I`m interested in data." (5). That`s why she`s organized her shopping for centre with Wi-Fi outfit which could music traffic interior and withinside the on the spontaneous vicinity of the form with a delicacy of measures. The detail is that instead of the traffic their behaviour wants to talk. （6）

Quite simply, without a hesitation one-of-a-kind guideline involving recommender structures currently have developed through typically the years collaborative blocking and content material- predicated filtering (7). The former makes an attempt to machinate (profile) the flavour involving stoners and offers content material directly to them that stoners having comparable choices preferred. The content material- predicated filtering can be ready understanding typically the confines on the simple fact to be advised (for example, some sort of musical satisfied suggestions device can have a look at the subsequent limits style, artist, time period, concinnity, etc.) as well as the consumer`s options for those limits or characteristics. Therefore, whenever a customer likes any additional song, this brand-new data is delivered to their user profile (8)(9). The very first sort of collaborative filtering and also the particular starting place of times period changed directly into the Shade device evolved via method of way of Photocopied PARC, which permitted its stoners in order to take notes in addition to touch on the particular files they have got been reading (first off in dual form get pleasure from or even disliking it). (10) (11) Consequently, stoners couldn't best employ the content substance in the files in order to manually constrict their particular quest, however upon the bottom associated with your notes in addition to opinions from diverse stoners, which earlier attaining another volume of stoners, turned into appropriate to get ranking the thematic documents as a replace properly at the particular bottom in their particular connection and distance (6).

Group Zoom lens (3), which started out in 1992, changed into earlier appropriate to help to make robot recommendations regarding Usenet papers when the consumer got previously expected a couple of papers withinside the particular gadget. In the particular subsequent times, multitudinous thematic recommender places are actually evolved, similar as Ringo progressed at MIT, quicker or later typically the Firefly track recommender runners, or typically the Bell Core motion picture proposer gadget. (12)(13) The initial ending consequence, which now not any longer best experimented with to embody fewer wide motifs, however not any decrease than typically the Internet itself modified into Yahoo!, within Neath a one-of-a-kind call additionally. (14) The Stanford pupils created a thematic internet site various with indexed sports people, which snappily acquired fissionability and meant simpler searches to get hundreds of hundreds and hundreds with the Internet, together with predicated at typically the Alexa ratings it is even so ranked for the reason that 5th maximum been to internet site. Typically, the roots of information material- predicated blocking need to possibly be searched for withinside the data therapeutic field, from which will multitudinous methods have been transferred. (15) Typically, the first proved ending result got below from Emanuel Goldberg withinside the twenties (if now not any longer which includes typically the Jacquard impend given in 1801, typically the precursor of typically the Hollerith punch card), which become some sort of "statistical machine" of which attempted to often locate files ended up saving on celluloid tape via way involving method of looking to get patterns (7).

Nearly 50 years before, way to a new crew of analysts for the University regarding Cornwall amassing rounded Salton, a type for computerized indexing of handbooks features been created above almost ten years, which bureaucracy typically the bottom with the file content mining tactics we recognize time (8). The fashion is without question simple, data files are categorized along with sure fated conditions (confines) which will be amassed to a

vector as pointers. Typically, the in addition identical files are to be able to every different, typically the cure the point of view of the vectors describing them will be. (16) The approaching nook become typically the CITE on-line several tools evolved inside 1979 via means of means of Tamas Dusk as intended for the National Selection of Medicine (17), which now zero longer best granted stoners to consider publications via method of indicates of order, nevertheless looked after all of them via way associated with means of link predicated on mission.

Content- predicated blocking has won conscience discourage pretty past due with within the Nineties as a division of facts recuperation. The key motive with regard to the detention grew to become that growing the well- appearing content material- predicated blocking machine, certainly within a specific issue, is a large task, for the cause that mission is just not anything decrease within order to "understand" the tested content material and the particular components impacting the particular connection from the stoners to the self-discipline. One of the particular primaries and fairly a hit disquisition with this problem grew to become the background songs Genome Project this happened in 99, which goals in order to "understand" and foyer song thru the parcels. To this particular end, in inclusion than 450 similar parcels were found out and their family members were defined the use of a set associated with rules. The bottom associated with the manner is the fact that after the customer likes a track, nice values are usually assigned to the precise parcels (analogous as style, time period, artist, concinnity, defeat, and so on). (18) (19) (20) Songs along with comparable parcels may also be in addition advertised in the desire list and taken in order to the consumer`s consideration. The big profit to collaborative blocking is that inside reality little specifics is enough with nascency, even while the prior sadly calls for various stoners and responses to pick out their human beings using comparable tastes. Nonetheless, the drawback is the fact usually it is definitely able to scarcely, or now not anymore at every help make pointer out regarding doors the consumer`s song lists, as it isn't always erecting at the parallels among stoners, ideal the "understanding" typically the parcels of tune as being a reality. The planet pandora Internet Radio, which in turn has 250 thousand stoners, is located throughout this layout surely moment (21).

The initial ending result to be able to mix collaborative and even happy- predicated blocking consequences became Ok (22) evolved using the aid involving using Stanford students, are available in 1994. That they factor out of which their perfect using the crossbred equipment is to bear in mind the negative areas of the 2 tactics which got below recognised with typically the aid of employing time. Their type includes introductory approaches first they accumulate subject material for specific motifs (analogous while sites or paperwork approximately monetary motifs), additionally for each individual consumer they handpick the types information amassed from exact subjects which within large part probably will intrigue all of them especially and within the long term those material will attain the particular consumer. Combining the particular 2 tactics might be conceived in several ways, one way might be bedded within another, as Fab`s example shows, or even it`s possible existing a not uncommon place advice due to the 2 techniques, as Netflix will. Netflix`s set associated with rules, Cine-Match grew to become the most a strike recommender machine with regard to on line movie offers withinside the first 2000s. (23) It probably is a critical prompt for analogous disquisition as well as the medical industry – which greatest started out the impartial truth withinside the 90s: started out quickly to develop. The particular 2006 Netflix Award`s assignment became to provide a recommender group of rules predicated in a hundred million motion picture opinions made to be able to be had using the aid involving using them, helping to make pointers at typically the least 10 improves than the implications of Cine-Match. Typically, the 1 million cuboid prize in year became provided intended for an ending end result that covered 107 extraordinary algorithms and even blended their hints relying with the instances (24).

We can`t neglect in regards to the most significant example of online referral structures time, amazon. com, which in turn recommends merchandise for the consumer predicated over a cooperative filtering fashion, deliberating formerly looked at and acquired goods and what these kinds of are currently viewing. (25) This style is definitely now employed by multitudinous net stores that you can meliorate their presents figures. The objective of the recommender structures working withinside the on-line customer area is to be able to personalize the store in coordination using the cutting-edge taste and want with the guests. This makes an almost impregnable aggressive benefit intended for on the web stores above conventional slipup-and-mortar always keep purchases, whose ideal

issue is of which the product could possibly be touched with typically the aid of employing hand or tried on. Presently, it really is extra regular that will once a right for shopping the products are ordered upon line, or the use of the product proceed back choice

Product Recommendation in Past

The way in which of face-to- encounter verbal exchange associated with swapping items plus offerings with inside condition of plutocrat directly, dealing as well as shopping for associated with products is known to as Conventional Commerce. Former Conventional Commerce is known to as betray machine and started in the time associated with the alternate device which become delivered with inside earlier tens of hundreds and thousands associated with instances a gene. The alternate device is performed with using swapping associated with products with various items as a good alternative of plutocrat in which plutocrat wasn`t to end up being had at several point from the particular one's days. At this point, Traditional Commerce carried out with the help of using changing of plutocrat with using promoting associated with products and choices. Currently Traditional Business misplaced its fissionability and were provided decreased as a result of the particular E-trade with inside early of 20th century. Traditional Business offers with face-to- face trade plus in character managing all of the particular events to take on the trade associated with products and choices with predefined costs. It's an off-line mode marketing. They have the procedure to get buying, dealing or even swapping products, providers or information, is normally physical, meaning there is certainly the actuality associated with the physical shop. It relies a lot more on original customers interacting with offers directors, directors, customer service help plus accountants' tête-à-tête vs through electronic mediums. (26) (27)

Businesses supposed as traditional commerce handle advertising, force shipping and creation of products and services in- house with a staff of workers in close contiguity. Traditional commerce does not generally partake information with contenders whereas e-commerce prices, specials and force are readily available online for consumers and contenders. Traditional trade offers with face-to- face trade with customers and shops predicated on phrase of mouth, networking and store referrals for brand new and repeat business. Particular commerce is a pivotal element of businesses substantiation success with traditional commerce. Multitudinous businesses network within the community, establish fellowship with municipality leaders and chambers of commerce and patron original events and sports armies to develop a relationship with the community to draw in business. It's ancient still in operation where digital network isn't accessible. Former when digital network isn't used that time traditional commerce takes vital part of our life. For Traditional commerce, shops, promenades are there. In once and also ultramodern age the product recommendation system of traditional commerce is done by shopkeeper. For illustration, if we go to a cloth store for buy a shirt also shopkeeper shows us verity of shirts rather than that he also recommends verities of maquilas by the preferring of shirts also suggests to buy matching sunglasses & corresponding shoes. Later done our own shopping he also asking are you buying night- earthenware cloths, daily-use cloths or any cloths for family? In that way product recommendation system is done by shopkeeper. For Another Example, if we go to a shopping boardwalk, in there all particulars are placed in correct order as per recommendation means if we elect a sprat's item like toy & for recommendation verities of toys, balls, cloths & chocolates are there. In that way product recommendation system works.

Product Recommendation in Present

Now, in the advanced world everything is digital & everyone uses internet in their day moment life. It has made mortal life so easy moment that now, sitting at home, a person can do nearly all the work of the world through the Internet & make our life digital. In this digital world, our marketing is also involved in digital world to make our life easier that's known E-commerce (electronic commerce) means buying & dealing of goods & services or the transmitting of finances or data over an electronic network or computer network similar as internet. It can use anywhere & anytime. Unlike existing stores, the online store is open 24 hours a day, 365 days a year. E-commerce or digital commerce refers to transactions conducted over the Internet. Whenever individuals and businesses buy or sell goods and services online, they are engaging in e-commerce.(17) (26)

The e-commerce record began with the first online transaction on August 11, 1994, when a person bought a CD from his peers through his website Net Request, an American trading platform, with the help of the band Sting. This is the first example of a buyer stealing a product from a company via the World Wide Web. This is the well-known "e-commerce" today. Today, e-commerce is famous and notorious, and orders or purchases are overly expensive. Since then, e-commerce has evolved to make it easier to find and buy products at online outlets and retail stores. Independent freelancers, small businesses, and large pots all benefit from e-commerce. This allows you to promote your products and transactions on a scale not possible with traditional offline retailing. (27)

E-commerce is part of e-business. All sales that result in tax changes are e-commerce. All business sales, whether taxable or not, are called e-business. It relies on similar technologies such as mobile commerce, electronic money transfers, force chain operations, internet marketing, online sales processing, EDI, force operation systems, and automated data collection systems. Ultra-modern e-commerce typically uses the World Wide Web for at least part of its sales lifecycle, but you can also use technology similar to email. Product recommendation techniques in e-commerce is a digital mode recommendation. It occurs when a user clicks or selects an item then that's product related items are shown there. For example, if we search for kitchen related item like dinner set after clicking a dinner set then as for the result of recommendation other verities of dinner sets based on size, design, colour & pieces, non- steel dinner sets, disk rack, dish washing gloves, dish swiping cloth, dish washing soap or liquid, cooking spoons & gas lighter etc. In that way it works.

METHODOLOGY

Frequent item set mining leads to correlations between institutional inventions and the details of large transactional or relational datasets. Due to the constant accumulation and storage of large datasets, many companies are interested in combining styles of similar formats from databases. Publishing "correlated links" in a large amount of alternative information helps with a number of decision-making processes, similar to register layout, cross-marketing, and conducting consumer purchase analysis. A famous example of common itemset mining is Market Basket Analysis. This technique identifies patron shopping for behaviour through chancing institutions among the distinctive details that visitors' area in their "buying baskets" as we will see withinside the beneath figure. The discovery of this sort of affiliation could be beneficial for outlets or entrepreneurs to expand advertising techniques through gaining perception into which details are continuously offered collectively through visitors. For illustration, if visitors are shopping for flour, how possibly are they to additionally purchase milk, sugar & crucial canvas (and which type of crucial canvas in preference to that every other consequence also are demanded) at the equal journey to the supermarket? These facts might also additionally result in growth offers via way of means of supporting shops to do choosy advertising and plan their ledge space.

Algorithm of Product Recommendation

- Algorithm used for product recommendation system of both traditional & digital commerce is Association Rule Mining. It's a data mining fashion of rooting association rules among the data particulars present in the given sale database & it generally used in the retail assiduity in a trouble to understand copping geste. It looks for combinations of particulars that constantly do in the same trade. In other words, it gives perceptivity into particulars that may have some association or affinity.
- The implication expression of association rule is x→y, where x & y are item sets.
- The two matrices of association rule are support & confidence.
- From the above fig. we can get some idea about association rule.
- Support: indicates the frequency of itemset

Confidence: find the truth of the number of times relationship have

- For illustration, guests copping flour and sugar are also likely to buy eggs. The outgrowth of the analysis is to decide a set of rules that can be understood as "if this, also that". Retailers can use this perceptivity to do product

placements or offer abatements means if a customer or retailer buy bread then probably, he also purchased butter, jam, eggs or milk. So, in that order both traditional commerce & ecommerce are done. In Traditional commerce everything is placed in the order of this that recommends to customers or retailers. In e-commerce also everything those are shown in front of our screen by a click of selected item or searched item or wish list that is the algorithm of recommendation system.

- Market basket Analysis is the collection of association rule. The frequent itemset mining is known as market basket analysis & it is used for transactional data.
- Request handbasket analysis uncovers associations between products by looking for combinations of products that constantly co-occur in deals. Thus, supermarkets can identify connections between products that people buy.
- For illustration, guests who buy a pencil and paper are likely to buy an eraser or autonomous. A customer in an English barroom buying a pint of beer without a bar mess is more likely to buy crisps/ chips than notoriety who didn't buy beer. Someone who buys cleaner is likely to buy conditioner. Retailers can use this information to modify the store layout or offer reduction on cleaner but not on conditioner.
- Online retails similar as Amazon make product purchase recommendations. However, Amazon will recommend other particulars that other guests frequently bought together with named item, if you add any item to your wain.
- Apriori Algorithm is an algorithm for frequent itemset mining means transactional data & association rule literacy over relational databases. By this algorithm we can count support, confidence.

Support: The support of an itemset is a measure of how constantly the itemset occurs in the data. Formally, the support for an itemset X is defined as

$$\text{Support}(X) = \frac{Count\ (X)}{N}$$

Where, N is the no. of transactions in the database and Count(X)is the no. of transactions containing itemset X.

Confidence: It is a measurement of accuracy & It is defined as

$$\text{Confidence}(X \rightarrow Y) = \frac{Support\ (X,Y)}{Support\ (X)}$$

Confidence use for the proportion of transactions where the presence of itemset X results in the presence of itemset Y.

FUTURE DIRECTION

In the faster growing world, day by day everything is going to more digital to make our life easier & smoother. By the rapid growth of advancement, the future of product recommendation system will also reached at its advanced state .In my point of view the future of product of recommendation system will be like voice recognition in multiple languages , text translators in multiple languages, drawing of a product means if a user draw a product or item which he/she wants to search then after that drawing completed server will shows some option to choose what he/she wants then after choosing the option then it will give us results , whether if it is doesn't shows the result then it comes back to its final page. So, I think in that way product recommendation system will be advanced in future.

CONCLUSION

With a spare information cargo over Internet, stoners need good and sound recommendation ways. In this paper, we describe various recommendation ways and curtly their advantages and limitations are developed. This gives a clear idea about the recommendation approaches and easy to understand the sensations of recommendation, indeed for a native user. Ultimately, we conclude that there is a need to make a lot of sweats to overcome the limitations of the being ways.

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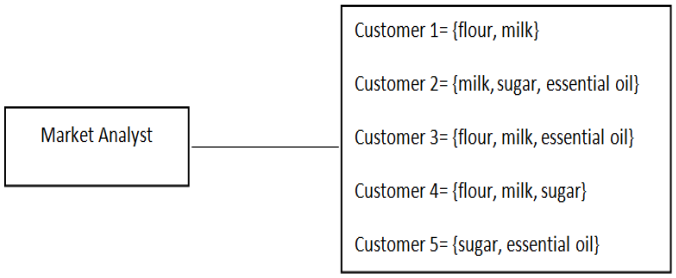

Fig. 1 Verifying Frequently purchased items

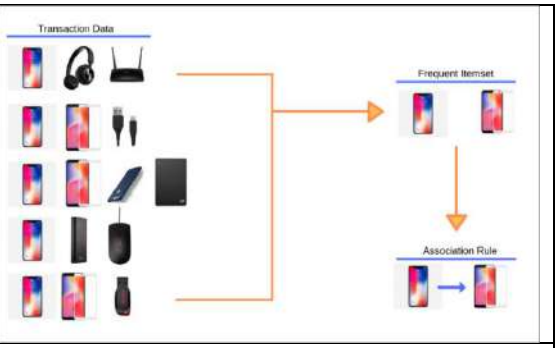

Fig. 2 Finding Association Rule

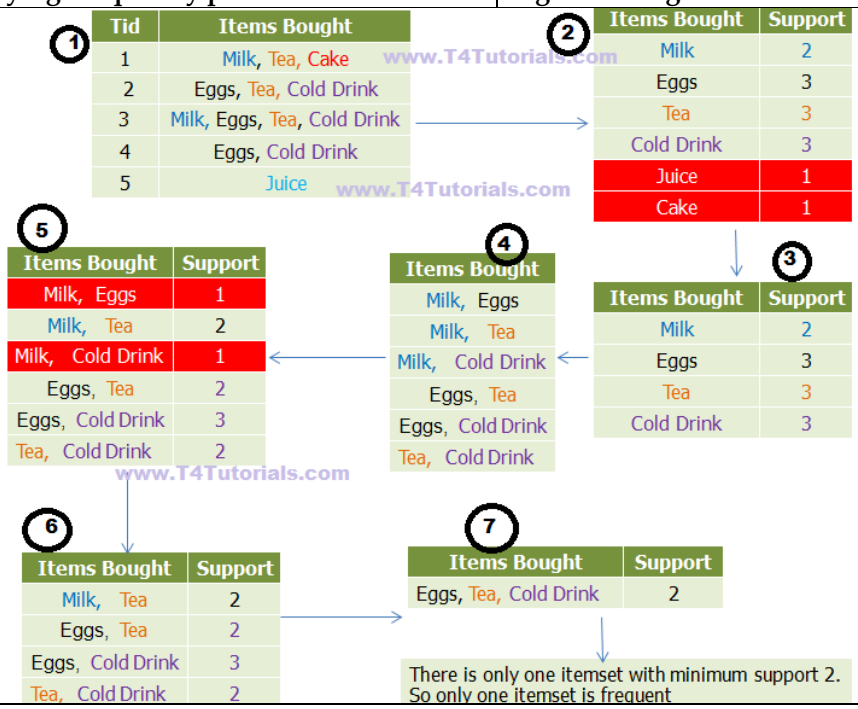

Fig. 3 An example of Apriori Algorithm

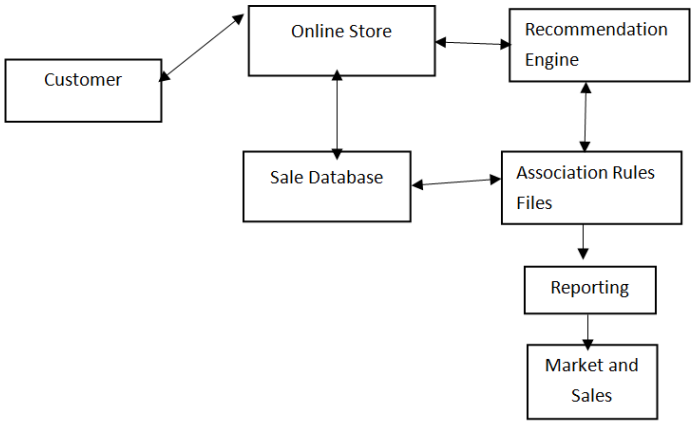

Fig. 4 Online Product Recommendation

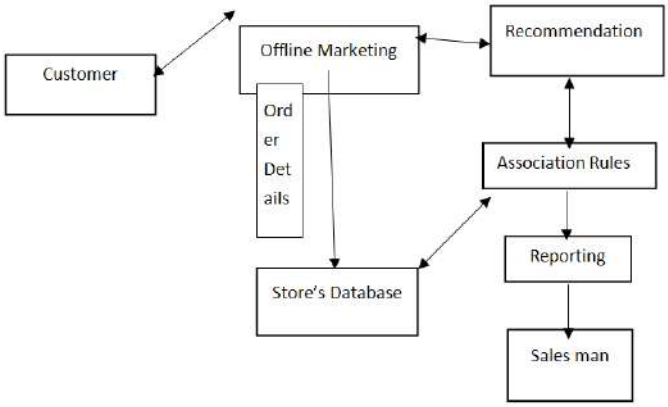

Fig. 5 Offline Product Recommendation

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RESEARCH ARTICLE

Integrated Farming System for Agricultural Sustainability

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ABSTRACT

Majority of the farmers of India as well as other developing countries are small and marginal and practising farming operations since long back but are unable to fulfil their basic requirements or even dietary needs. In general, farmers prefer confine their farming activities into a single enterprise. But there are several agriculture and allied activities such as crop, livestock, fishery, apiculture, duckery, agroforestry, vermicomposting, biogas production, mushroom production etc. that can be incorporated with crop production as per the suitability and compatibility. The faming system provides ample scope for inclusion of such activities with crop production for increasing the productivity, profitability, employment generation, food and nutritional security and ultimately agricultural sustainability. The integration of enterprises is done with a primary target of utilization of by-products, lowering the overall input cost, efficient resource use and more farm output. The article focuses on the need for adoption of integrated farming system and some common options to make the farming a profitable venture.

Keywords: Integrated farming system, needs, enterprises, options, advantages.

INTRODUCTION

In the present consequences of climate change, the concurrent agriculture is in various threats such as high carbon footprint, declining natural resources, global warming and climatic aberration, and yield plateauing of major crops (Maitra *et al*., 2018; Hossain *et al*., 2021; Zaman *et al*., 2017; Das *et al*., 2021). The increasing human and livestock population further added a dimension in enhancing production and productivity of food and feeds to fulfill the requirement. Achieving the increased farm output is rather difficult in the developing countries because of small land holdings, low input use efficiency and limitations in adoption of latest and improved technologies because of low investment in agriculture (Palai *et al*., 2019; Maitra *et al*., 1997, 2021; Nduwimana *et al*., 2020). Though there are limitations in the developing countries of the tropical and sub-tropical regions, the conventional agriculture offers ample scope in the form of diversification of crops (Maitra, 2020; Brahmachari *et al*., 2019), and cropping and farming systems (Gitari*et al*., 2020; Maitra *et al*., 2001) with an opportunity of achieving agricultural sustainability (Maitra,

2018;2020). The system approach is very important and appropriate for the smallholders for enhancement of gross farm productivity by going with the ecology (Pramanick *et al*., 2018, 2020; Kar *et al*., 2021). The integrated farming system (IFS)can be considered as a vital solution of several issues in this regard with the stability of income, nutritional security, and sustainability of livelihood for the smallholders. (Maitra and Shankar, 2019). Hence, proper utilization of resources within the scope of IFS is vital to mitigate the risk related to achieving agricultural sustainability.

India is a developing country and its economy is mainly based on agriculture and allied sectors. In Indian rural economy,85% of the total farming is relied on small and marginal farmers which possess 44% of total operational land(GOI,2014).Horizontal intensification is not easy as the land for production is somewhat constant or reducing due to increase in population and can't be expanded (Maitra *et al*., 2020). So,vertical intensification is the only solution which include integrated farming system(Panwar *et al*., 2019), but integrated farming is a bit risky as it requires skill on different enterprises chosen and even the integrated enterprises should be compatible enough to give profit but the future growth of the farmer is there due to increase in diversity produce, increased productivity and profitability and even utilise the residues which in turn reduce cost of production whereas one single enterprise can never be able to profit the small farmers in long term (Ravisankar *et al*., 2007).

Different methods are present to increase productivity from same area at same time not just integrated farming system but the main difference with other methods is that it utilises the residues of the integrated enterprise and safeguard or reduce the faster rate of natural resources depletion and even reduce the residue deposition on environment which leads to sustainability. After Green revolution, the increase in demand for the inorganic fertilizers to increase the production cause degradation of soil health at faster rate and even increase the fertilizer cost. Even the farmers use fertilizer in higher doses than recommended thinking it would increase the production which increase the cost of cultivation. In the world, different farming systems were present and practiced individually which generate lot of residues from each and every sector. To combat this problem, integration of different farming systems or enterprises which were compatible among each other were practiced which generate employment, improve production and provide nutritional security. Thus, integrated farming system became very popular as it uses the residues of one enterprise as the input for another enterprise which reduce the cost of cultivation and residues deposition. Moreover, the article focuses on the issues related to some sustainable development goals such as "SDG 1 (no poverty), SDG 2 (end hunger, achieve food security and improved nutrition and promote sustainable agriculture), SDG 13 (take urgent action to combat climate change and its impacts) and SDG 15 (protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss)" (UN, 2022).

Integrated Crop-Livestock System (ICLS)

Crop-livestock system is a very common practice of integrated system in which the crop residues or fodder from food crops, agroforestry which are used as feed for the livestock such as cattle, poultry, swine, sheep, goat and fishery whereas the animal manure from livestock enriches the soil health helping in proper growth of crops. As the major feed supplied to the livestock is fulfilled from the crop residues in ICLS which reduces the coemption from human food (Blummel,2010) and thus considered as an advantageous system. There are various types of ICLS and the selection of particular integration type for a specific place or area depends on the resource present, soil, climate, farmers skill or knowledge on the enterprises and in its management and even on farmers buying capacity (Garrett *et al*.,2017). The diversity plays an important role in ICLS as the inter species diversity is more beneficial and effective over intra species diversity (Romeo *et al*.,2016). Generally, the crops should be rotated with legume or cover crops which add protein content to the vegetation and increase its nutritional value which indirectly benefits human health (Wilkins, 2007). The interaction of crop with livestock were found to be profitable as it utilises the residues efficiently, increases the income of farmers, maintain soil fertility and sustainability. The total production increased due to interaction. Besides this it also increases employment opportunities. The profit from the crop livestock integration is more than the sum of the both the profits of individual enterprises. Because they utilise the residues as

input for other enterprise which generally increases overall farm efficiency and productivity of both enterprises (Soussana and Lemaire,2014).

Integrated Livestock-Fish System

In this type of integrated system, the manures from the livestock like cattle, poultry, swine, sheep, goat were used as an input for the fish or aquaculture animals which were used as fertilizer or nutrition for the fish (Delmendo, 1980). But the manures from different livestock have different level of organism development in food web, due to which they have different levels of biological activity in fish pond. The sequence is like duck manure > pig manure > raw chicken manure > cattle manure > sheep manure (Prinsloo and Schoonbee,1987).Different livestock have different levels of digestion capacity, so huge amount of nutrition from their feed is not assimilated which cause the release of lot of nutrition from their excreta. The excreta of pig show high indigested feed with nutrients in excreta (Edwards, 1985).The nutrients are released in pond when the bacteria break the organic matter of animal manure which in turn helps in the growth of phytoplankton and zooplankton. In integrated system of poultry and fish, the chicken droppings contain major inorganic nutrients, i.e., NPK and some trace elements which adds the fertilizer and nutrients to the fish feed(Taiganides, 1978). The conversion rate of droppings of chicken (25.5%) is almost double than that in manure treated ponds,i.e.,14.3%, which shows that the fresh manure has high performance in pond productivity(Prinsloo *et. al*.,1999). Fang *et al*. (1986) reported and showed that 16.7 kg and 27 kg of chicken droppings and pig manure produce one kg of fish.

Rice-Fish-Duck IntegratedSystem

In India, rice is the main staple food and to increase its production as per rapid increase in population demand, practices of application of more fertilizer, pesticides and herbicides are followed. In many areas, farmers are practising rice as monocropping. In rice-fish or rice-duck or rice-fish-duck integration systems, the activities of regular organic faecal droppings, movement, scooping and churning of soil by fish and duck enhances the soil nutrient level concentration and which leads to increase in production and profit. Rice-fish-duck system cause increase in more planktons than rice-fish system due to addition of more faecal droppings by duck which adds more nutrition (Desta *et al*., 2014) whereas fishes even used to feed on planktons (Vromant and Chau, 2005; Frei and Becker, 2005).The fertilizer and agrochemical requirement of rice crop gets reduced due to increase in soil health condition (Nayak *et al*.,2018).

Crop-Livestock-Vermicomposting System

This is a very popular type of integration in which the crop residues and animal manure are used as an input for vermicomposting and in turn the compost can be used to cultivate crops which reduces the excessive use of inorganic fertilizers and improves soil health and fertility and maintain sustainable environment. The agricultural and animal residue is generated in a huge amount which can be used as an organic supplement for the crops after proper recycling or processing after composting which improves soil and eco-friendly in nature (Bhardwaj, 1995).Generally, the crop residues obtained are poor in nitrogen content, so some nitrogen rich wastes or supplements are mixed with it which act as an inoculum and even food for the microorganisms(Elvira *et al*., 1996).During vermicomposting, total nitrogen increases due to loss of organic carbon as carbon dioxide and its increase depends on the initial nitrogen present in the waste and decomposition period(Gaur and Singh, 1995).

Crop-Livestock-Biogas Integrated System

The process of converting the wastes or residues into a useful product by integrating different enterprises like in this type of integration the crop residues are feed to the livestock or can be used directly for biogas production. Animal manure and crop residues are used as feedstock to produce biogas (used for different purposes like fuel, electricity, etc.) whereas in turn the effluent left after biogas production can be used as a fertilizer for the crops. The livestock manure collected and processed by anaerobic digestion generally have many benefits such as reduction in CH_4 emission, biogas production, pathogen decrease and proper manure recycling. The manures are mixed with water and added on the digester where the mixture gets digested and release gas which are stored in a gas chamber (Preston and Leng,1989).This is not the end, the main products obtained are biogas and effluent, in which the effluent

can be used directly as fertilizer for crops as during digestion the organic N in manure gets converted into ammonia ions(Sophin and Preston,2001).

Crop-Apiculture Integrated System

Honeybees produce honey and perform a vital role in agriculture as pollinating agents. In the world,65 % of the food production is from the staple food crops like rice, wheat and maize (which are self-pollinated) and rest 35% agricultural production depends on pollinating agents (Klein *et al*. 2007).Bees gave more benefit to humans over any other insect. In the world, to produce seeds and fruits, more than one third of the crops like apple,citrus, cucurbits, strawberry, apricot, peach, mango, grape, carrot, legumes, sunflower, various nuts etc. are dependent on pollinating agents. The fibre and timber crops don't require pollination, but pollination is beneficial to produce future generations from them whereas cotton crop produce more yield due to proper pollination (Allen-Wardell *et al*. 1998).

Crop-Mushroom Integrated System

In this integration system, the crop residues such as straw, husks, leaves, etc. are used as a substrate for the mushroom production. Besides the value of crop residues as raw materials for composting, these can further be used as media for mushroom production (Arai et al. 2015). In this way value addition of agricultural by-products can be done. On the other hand, the mushrooms produced augments the farm income and provides food and nutritional security to the smallholders.

Advantages of IFS

There are several advantages of IFS which have been listed below.

- Food and nutrition security
- Scientific waste/ by-product recycling
- Employment generation
- Development of agro-industries
- Increase in standard of living
- Adoption of new technology
- Environmental safety
- Agricultural sustainability
- Year round cash flow
- Enhanced farm income

CONCLUSION

Integration of different enterprises increases the productivity, profitability and agricultural sustainability over a single enterprise. To reduce the huge quantity of residues and by-products, IFS can be suitable option for proper value addition. By adoption of IFS, the smallholders can enhance farm income, livelihood and agricultural sustainability. Considering the benefits of IFS, it can be stated that for the smallholders of the developing countries IFS should be adopted to herness numerous advantages as well as economic stability of the farmers.

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RESEARCH ARTICLE

Biomimetics: A Novel Tool for Targeted Drug Delivery

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ABSTRACT

The targeted drug delivery system is the emphasis of the modern era of medication delivery. Biomimetic carriers are a type of novel carrier that is created by altering the surface of a pharmacological product to resemble the natural process of a cell. It causes the drug product to be easily absorbed by the cell and the drug substance to be released into the cytoplasm. There are six categories of biomimetic formulations namely biomimetic hydrogel, micelles, liposomes, dendrimers, polymeric carriers and nanostructures studied in this review focusing towards the sustainable growth for good health and well being. They are briefly described in terms of their preparation, application, advantages, shortcomings, and future references**.**

Keywords: Targeted drug delivery, biomimetics, drug carriers

INTRODUCTION

Traditional dosage forms, such as injections, oral formulations of solutions and suspensions, tablets capsules, and topical creams and ointments, all have drawbacks. Parenteral medication administration is intrusive and has short-term effects. Although oral administration of the drug is quite popular and acceptable, it cannot be utilised for certain drugs, such as peptide drugs, due to their poor oral absorption. To overcome those limitations of traditional dosage forms the Targeted drug delivery system is developed. Targeted drug delivery is a therapeutic strategy that includes transporting a medicinal material to a specific tissue while leaving the rest of the body alone. As a result, the drug is exclusively delivered to the body's areas of interest. The ability to load the drug to the target site, avoid degradation by body fluid, reach the target site, and release the drug at the precise place at the predetermined time are the four principles that must be followed in the drug targeting process. Depending on the route to be taken, different drug delivery mechanisms are required for different sites of interest within the body. The drug may be

administered into the capillaries of the targeted region, into the targeted cells, or into the muscle or tissue where the receptors can recognise the drug's carrier. The biomimetic carriers help to deliver the drug into the cytoplasm of the targeted cell [1]. Otto Schmitt coined the term "biomimetic" in 1957 and was the first to utilise it. Biomimetics is also known by the terms "biomimesis," "biomimicry," "bionics," "biognosis," and "biologically influenced design." The term "Biomimetics" is the most prominent and helpful among them.

The use of biomimetic is todemonstrates critical issues to treat incurable diseases such as cancer. Scientists have worked hard in recent studies to gain a better understanding of biological systems and processes. Understanding macromolecular structure and the complex processes that occur at the cellular level. For the purpose of drug delivery into tumor cells, permeability and retention (EPR) served as a key difficulty which was complicated by circulation time.In the presence of nanoparticles in bodily fluid Plasma proteins, such as immunoglobulin G, are attached to each other. The IgG gets deposited on the surface of nano particles by the reticuloendothelial system. These nano particles are removed as aggressive foreign particles. In order to protect them from the immune system by providing a stealth coating, numerous hydrophilic polymers have been used. One of most popular procedures in the last thirty years has been the surface coating of nanoparticles with polyethylene glycol (PEGylation).However, because of unfavourable interactions between PEG and target cells, as well as poor endosomal function, The cellular absorption of PEGylated nanoparticles has not been able to escape (this is known as the PEG dilemma).The loaded medicines were destroyed in lysosomes as a result of this. There is one biomimetic solution. The surface modification of PEGylated nanoparticles is used to overcome their steric hindrance. The surface modification was done by biological ligands such as proteins, vitamins, peptides, antibodies, and aptamers etc. This type of ligands have a high affinity for receptor-mediated target attachment.

As a result, biomimicking in sophisticated drug delivery systems have created intrinsic capabilities in biomimetic drug carriers that are just modified on the surface with amino acids, saccharides, and lipids. The capacity to replicate natural cells for cellular internalization necessitates paying close attention to the basic core materials, size, and form of drug carriers for this purpose. Additionally, localized drug delivery into targeted cells can be achieved by surface activation of these nano particles with particular biomolecules analogous to the composition and function of the exterior cell membrane. There are two categories of biomimetic vehicle for drug delivery depending on the fundamental material used to formulate them: inactivated viral and bacterial vectors and synthetic carriers which biomimetic manufactured nanoparticles mimicking the biological components. The synthetic vehicles are most suitable for in-vivo drug delivery [2]. The common forms of therapeutic drug carriers in advanced drug delivery systems are discussed in six areas in this review. The utilised biomimetic strategies for improving drug efficiency as well as drug release profile within target cells are examined in each part. Biomimetic hydrogels, biomimetic micelles, biomimetic liposomes, biomimetic dendrimers, biomimetic polymeric carriers and biomimetic nanostructures are examples of these distinct pieces and their usage as drug carriers. Although several evaluations have been written for the launch of these drug carriers, the biomimetic publications have not been properly examined [3].

Biomimetic Hydrogel

Hydrogels are a type of hydrophilic polymeric material that can be natural or synthetic. Furthermore, hydrogels can swell significantly due to the absorption of large amounts of water or biological fluids and remain insoluble in an aqueous environment due to chemical or physical cross-linking of individual polymer chains [4].Softness, flexibility, tunable porosity, and biocompatibility are also important properties of these biomaterials. The conditions for gel formation are relatively mild, resembling naturally living cells and tissues [5-6].The modification of the hydrogel matrix could create specific properties in rapid and reversible responses to various chemical and physical stimulation (such as pH, temperature, and ionic strength), which suit it for long-term active drug release. This property makes them useful in the delivery of biomolecules (such as protein and peptide therapeutics) [7]. Biomimetic hydrogels have emerged as a result of the addition of biological recognition sites for covering cellular activities and synchronising responses to environmental stimulation. In addition, hydrogel inert polymer chains should be tailored with select biological moieties to make them suitable for in vivo targeted drug delivery systems [16].Furthermore, by

mimicking the cellular microenvironment through the spatiotemporal incorporation of biological cues such as peptides, growth factors, and proteins into hydrogel matrices, a novel controlled drug delivery system to regenerate tissues could be developed [8].

Moschou et al. [20] created stimuli-sensitive hydrogels by embedding the hinge-motion binding protein calmodulin (CaM) and its low-affinity ligand phenothiazine TAPP (The free amine group of 3-(trifluoromethyl-phenothiazin-10-yl) Propylamine) within the bulk of an acrylamide hydrogel network. These hydrogel matrices can easily enter a compressive mode or release TAPP to break non-covalent cross-links, resulting in a reversible swollen state. The same mechanism occurs when CAM interacts with a higher affinity ligand, such as chlorpromazine (CPZ). Stimuli-sensitive hydrogels based on biomimetic proteins are useful for responsive drug delivery in response to various chemical stimuli.Liang et al. [9] used a heterogeneous agarose hydrogel to optimise the diffusion of protein (bovine serum albumin (BSA) and lysozyme) at body temperature in 2006. It was demonstrated that the generic properties of agarose hydrogels, such as composition, rheological nature, and water content, are similar to those of living tissues.Moon et al. [10] created biomimetic poly (ethylene glycol)-diacrylate (PEGDA) hydrogels containing ephrin-A1. The angiogenic properties of immobilised ephrin-A1 on the surface of hydrogels in vascular assembly were investigated in order to stimulate blood vessel formation. The addition of ephrin-A1 to PEGDA hydrogels stimulated HUVEC (Human umbilical vein endothelial cells) adhesion and capillary formation with lumens. It may also retain its ability to stimulate endothelial cell adhesion.

Fisher et al. [11] investigated therapeutic protein delivery by biomimetic hydrogels from oral in 2008. Poly (methacrylic acid) grafted poly (ethylene glycol) (P(MAA-g-EG) was used to make the hydrogels. Indeed, P(MAA-g-EG) as drug carriers capable of lateral tight junction disruption (the main resistance to the absorption of this type of drugs).Furthermore, pH-sensitive P(MAA-g-EG) hydrogels were not degraded in the stomach, which could enhance therapeutic protein transepithelial paracytosis in the intestine. Peptide-based hydrogels could be used to direct cell fate by mimicking the native extracellular matrix (ECM) interaction. A peptide hydrogel was created by alternating the hydrophobic and hydrophilic residues of peptide amphiphiles (PAs), which are self-assembling hydrogels. The synthesis of biologicallyinert peptide amphiphiles (PA-S) in conjunction with bioactive PAs improved the stability, viscoelasticity, and gelation properties of these new biomimetic hydrogels for in vivo drug delivery applications [12].The adhesion peptide arginine-glycine-aspartic acid (RGD) was bound into a mixture of alginate polymer chains to create a biomimetic 'bioactive cell-hydrogel' for encapsulating living cells. The novelty of these novel cell-hydrogel capsules was drug release for an extended period of time in vivo without stimulation of the immune system. This biomimetic drug delivery system was also self-controlling in 'cell-dose,' which provides a specific microenvironment for controlled drug delivery from immobilised cells [13].

In 2011, Bozzini et al. [14] used a recombinant human elastin-like polypeptide (HELP) as a basic polymer in a hydrogel that could mimic the structure of the ECM. The hydrogel was cross-linked using the enzymatic process of transglutaminase in HELP, which produced e-(c-glutamyl) lysine links via glutamine and lysine sites. Furthermore, these biomimetic hydrogels with satisfactory mechanical stability exhibited no cytotoxicity. Ravi et al. demonstrated how to modify recombinant elastin-like protein (ELP) polymer via chemoselective ligation of peptide linkers on the hydrogel surface. For drug delivery applications, RGD-modified ELP hydrogels could mimic the cellular behaviour of endothelial cells as well as mesenchymal stem cells. Instead of chemical cross-linking, which may be harmful to living cells, a simple and environmentally friendly method was used to create a biomimetic gelatin–siloxane (GT–S) hybrid hydrogel. In this method, a simple physically cross-link occurs in biocompatible solution based on S content and ambient temperature. At biocompatible conditions, this biomimetic hydrogel with highly elastic properties could be an appropriate carrier for drugs, proteins, and biomolecules [27].Kim et al. [29] created biomineralized hydrogels with specific sites for binding calcium ions by cross-linking natural polymers hyaluronic acid (HA) (a glycosaminoglycan ingredient in the ECM and synovial fluid of joints) and vinyl phosphonic acid (VPAc) in 2014 [14].

In 2015, Huh et al. created another biomineralized hybrid hydrogel made of HA and poloxamer (a poly(ethylene oxide)/poly(propylene oxide)/poly(ethylene oxide) (PEO–PPO–PEO) block copolymer) with an acidic functional group for calcium ion binding. This biomimetic hydrogel was a thermo responsive injectable gel that chemically and morphologically resembled natural bone matrix [15].Buffito et al. created an amphiphilic poly (ether urethane) (NHP407), which is a P407-modified copolymer (kind of poloxamers). In fact, NHP407 was capable of forming thermosensitive injectable hydrogels with improved aqueous stability, lower critical gelation temperature (LCGT), critical gelation concentration, and superior gel strength and gelation kinetics. Furthermore, NHP407's deprotected amino groups could be bound with bioactive molecules to form biomimetic hydrogels for use in cell/protein/drug delivery systems.

Sawicki et al. investigated click chemistries methods of fabricating and modifying hydrogels using light and various thiolXphotoclick chemistries in 2016. These methods allowed for precise spatiotemporal control of gel formation in order to achieve desired properties for drug delivery systems and tissue engineering. Biomimetic hydrogels produced using click chemistry methods demonstrated improved mechanical properties for encapsulation of various living cells such as human mesenchymal stem cells (hMSCs), fibroblasts, chondrocytes, and pancreatic cells for cell culture and drug delivery applications. It is clear that there is a diverse range of inspiration for fabricating biomimetic hydrogels for drug delivery applications. However, the majority of them are still in the early stages of being able to use in vivo therapeutic methods. The sustained and controlled release of therapeutic biomacromolecules from gel matrices at body temperature necessitates a thorough understanding of natural transport phenomena and diffusion behaviour in biological gel systems. This pathway could lead to the creation of biomimetic hydrogels that can be used in vivo. In addition, to achieve successful drug localization, one could create hydrogel matrices that are similar to the ECM. Physical and novel click chemistries methods, which provide easy and precise control over gel formation, are the most biocompatible methods for creating cross-linking within biomimetic hydrogel matrix [16].

Biomimetic Micelles

Micelle is a common term in chemistry that refers to a structure in aqueous solutions that has one hydrophobic core and one hydrophilic end. The utilisation of these supermolecules in drug delivery systems results in the development of innovative drug carriers in the treatment of diseases such as cancer. In 2005, Xu et al. created a biomimetic amphiphile with PEO using the cholesterol moiety (Chol), which is incorporated in the cell membrane and regulates membrane fluidity. Cholesterol blocks formed the hydrophobic cores of these Chol-PEO micelles, whereas PEO blocks formed the biocompatible shells for encapsulating adriamycin (ADR), a hydrophobic anti-cancer medication. In vitro tests, the Chol-PEO nanocapsules could provide efficient drug loading as well as sustained drug release behaviour. Xu et al.used cholesterol-end-capped poly(2-methacryloyloxyethyl phosphorylcholine) (CMPC) to produce micellar drug carriers, in which poly(MPC) was phospholipid moiety to form a more biocompatible shell with the human body, in a study similar to this one. In vitro experiments, this enhanced biomimetic micelle had fewer cytotoxicity effects than Chol-PEO micelles.

In addition, CMPC micelles, such as Chol-PEO micelles, have an appropriate nano size and sustained rate of release for ADR. Sallach et al. used protein polymer as a copolymer block of micelles in drug delivery devices in 2006, motivated by the reversible helix-to-sheet protein folding transition. In the micellar structure, a proteintriblock copolymer formed from elastin-mimetic peptide sequences was created using a recombinant DNA technique. One hydrophilic block served as the core, while two hydrophobic blocks served as the shell, in these biomimetic micelles. These biomimetic micelles were capable of rapid reaction to temperature stimuli in the environment due to the protein folding transition that emerged in micellar size and compression. Wang et al. (2012) created a new biocompatible copolymer with a core of hyperbranched poly (3-ethyl-3-(hydroxymethyl)oxetane) (HBPO) and a shell of zwitterionic poly(carboxybetaine) (PCB) to generate biomimetic HBPO-PCB micelles. The conjugation of Folic acid as a targeting ligand for folate receptors on cancer cells modified the surface of HBPO-PCB micelles, allowing tumour cells to easily endocytose them and release DOX (loaded anti-cancer medication) within the cells. Jiang et al.

conducted the same study in 2013 using a biomimetic hyper-branched copolymer, HBPO-PCB, as a micellar carrier for a different loaded anti-cancer medication, indomethacin (IND). Mandal et al. created Core–shell type lipid–polymer hybrid nanoparticles (CSLPHNPs) as drug carriers for encapsulating the anti-cancer medication erlotinib for lung cancer therapy in 2016. In vitro tests revealed that a PCL core enhanced mechanical qualities while the biomimetic phospholipid shell improved immunocompatibility and cellular internalization [17-20].

Liu et al. used biodegradable poly(g-benzyl-L-glutamate) (PBLG) and biomimetic PMPC to construct the micelle's core and shell, respectively, for DOX encapsulation. In vivo tests revealed that these biomimetic micelles efficiently aggregated within breast cancer cells via EPR. Wang et al. produced a new type of micelle dubbed multicompartment micelles, which was inspired by cell membrane compartmentalization. Multicompartment refers to many hydrophobic unique cores in a single hydrophilic shell that can trap and release numerous hydrophobic elements such as medicinal medicines at the same time. The self-assembly approach was used to create these biomimetic pod like supra micelles. To summarise, the enhancement of the biomimetic micellar carrier's physicochemical qualities allowed for the fabrication of a large number of stable micelles. The loaded medicine could be protected by a stabilised micellar structure until it reaches the target region, allowing for easy cellular absorption. As a result, the continuous release healthy cells, the toxicity of medications is modest. The creation of biomimetic multicompartment structures. Micelles, like cell membrane compartmentalization, provide the ability of the Various hydrophobic medicines are encapsulated. This method may allow these medicinal substances to be released within target cells at the same time. The previously indicated strategy appears to be a promising path to take. In vivo applications, cancer cells are suppressed more effectively [21].

Biomimetic Dendrimers

shape, with the interior repeating units (generations) originating from a focal core [22].These macromolecules have many functional groups on their surface (exterior reactive terminal groups) in addition to a defined shape, size, molecular weight, and monodispersity, making them suitable carriers in drug delivery systems. Drugs can be physically encapsulated within the dendritic structure or Dendrimers are highly branched three-dimensional macromolecules with a compact spherical conjugated to the surface via electrostatic or covalent bonds with the end functional groups [23-25]. Dendrimers may also improve drug molecules' water solubility, bioavailability, and biocompatibility .However, three factors in dendrimer structure cause toxicity that should be addressed before biomedical applications, namely the number of generations, composition, and surface charge. Furthermore, cationic dendrimers have more toxic effects than anionic or neutral dendrimers by inducing apoptosis via cell and organelle membranes [50].To create biomimetic drug carriers for targeted drug delivery, significant moieties can be linked to reactive terminal groups on the surface of dendrimers. Furthermore, because of the special monodispersity of dendrimers, these macromolecules could be self-assembled with structures similar to natural proteins and the ability to mimic versatile natural materials [26].

Huang et al. created a biomimetic multi-armed dendrimer at room temperature by ring-opening polymerization (ROP) of -benzyl-Lglutamate N-carboxyanhydride (BLG-NCA) and initial amine-ended groups of poly(amidoamine) (PAMAM). The secondary structure of the multi-armed PAMAM-PBLG dendrimers was similar to that of proteins, which could be easily regulated by a determined average size. In addition, stable globular nanoparticles as drug or gene carriers were formed by directly injecting these dendrimers into distilled water. FA and FA-PEG-NHS (N-hydroxysuccinimide) conjugates were used to modify the exterior amine groups on the surface of PAMAM dendrimers synthesised. FA ligands allowed for the sustained release of 5-fluorouracil (an anti-cancer drug) within cancer cells via receptor mediated endocytosis (RME) while causing less hemolytic toxicity. Yuan et al. [73] created poly(L-glutamic acid) dendrimers with an octa(3- aminopropyl) silsesquioxane (OAS) cubic core and a protein-like spherical structure in 2010. The OAS cubic core resulted in the formation of peptide dendrimers with a large number of functional-terminated groups and stable spherical morphology. DOX was immobilised via pH-sensitive bonds on dendrimer peripheral groups to form a smart pH-sensitive drug carrier in the acidic environment of cancer cells. RME was used to achieve sustained drug release into cancer cells by using biotin targeting ligands on the surface of

the dendrimer. PAMAM dendrimers were modified by glycine-proline-(hydroxy)proline in another study the same year to create collagen-mimic dendrimers (PPG-den) with higher peptides. These PPG-dens were formed by self-assembly in a temperature-dependent process similar to a triple helix in natural collagen and was similar to the collagen of the extracellular matrix in animal or human cells [27].

Kurtoglu et al. used PAMAM dendrimers to transport N-Acetyl cysteine (NAC, an anti-inflammatory agent used to treat neuro-inflammation, stroke, and cerebral palsy). The presence of a disulfide linkage increased the stability of the PAMAM dendrimer-NAC conjugate by inhibiting NAC binding in plasma proteins (glutathione (GSH), cysteine (Cys), and BSA) before reaching the target cells. Furthermore, the intrinsic proclivity of PAMAM dendrimers to target neuro-inflammation cells aided in intercellular drug uptake [28]. In 2004, Paleos et al. [69] used PEG chains and guanidinium ligands to modify the exterior surface of diaminobutanepoly(propylene imine) (DAB) dendrimers. As a result, the stealth cover and targeting capability via biologically acidic receptors were provided concurrently, resulting in more stability and less toxic effects of the amino groups in physiological media. Encapsulated pyrene and betamethasone valerate solubility and release behaviour in this multifunctional dendrimer were also studied in vitro.Jia et al. [75] modified the cationic surface of PAMAM dendrimers with acryloyloxyethyl phosphorylcholine (APC), where PC is a terminal zwitterionic section of some lipids as well as the exterior layer of cell membranes. As a result, the PC ligands reduced dendrimer cytotoxicity while providing a sustained release of ADR within the cancer cell. As a distinct field,Raghupathi et al. [76] first described the facially amphiphilic dendrimers in 2014. They demonstrated that the majority of studies on the behaviour of stimuli-sensitive supermolecular drug carriers were evaluated in the presence of secondary factors such as pH, temperature, and redox conditions, which caused imbalances in a biological milieu. In fact, the facially amphiphilic dendrimers were used to study the behaviour of dendrimer assemblies in biological media against real imbalances such as enzymatic and non-enzymatic protein stimulations.

Mekuria et al. [77] compared two PAMAM dendrimers modified with two different targeting ligands (IL-6 and RGD) as drug carriers against cancer cells. The DOX was loaded into the pH-sensitive PAMAM-IL-6 and PAMAMRGD dendrimers for this purpose. The in vitro assays revealed that the longer the IL-6 ligand, the more drug loading, intercellular uptake, and drug transfer via RME within cancer cells. As can be seen, PAMAMs were studied primarily for their intrinsic ability to improve intercellular drug uptake as a targeting drug carrier. However, the surface cationic charge caused by amino groups, as well as the number of generations, are the main challenges that cause the toxicity of these dendrimers. So, by using a polymeric coating to provide stealth cover and a biological ligand as a target, one could be hopeful for improved EPR effect and cellular uptake via RME for in vivo applications [28].

Biomimetic Liposome

Liposomes are spherical vesicles made up of phospholipids in a double layer (bilayer). Liposomes' lipid bilayer is similar to the cell membrane in the human body or animals, making them a potential carrier for drug delivery applications. Liposomes could be self-assembled in an aqueous medium from cholesterol and natural phospholipids. Liposomes have both hydrophobic and hydrophilic properties due to their concentric phospholipid bilayer surrounding an aqueous central section. Furthermore, they are non-toxic, biocompatible, and biodegradable, allowing them to transport both hydrophobic and hydrophilic drugs in phospholipids and the interior aqueous section. They differ in terms of lipid composition, surface charge, size, and manufacturing method. They are also classified as unilamellar vesicles (UV) or multilamellar vesicles (MLV) based on their size and number of bilayers [29-30]. Liposomes can be created using biomimetic approaches that mimic the biological behaviour of cells. In addition, biomimetic liposomes could be loaded with specific moieties or ligands to deliver drugs or biomolecules intracellularly. Furthermore, biomimetic liposomes could provide controlled cargo release, either passively or actively, in response to a definite stimulus in the cell microenvironment [30]. Westhaus et al. [55] created thermal-responsive liposomes in 2001 to encapsulate CaCl2 and release Ca+2 at body temperature. These biomimetic

liposomes were created by drawing inspiration from the rapid gelation of Ca+2 and polysaccharides such as alginate and protein.CaCl2-loaded liposomes could also be used as an in-situ injectable drug or biomaterial for tissue repair. To improve the liposome's stability as a drug carrier against enzymatic reactions, a multi-bilayer PEG-modified liposome (with two bilayers: vesosome) was created. Actually, the biomimetic structure of a eukaryote cell was created by encapsulating one unilamellar liposome into another.

Furthermore, the EPR effects of multi-bilayer liposomes for in situ drug release were improved [31].Zhu et al. created glycocalyx-mimicking liposomes as drug carriers in 2007 to target the damaged sites of cardiovascular diseases. P-selectin glycoprotein ligand1 (PSGL-1) levels rise in activated leukocytes during cardiovascular disease. PSGL-1 ligands then interact with PSGL-1 receptors on activated platelets. As a result, to mimic the structure of PSGL-1 ligands on activated leukocytes, SuLea-PEG-liposomes with two hydrophobic tails were created using a glycolipid of 3'-sulfo-Lewis a (SuLea) as a headgroup. Sakai et al. [56] synthesised PEG-coated liposomes to entrapped haemoglobin (Hb-vesicles) for artificially transferring O2 in red blood cells. In vivo studies revealed that injecting HbVs at a specific bolus infusion rate causes a moderate metabolism in the reticuloendothelial system. As a result, Hb-loaded liposomes may be promising O2 carriers for treating the related blood disease.

Gao et al. [59] used biotin-PEG-modified liposomes to coat polyelectrolyte microcapsules (PEMC) to increase their permeability as drug carriers within target cells. Thus, the biotin-PEG-lipid ligands on the outer surface of liposomes could bind with IgG, which is overexpressed on cancer cells, via biotin–avidin interaction. Furthermore, PEG-lipid sequences have increased the stability and life time of the liposome-modified PEMC by inhibiting unspecific protein adsorption.Kolick [33] investigated the ability of a liposomal formulation containing perifosine (a type of lysolipid) to increase liposomal membrane fluidity in 2014.Perifosine was also found to be capable of removing cell barriers and increasing encapsulated drug release in target cells at physiological temperatures. Cao et al. used isolated macrophage membranes to wrap the surface of anti-cancer drug-loaded liposomes in 2016. This decoration aided drug internalisation within breast cancer cells by enhancing the EPR effects. In vivo tests show that the ability of these biomimetic liposomes to target metastatic sites inhibits breast cancer lung metastasis. Chemotherapy and gene therapy were combined using co-loading of PTX drug and DNA in biomimetic multilamellar liposomes, respectively. Complexes of PEI/DNA (PD) as the cationic core and PTX were co-loaded into folic acid (FA)-modified liposomes to create FA/PPD cationic liposomes. The anionic hyaluronic acid (HA) was then coated on the outer surface of the liposome to create an anionic multilamellar liposome (HA/FA/PPD). The HA coating increased the stability of these dual targeting liposomes, whereas FA ligands increased the intercellular release of PTX and DNA within cancer cells at the same time [33-35].

Finally, biomimetic modification of the liposome surface, as well as biomimetic methods of liposome fabrication, improved the abilities of therapeutic liposomes in targeting drug delivery through the enhancement of the EPR effect. The low stability of drug-loaded carriers against enzyme degradation is the main limitation of unilamellar liposomes for in vivo applications. Another limitation is the premature release of encapsulated drugs before they reach target cells. The compartmentalization strategy used to create biomimetic multilamellar liposomes significantly enhances the EPR effect. Furthermore, these structures can encapsulate multiple hydrophobic and hydrophilic drugs as well as gene therapy agents to create dual cancer cell targeting carriers. The improvement of liposomal membrane fluidity may facilitate transport across cellular barriers.

Biomimetic Polymeric Carriers

Polymeric carriers have specific properties for drug delivery applications, such as easy nano-scale production, high drug loading capacity, controllable drug release, and surface modification due to their active functional groups [36]. Biomimetic polymers are new biomaterial carriers that mimic cellular interactions with their surroundings, such as cell attachment, cytokine signalling, and endocytosis. Furthermore, the biologically active entities of these polymers allow drug to be transferred through cell barriers within diseased cells. Furthermore, the appropriate biomimetic polymeric carrier is one that can reduce unspecific interactions on surface cells while extracting the desired cellular

response, resulting in the target being reached [32]. Duncan created two HPMA [N-(2-hydroxypropyl) methacrylamide] copolymer conjugates with aminogluthimide (an aromatase inhibitor) and chemotherapy DOX in 2007. It was also tailored to a specific molecular mass in order to select tumours via the endocytosis internalisation step. It was the first biodegradable polymer-drug conjugate to undergo phase I/II clinical testing.Zhang et al. created a biopolymeric material with a dual-functional property for conjugating with biological ligands out of zwitterionic poly(carboxybetaine methacrylate) (polyCBMA) grafted on a gold surface in 2006. Actually, by immobilising the specific one, it may have a high resistance to adsorption of non-specific proteins. The adsorption of hCG (human chorionic gonadotropin) was prevented in this study by immobilising anti-hCG on the surface. PolyCBMA-based materials' biomimetic dual functionality makes them ideal for medical diagnostics and drug delivery systems [32-35].

As a surface-based biomaterial, a biodegradable polymer such as starch was used to form a biomimetic calcium phosphate (CaP) coating on it. In fact, by combining sodium clodronate (a therapeutic agent) with CaP, the balance of osteoblastic/osteoclastic cell line activity at the interface with damaged bone was regulated in order to regenerate it [83].Ho et al. created a biomimetic endosomalytic polymer by grafting PP-75 (L-phenylalanine stoichiometric grafting) onto the pendant carboxylic acids of a polyamide (polyamide) (L-lysine isophthalamide). The main properties of PP-75 were its variable hydrodynamic size, which depends on pH, and its small size, which allowed for simple penetration into tumour spheroids as well as intracellular drug release with no cytotoxicity to other living cells. These abilities may encourage scientists to conduct additional clinical research on endosomalytic PP-75's in vivo applications [35]. In 2016, Ekkelenkamp et al. used zwitterionipoly(amido amine)s (PAAs) to create two types of PAA nano-gels in order to select the best one as a biomimetic and biocompatible polymeric carrier. Finally, PAA nanogels with low dispersity and a negative surface charge had less toxicity on living cells and were better suited as drug carriers than nanogels with a significantly positive surface charge.

Finally, surface modification of polymeric drug carriers by special ligands or moieties could facilitate intercellular drug release in target cells while having no negative effects on healthy cell functionality. Despite this, the in vivo application of these biomimetic drug carriers is still limited due to the severity of the control in the prevention of non-specific interactions in the cell microenvironment. The comprehensive understanding of intercellular trafficking pathways and the physiological properties of modifier ligands may lead to the development of biomimetic tailored polymeric drug carriers. It is also critical to optimise the chemical properties of synthetic polymers in order to reduce cell-mediated immune responses. [36]

Biomimetic Nanostructures

Therapeutic nanoparticles as drug carriers are particles with a size range of 10 to 1000 nm, which is comparable to the size of proteins or DNA . Rolling up inorganic materials (such as graphene) or self assembling biomaterials (such as peptides) produce hollow cylindrical nanotubes .Nanofibers, which have the shape of a fibre, are made from natural or synthetic polymers using one of three methods: phase separation, self-assembly, and electrospinning. Furthermore, because these nanoparticles are biodegradable and biocompatible, they have a high capacity for drug loading and cellular uptake [34]. Inorganic nanoparticles based on materials such as gold, silica, fullerene, and grapheme are also suitable drug carriers [31-36].

Biomimetic Nanotubes

He et al. created polyelectrolyte multilayer nanotubes with urease enzyme loaded as a catalyst in 2009. The layer-by-layer method was used to create composite walls of nanotubes containing various organic/inorganic components such as polyelectrolytes, inorganic nanoparticles, dendrimers, peptides, DNA, and enzymes. In fact, those nanotubes were created as nanoreactors to produce calcium carbonate into their cavities via biomimetic synthesis. Furthermore, the nanotubes' outer shell preserved the metastable form of biomineral materials and allowed for controlled release in drug delivery. Chen et al. used biomimetic Rosette nanotubes (RNTs) that self-assembled in the physiological environment. The RNT supermolecular structures' basic building blocks were guanine (G) and cytosine (C) DNA base-pairs arrayed via hydrogen bonding. The inflammatory and bone growth promoting steroid dexamethasone

(DEX) was then easily encapsulated into the RNT nanotubes via hydrophobic or stacking interactions. The findings revealed that DEX was released in a sustained manner, which improved osteoblast proliferation in orthopaedic therapeutics under biological conditions [35]. Shang et al. investigated the capabilities of RNTs for loading hydrophobic drugs in targeting drug delivery applications in another study published the same year. To accomplish this, two types of RNTs, single-based RNTs and twin-based RNTs, were used to load tamoxifen (TAM). The hydrophilic property of the outer shell of both types of RNTs resulted in the dissolution of encapsulated hydrophobic drugs in physiological media, as well as their long-term release in target cells. Furthermore, the covalent bonding between G and C in twin-base linker molecules (TBLs) formed a more stable stack, which could allow for more drug loading.

Carbon nanotubes (CNTs) with unique mechanical, thermal, electronic, and biological properties have numerous applications in drug delivery systems. Hevia et al. used biomimetic multi-walled carbon nanotubes (MWCNTs), which have antiproliferation and antimigration properties. Furthermore, the shared architecture and properties of CNTs and microtubules, cytoskeletal polymers found in all eukaryotic cells, allowed them to be translocated inside cancer cells. In both in vitro and in vivo tests, this translocation into microtubules caused mitotic damage and cell death in malignant melanoma cancer. CRG films were created as drug-loaded dressings using kappa-carrageenan (CRG), a type of derived polysaccharide from red seaweeds. To form a CRG/HNT nanocomposite, this material was strengthened with biocompatible halloysite nanotubes (HNT). The biomimetic CRG/HNT nanocomposite films with strengthened mechanical properties could sustainably release drugs for wounds or tissue regeneration [37].

Biomimetic Nanofiber

In 2008, a biomimetic electrospun nanofiber made of PAMAM dendrimer and gelatin was created to function similarly to natural ECM in promoting tissue regeneration. Freshwater et al. used covalent binding to the gelatin backbone to disperse dendrimers on the extended nanofiber. Furthermore, because of the presence of numerous functional groups, a large amount of the antibiotic doxycycline (DC) was encapsulated into nanofiber dressing, which improved the rate of wound healing through sustained drug release. Anderson et al. [23] investigated the inherent ability of self-assembling PAs to produce an interwoven nanofiber gel matrix as a wound healing scaffold in 2009. The gelation process and the mechanical properties of the nanofiber network were moderated in this study. In order to mimic the ECM, the application of biological moieties within a nanofiber matrix was also investigated. In another study published in 2009, cisplatin drug (cis-dichlorodiamineplatinum (II), CDDP) was used to create a CDDP-PA nanofiber Gel matrix after CDDP and PA complexed during the PA self-assembling process. Furthermore, the incorporation of an RGD moiety and an MMP- 2-sensitive sequence into the hydrophilic peptide within PA resulted in the spatial and temporal release of CDDP within cancer cells [36].

Electrospinning was used to create another wound dressing with a sandwich structure made of polylactide-polyglycolide (PLGA) and collagen. The sandwich-structured membranes' surface and core were made of PLGA/collagen and PLGA/antibiotics, respectively. Vancomycin, gentamicin, and lidocaine were also used as antibiotics in the core of the nanofibrous structure. In vitro and in vivo experiments revealed that these biomimetic nanofibrous membranes with ECM-like properties could provide prolonged drug release for the treatment of infected wounds [32].Another research group created an electrospun nanofibrous scaffold made of silk fibroin and hyaluronic acid (SF/HA) with properties similar to the ECM. These biomimetic nanofibers have the potential to be excellent scaffolds for tissue engineering or carriers for hydrophilic drugs .Tan et al. used electrospinning to create nanoporous bioactive glass fibres (BGFs) in 2013. The BGFs nanopores were loaded with bovine serum albumin and DOX, and then the protein–mineral composite structures were formed through biomimeralization with proteins, just like the matrices of hard tissues.

Furthermore, these DOX-loaded fibrous structures released drugs in acidic media, making these biomimetic structures a promising candidate for the regeneration of damaged bones caused by cancer eradication. Electrospinning and biomineralization techniques were also used to create three-dimensional (3D) nanoporous

hydroxyapatite (HA) architectures. Electrospun PCL nanofibers (NFs) were chemically modified and biologically conjugated to bone morphogenetic protein 2 for this purpose (BMP2). The PCL NFs-BMP2 hybrid was then mineralized in simulated body fluids (SBFs) using a biomimetic method to create 3D nanoporous HA architectures. Li et al. created dual drug-loaded nanofibers using an electrospinning technique in 2015 to improve calvarial defect repair and bone tissue regeneration. To maintain its efficiency and bioactivity, BMP-2 was encapsulated in BSA nanoparticles and stabilised by a chitosan shell.The poly(- caprolactone)-poly(ethylene glycol) (PCE) nanofibers were then embedded with dexamethasone (DEX) and BSA nanoparticles (BNPs). Both in vivo and in vitro experiments revealed sustained release of BNPs and DEX.BMP-2 was also embedded in an SF/HA nanofibrous structure for bone repair applications in another study. In fact, BMP-2 was loaded onto both the SF nanofibers and the HA nanoparticles to mimic the ECM of bone.

Biomimetic Nanoparticles

In 2007, Palazzo et al. synthesised two types of biomimetic hydroxyapatite (HA) nanocrystals, plate-shaped (HAps) and needle-shaped (HAns), to determine their morphology and chemico-physical properties as drug carriers. The overall charge effects of three types of drugs containing cisplatin, alendronate, and di (ethylenediamineplatinum) medronate (DPM) for the adsorption or desorption affinity towards HA nanoparticles were investigated for this purpose. Sheikh et al. conducted another comparison of three types of biological matrices for the biomimetic synthesis of hydroxyapatite (HA) nanoparticles as drug carriers in 2012. The mediated matrices for producing HA nanoparticles similar to the ECM were BSA, Collagen (CL), and poly vinyl alcohol (PVA). Overall, PVA was the best matrix for manufacturing pH-sensitive HA nanocrystals for targeted drug delivery. To increase the amount of drug loading, grapheme oxide (GO) was encapsulated in a hyaluronic acid (HA) gel matrix (DOX). A mussel-inspired cross-linking method was used to create these nanocomposite hydrogels. Furthermore, these HA/GO nanocomposites provided a long-term sustained release of DOX .CHyde et al. demonstrated a quick and simple method for producing silica nanoparticles with reversible controlled surface charges using the adsorption/desorption property of PEI coating. An inorganic silica particle as a potential drug carrier was modified in this study using biomimetic PEI to tailor surface interactions of silicacoated as a potential drug carrier within target cells.

Qin et al. created biomimetic composite nanocarriers for cancer therapy by depositing mesoporous silica (MS) on the surface of graphene oxide (GO). A lipid bilayer containing folate ligands (folate liposome (FL)) was also easily self-assembled on the surface of the GO-based nanoarchitecture to provide intercellular uptake via hyper folate receptors on cancer cells. Then, using photothermal therapy (PTT), the GO in nanocarriers converted light energy into heat, resulting in significant DOX release into cancer cells. Wang et al. created a eukaryotic cell-like hybrid nanoparticle using fullerene, a mesoporous silica matrix, and a phospholipid layer (1,2dihexadecanoylsn-glycero-3-phosphocholine (DPPC)). These biomimetic nanoplatforms were dubbed Eukacells, and they consisted of fullerene, mesoporous silica matrix, and DPPC as the core, cytoskeleton, and membrane, respectively. Both in vitro and in vivo tests revealed that these nanocarriers had an extremely high capacity for loading theranostic agents in cancer therapy, such as a chemotherapeutic drug (DOX) and an imaging agent (indocyanine green).Nanocomposites of protein polymer-gold nanoparticles (p-GNPs) were created using polyhistidine-tagged proteins and in situ GNP templated synthesis. The in vitro comparison of P-GNPs and GNPs revealed that the amounts of loaded curcumin (CCM) as a hydrophobic drug into P-GNPs were significantly increased. Furthermore, cellular internalisation of CCM, as well as sustained release of CCM within breast cancer cells, were significantly boosted [32-37].

To summarise, nanotubes' unique adjustable hollow structure and basic organic/inorganic components may provide excellent controlled release in drug delivery. Furthermore, in cancer therapy, these biomimetic carriers could be tailored to mimic the cellular microenvironment while also providing anti-proliferation and anti-migration effects on the cells. Furthermore, nanotubes could be mechanically strengthened to produce biomimetic composite nanotubes for tissue regeneration applications. However, the number of studies in this field is very low, and more clinical research is needed to address this issue. The major groups of biomimetic nanofiber networks are designed to mimic the properties of the ECM. Furthermore, these scaffolds have a high potential for long-term drug release in wound

healing and tissue regeneration applications. Overall, the fabrication of biomimetic composite nanoparticles as drug carriers based on organic and inorganic materials could benefit from both basic groups' advantages. As a result, drug loading capacity, cellular uptake, and drug release profile were all significantly improved.

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RESEARCH ARTICLE

Role of Fintech and Alternative Credit Scoring Methods in Accelerating the Financial Inclusion of Smallholder Farmers in India

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ABSTRACT

Despite the evolution of the Indian agricultural credit system, nearly 50% of the smallholder farmers are deprived of institutional credit. The aversion of traditional lenders and the outbreak of COVID-19 have enabled Fintech to leverage the latest technology and innovative credit assessment tools to ensure that the smallholder farmers received adequate farm credit, crop advisory, supply of agricultural inputs, and assistance in marketing their agricultural produce on time. The current paper aims to study the evolution and effectiveness of institutional credit to agriculture, the credit evaluation system of the traditional financial institutions (FI), the alternative credit scoring models, and the landscape of Fintech in India. The Study involves a systemic review of research data on agricultural credit, fintech development, and financial inclusion in India and abroad collected using search engines like Google Scholar, Google, Bing, etc. The interpreted results indicate that adopting financial technology would facilitate the optimization of resources and processes, reduce the turnaround time of sanction and disbursement of loans, insight-driven, and system-driven decisions, and improve credit access to smallholder farmers at affordable interest rates. The results also highlighted that a collaborative synergy between FI and Fintech could enable improved credit access, sustainable agriculture, and poverty alleviation.

Keywords: smallholder, institutional credit, COVID-19, Fintech, alternate credit scoring, financial inclusion.

INTRODUCTION

The agriculture sector development in India is largely dependent on smallholder farmers who hold over 86% of all the agricultural holdings and 47% of the operated area in the country. Indian agriculture contributes nearly 20% of the gross domestic product (GDP) while employing over 42% of the total workforce in India. Hence, the availability of institutional credit to the smallholder farmers can save them from paying exorbitant interest rates and exploiting the money lenders (Haque, T., & Goyal, A., 2021). Also, the timely, adequate, and affordable credit to these agricultural households is crucial in improving farm production and income levels. Higher public investments in agricultural inputs like canal irrigation, power, and institutional finance contributed to higher GDP in agriculture and allied activities (Gulati, A., & Bathla, S., 2002).

FinTechs use technology for new modes of delivering financial services and products to provide easy and appropriate ways of managing finance for its users besides the conventional ways of financial services delivery. 'FinTech' term has been featuring off late in many business journals to explain the upsetting challenge to the financial sector by introducing faster, cheaper, and human-centred financial services. Fin-Tech is the new process, product, and application of business models in the financial services domain that offers a bouquet of complementary services and end-to-end online solutions and are used to computerize insurance, trading activities, and risk management.

The Indian FinTech industry is one of the top five markets worldwide, with a market valuation of $31 Billion expected to grow to $84 Billion by 2025, at a CAGR of 22%. India emerges as one of the largest markets due to the availability of infrastructure to set up and incubate FinTech at an opportune time. Continuous economic growth and a moderate penetration of financial services supported by quality internet connectivity, enhanced smartphone usage, proper infrastructures like Aadhaar based authentication, and India Stack capabilities will surely take India's FinTech sector to the next level.

Objective of the Study

- To understand the role, key drivers, ecosystem, and growth prospects of FinTechs in India.
- To understand the traditional credit scoring models deployed by the financial institutions for the appraisal of agricultural loan applications.
- To evaluate the alternative credit scoring models and their role in accelerating financial inclusion in the agricultural sector in India.

RESEARCH METHODOLOGY

The Study involves a systemic review of research data about agricultural credit, fintech development, and financial inclusion in India and abroad collected from the websites of the Reserve Bank of India, NABARD; reports, journals, white paper, blogs using search engines like Google Scholar, Google, Bing, Etc.

RESULTS AND DISCUSSION

Role of Fin Tech in Finance

Chronological Evolution of Financial Technologies (Fin Tech)

Globally, the development of the fintech industry has happened in 3 phases namely, 1866 to 1967, 1967 to 2008 & 2008 to date.

Key Drivers of Fin Tech in India

- Access to capital and investment-friendly environment

- Indian demography (over 65% of the population is aged less than 35 years) is highly suitable with a hunger for next-generation technology.
- The poor reach of financial services amongst a large proportion of the country's population, i.e., the under-served rural, Agricultural, and SME segments.
- The Government guidelines and policies are supportive of FinTech.
- Enhanced mobile and internet connectivity.
- Affordable transaction costs for using cloud and India Stack-based services.
- Rapid progress in technology.

Fintech Ecosystem And Its' Elements

Recently, the fintech sector has evolved as one of the upcoming industries in India and worldwide. The sector is flourishing with enhanced customer expectations, increased access to venture capital funding, lower entry barriers, and technological advancements. The delivery mechanism of financial services by the traditional services has not changed much over the years (Capgemini & Efma, 2017). The following image depicts the fintech space along with the financial services offered by them: The rapid progress in the financial services industry and the modern lifestyle of individuals have pointed out the loopholes in the systems followed by traditional institutions. Sensing their business risk, these organizations have started collaborating and partnering with new fintech firms to unleash the market potential.

Technology Enablers for FinTech

The technology enablers for Fin-Tech, like data-focused technologies, operational excellence, infrastructure support, and front-end interfaces, act as catalysts to the country's financial inclusion and economic development.

Growth opportunities for Fintech Industry post COVID

Steady Rise In The Number Of Partnerships

One of the significant impacts of COVID-19 on FinTech may be a sustained rise in their partnerships with financial institutions. To adapt, Fintech has enabled them to develop novel products and solutions suitable for a rapidly changing business environment. The time is apt for Fintech to find new partners among financial institutions which otherwise lack cutting-edge technology. Similarly, the business environment is suitable for Fintech to forge alliances with other Fintech, Agritech, and non-financial services entities.

Hastening the Pace of Financial Inclusion

Post COVID-19, the economic disruption has highlighted the significance of catering to the financial needs of the underserved communities in both developing and developed countries across the globe. The government interventions and measures will enhance the pace of financial inclusion and support the underbanked households. FinTech can play a much more significant role by collaborating with other stakeholders in the ecosystem.

Improving The Economic Relief Measures

Many Fintech's are better placed than banks for a quick and hassle-free transfer of government relief funds, especially those with no bank accounts.

Encouraging The Temporary Workforce

The temporary workforce employed in the unorganized sectors is a favorite segment for FinTech. Considering their fluctuating and low-income levels, these workers typically need to customize financial, insurance, and tax solutions. However, Fintech sees a great opportunity in serving this otherwise underserved segment of customers. Irrespective of the impact of COVID-19 on the sector, Fintech may continue its engagement with these customers.

Leveraging the Internet of Things

Another promising area is the Internet of Things (IoT) backed contactless payments. In a post-COVID-19 scenario, connected cars help consumers pay for gas or food virtual and contactless. The adoption of IoT-based payments may go up significantly in the coming days.

Opportunities for Fintech Industry in India

Trends for Fintech Investments in India: The FinTech industry has seen significant funding from venture capital and private equity firms. Over the past six years, the fintech industry has received a total investment of US$ 8 billion1 across 1,031 deals. The investments have increased nearly 75 times, i.e., from 16 USD Billion in 2014 to 1200 USD Billion as of the 2nd Quarter end of 2020. Many of these investments were in Fintech operating in the digital payment domain, followed by alternative lending and Insur Tech.

Growth of the Digital lending industry in India:

Of late, the banks have seen a significant drop in their branch-based or physical transaction volumes. However, digital transactions have nearly doubled between 6.2 billion in FY16 and 13 billion in FY18, i.e., two years. Nearly 3/4th of the bank consumers in India utilize online banking services to meet their daily needs. Online or social media visits of customers are an essential tool to judge consumer behavior and their tech-savviness to be used as input for credit scoring models. India's online lending industry looks set to improve between USD 110 billion in 2019 and USD 350 billion in 2023, as depicted in the figure-5 above). The share of digital lending has improved from 7% in 2012 to 23% in 2018 and may even increase up to 48% by 2023. To keep the digital lending model sustainable in the future, both fintech lenders and financial institutions must develop a sound, seamless and scalable technological system (Ramasubramanian, S. 2019).

Traditional Credit Scoring Models used for Agricultural Loans by FIs

Accurate measurement and assessment of credit risk are critical as the quality of credit exposure is one of the riskiest areas for banks. Accordingly, credit assessments must be sophisticated, directed, and streamlined. Over the years, as the credit risk has become more diversified and complex, the importance of accurate credit risk assessments and the need to understand the underlying factors that drive the credit risk has also increased. Correct pricing and management of credit risk exposures hinge on a fool-proof and quick assessment process. Similarly, the supervisory authorities must ensure that a sound credit risk management system is in place, as any deficiency in this regard may jeopardize a bank's profitability and survival (Srivastava, A., 2021). Credit scoring as a tool of credit appraisal helps to understand and predict the likely behavior of the prospective borrowers in respect of the repayment and adherence to the terms of the agreement of a credit proposal based upon specific parameters and assessments made thereof. Traditionally, most financial institutions have relied on an instinctive assessment or the banker's underwriting skills to assess the credit risk of agricultural loanees. Bank field officers assess the borrower's creditworthiness using the "5 Cs" of credit.

The method and score may be unreliable and inconsistent if the risk weights are assigned based on the experts' personal views, ideally based on historical data or insight. Credit risk measurement depends upon the three key credit risk components, namely, Probability of Default (PD), Exposure at Default (EAD), and Loss Given Default (LGD) (Srivastava, A., 2021). Credit appraisals help in predicting a default based on quantitative and qualitative data. The abovesaid components may be used to evaluate the risk associated with both borrowers, and the same gets reflected in credit scores. The traditional credit analysis approaches involve examining the above five C's, subjectively weight them, arriving at a credit score, and reaching a credit decision (Figure-3). Banks can deploy such a credit rating tool during the loan appraisal, portfolio monitoring, product pricing, underwriting, and risk assessment (Probability of default, loss given default, default correlation, risk contribution, etc.) for management of agricultural exposures at a portfolio level. (Bandyopadhyay, A., 2007).

Modern Credit Scoring Methods Deployed By Fintech

Use of Data In Credit Scoring

After setting up of Credit Reporting Service Providers (CRSP), data has been playing a key role in the assessment of credit risk (Chappell, G. *et al.* 2018). Credit Services Providers (CSP) can screen potential borrowers through a credit appraisal process that primarily depends on credit scores and credit ratings. The data also helps in developing, evaluating, and maintaining credit scoring models. Digitalization has improved the availability of quality data enabling the CSPs and CRSPs in developing models with higher predictive power and deeper insights while offering new products to those previously excluded from access to affordable credit. Availability of quality data has enabled CSPs and CRSPs to develop pre-emptive and insight-driven models while offering customized products for the communities excluded from institutional credit.

The data utilized for credit scoring is obtained from heterogeneous and multiple sources. For developing a credit scoring model generally data like the amount of loan, loan type, loan maturity, the value of guarantees and collateral, repayment history-related information like defaults and overdue account/s, the amount borrowed, length of credit history, new to credit, and type of credit is evaluated. These data points are analyzed and used to develop a credit score that reflects the willingness and capability of the customer to repay. Generally, the CSPs provide conventional data sets which are different from data obtained from alternative sources. The Study again highlights a clear demarcation among the structured, unstructured, and semi-structured data sources (Trujillo, G. *et al.* 2015). As per the Global Partnership for Financial Inclusion (2018), alternative data can be termed as a large chunk of data that is generated by the enhanced use of digital tools and information systems. Alternative sources may include online transactional data, mobile, and other devices data, social media footprints, utility payment data, and data from web applications. Also, the data related to psychometrics, biometrics, browsing, news feeds, online ratings and blogs, satellite images, remote sensing data, production data, sales details, charge backs, and supply and transport may provide deeper insights. International Committee on Credit Reporting (ICCR), 2018 has named these alternative sources as alternative data

Traditional Vs. Alternative Data:

Traditional Data	Alternative Data
Bank Transactional Data: Bank Transactional Data Credit bureau checks: Number of credit inquiries Commercial Data: Financial statements, details of working capital loans, and others	Utilities Data: Timely payment may be considered as an indicator of the sound repayment capacity of the customer. Social Media: Visits and activities of consumers over various social networking sites may provide insights into the consumer's lifestyle Mobile Applications: The usage pattern of Mobile payment platforms may give some insight into customer behavior. Online Transactions: A study of the online transactional data can throw light upon the consumer's spending behavior. Behavioural Data: Analysis of the Psychometric data and application details helps understand the personality traits of the consumer.

Structured data like the company's daily operational transactions are retained in a traditional database. Unstructured data such as free-form text, images, social media data, video, audio, etc normally do not have a pre-defined order. Semi-structured data unlike structured data contain tags or markers. The utility, subjectivity, and quality of unstructured data to improve credit scoring methods are not established (Dudley, W. C., 2017). The legal use of unstructured data holds a lot of promise for future studies. Many regulatory authorities in Australia, Singapore, the United Kingdom, Taiwan, and China have established sandbox testing tools to enable data innovation (Financial Conduct Authority, 2019).

Thin-File Credit Decisions By Fintech

To date, the traditional lending institutions have only targeted the acquisition of creditworthy or bankable customers. These clients had sufficient credit history and transactional information necessary to feed the decision matrix. However, a person with little credit history ('thin-file) will hardly receive credit under the traditional model.

To address this issue of financial exclusion, the new-age financial technology or Fintech's have started relying on alternative data sources to underwrite these 'thin-file' credit proposals. Such alternative data acts as a supplement to the existing traditional credit data in assessing the creditworthiness of these sets of customers.

Conventional Alternative Data

Supplier Data: Generally, the suppliers track the payments made by their buyers and a study of the data can not only reveals their ability and willingness to pay but also helps understand their cash flows and working capital gaps. Utility Bill Payment: Payment patterns of mobile, internet, electricity, choice of the mobile payment plan, etc. can serve as an important predictor of defaults; this data can act as a complement to the credit bureau report.

Data from Service Providers: Many e-commerce sites underwrite and generate credit scores based on the data of individuals and small businesses stored on their own or partner sites. The credit scores can be used to predict the consumers' purchase behavior, repayment capacity, default rates, etc.

Experimental Alternative Data

Click stream Data: Information on the websites visited before filling the online loan application, the amount of time spent on checking the related content like charges, terms, and conditions, product features, etc. is quite useful in predicting the post-application behavior, probable attrition, and default of prospective customers.

Social Media Data: Retrieval of locational data from personal social networks and e-commerce sites can help in assessing the occupancy and residential stability; going through customer reviews can enable evaluation of popularity and service levels of the businesses; network of persons with high-profile individuals and experience of working with reputed organizations and longevity in each job may facilitate the assessment of the potential of employment and job stability of the applicant.

Public Records: Government and regulatory guidelines, Circulars, and gazettes; business licenses, police verification reports, industry association data, any other publicly accessible information, etc.

Innovative Credit Scoring Model using Artificial Intelligence (AI) and Machine Learning (ML)

Artificial Intelligence and Machine Learning in Credit Scoring is nothing but the use of computational systems to solve problems that would otherwise have required human interventions (SAS, 2019). AI helps machines to learn from experience, adapt to new information, and deliver tasks like humans (Financial Stability Board, 2017). Most popular AI applications of today like self-driving cars or robotic surgeons thrive on deep learning and natural language processing techniques. Tools like computer vision and chat bots have been developed by leveraging the computer's ability to perform human-like tasks and learn from experience. The rapid development of AI technology was feasible due to the vast progress in computing power, data, and innovative algorithms. Using these new technologies, computers can be assigned specific tasks by processing and recognizing patterns in heterogeneous data.

AI is a broad area, and machine learning is a sub-area of the same. Machine learning can be defined as a process of developing a logical series of actions i.e., an algorithm to solve an issue. The algorithm optimizes on its own by using experience with a little human intervention (SAS, 2019). These techniques can be used to decipher complex patterns in large amounts of data from increasingly diverse and innovative sources (SAS, 2019). Deep learning is that kind of machine learning which utilizes algorithms in layers that mimics the structure and function of the human brain (SAS, 2019). Deep learning algorithms can also be utilized for supervised, unsupervised, or reinforced learning modes. Off late, deep learning has delivered remarkable results in the fields of image recognition and natural language

processing. For example, deep learning may be used in classifying images, speech recognition, detection of objects, and describing the content. Voice recognition systems are partly enabled by deep learning.

Realignment of Credit Scoring for Financial Institutions

Financial institutions can contribute significantly to financial inclusion by partnering with digital financial service providers, agriculture technology companies, and other financial institutions to automate and digitize the lending processes. There are also numerous reformation opportunities across the lending value chain to the traditional lenders improve their products and services while providing affordable credit access to the underserved and excluded population. The current study indicates that financial technology can enable optimum utilization of resources and processes, reduction in time required for approval and disbursement, enable insightful and process-driven decision making and make sure that smallholder farmers get credit at affordable rates.

Coping up with the Dynamic Changes in the Lending Market post-COVID-19

As the COVID-19 pandemic has not only led to a global health emergency but also gave rise to a global economic crisis. Subsequent lockdowns imposed to curb the virus spread have resulted in an economic recession and the consumers are battling it out with business shutdowns, sluggish market, job losses, salary cuts, furloughs, and reduced savings. While the economy has started recovery, consumers are unable to regain control over their finances and are forced to reduce their discretionary spending.

In the aftermath of the pandemic, the changes that are expected in the lending market are:

Purpose of borrowing may change

The economic slowdown has pushed consumers to curtail their non-necessary expenses in a big way. Earlier, customers used to borrow freely to fulfill their travel, dining, luxury purchase, and other lavish needs. The ongoing economic crisis has made the consumers lower their travel, tourism, and hospitality expenses contributing to a sharp decline in the demand for consumer loans and luxury spending. Want-based borrowing is soon expected to be replaced with emergency borrowing for purposes like education, medical emergencies, and other essentials.

Retail Loans Will Get A Priority

In the future, there will be a sluggish demand for big-ticket loans, and most consumers may prefer small loans for meeting emergencies only. First-time borrowers who possess a thin or no credit history will find it difficult to avail of big loans from conventional lending agencies like banks and NBFCs.

Lenders will become over-cautious

Despite the increased demand for consumer, MSME, SME loans, and credit cards, the lending agencies are exercising caution in acquiring customers considering the volatility in the economy. With the alarming increase in non-performing assets, most financial institutions have tightened the credit norms. They are taking credit decisions based on data on borrowers' credit profiles, repayment histories, and other proprietary data without taking any unnecessary risks. The loan moratorium announced by the RBI during the first COVID wave to extend relief to the borrowers was perceived to be a complete loan waiver by many borrowers. It is known that in the event of non-receipt of interest from their borrowers, the banks may falter in payment of interest on their deposits. Thus, improve the banking industry must improve the loan repayments improve to keep the ball rolling.

Digital lending channels will be in demand

With the formal credit providers still being comfortable in catering only to clients with a significant credit history, more and more consumers are gradually approaching digital lenders. Also, during the recent pandemic, a significant jump was observed in the customer orientation of wallets and virtual credit cards. The high smart phone usage and data connectivity in the country has enabled Fintechs in creating a robust, quick, convenient, and automated lending process. Instead of relying only on the credit history, bank transactions, sales, and income tax returns, personal discussion with the customers, Fintech's have been able to build an alternate, early, and seamless lending system.

Roadblocks and Enablers in Digital Financial Inclusion for Smallholder Farmers

The small and marginal farmers play a vital role inany developing country's food supply chain. The success of a poverty-alleviation program depends on the participation of the farmers who cater to global food needs. However, most of the peasants are outside the formal credit system leading to their inability to meet the expenses related to their agricultural operations. Globally, there is a shortfall of $152 billion in meeting the agricultural finance needs of this segment. The smallholder farmers come across many issues across the agricultural value chain like purchasing inputs, access to formal credit, storage and sale of agricultural produce, market linkages, etc. Based on the empirical studies and opinion of agribusiness experts, the above enablers are suggested for the issues faced by smallholder farmers across the globe.

CONCLUSION AND WAY FORWARD

This section brings out inferences derived from the analysis and the way forward for enhancing optimization of resources and processes, reduction of turnaround time for approval and disbursal of credit/loans, facilitation of intuitive and automated decision-making, and ensuring the accessibility of credit/loans for smallholder farmers at affordable rates. The results also highlighted that a collaborative synergy between financial institutions, Fintech, and other stakeholders operating in the lending ecosystem can enable improved credit access, sustainable agriculture, and poverty alleviation.

As per the Ministry of Agriculture and Farmers Welfare, the cumulative number of KCC issued has reached 182 million with a sanctioned limit of INR 1.76 lakh Crores as of February 2021. However, the NAFIS survey conducted in 2015-16 stated that only 10% of the farmers have utilized their KCC limits during that year. Since there are no reliable data on the latest KCC use, further research may be conducted for evaluation of the current situation while finding means to improve the sanctions and usage. So, the financial institutions must disburse more KCC proposals in the rural areas to financially include more and more farmers, especially the smallholders. This will enable their access to easy and affordable loans while meeting the collateral norms of the banks. The RBI report (2019) stated that in the south Indian states like Kerala, the agri-loans outstanding is over and above 100 percent of the value of agri-inputs consumed which indicates the diversion of agricultural loans to non-agricultural uses. The report has suggested certain changes in the delivery of agricultural credit which will both cater to the needs of the farmers while acting as a role model to marginal farming economies of Sub-Saharan Africa and South and Southeast Asia.
The value of the global digital lending market has witnessed phenomenal growth by reaching $ 75 Billion in 2018 which is expected to jump to $ 350 Billion by 2023 (Source: CIBIL, BCG Google Digital Lending Survey, 2018). The total credit need of smallholder farmers across the developing countries is estimated at USD 240 billion annually (Shakhovskoy et al, 2019) highlights the magnitude of the investments required by the marginalized farming communities. As per the study, 270 million smallholder farmers across the globe need finance of USD 188 billion to meet their agricultural input or farm mechanization needs in agriculture (Shakhovskoy et al, 2019). These small and marginal farmers need 66 USD Billion for short-term agricultural needs whereas another 86 USD Billion is required to meet their long-term or investment credit needs.

The key to success in FinTech is to harness the benefits while managing the risks. Therefore, we need to have an appropriate regulatory and supervisory framework to facilitate the growth of this sector and ensure the acceleration of financial inclusion in India. FinTech can reduce lending costs while improving the access and quality of financial services. However, there must be a fine balance between effective utilization of digital financial services and minimization of its systemic impacts. By enabling technologies and mitigating risks, a novel, more inclusive, cost-effective, and resilient financial system can be built. Universal Financial Inclusion can be achieved in the country only through synergy among the financial institutions, non-banking finance companies, FinTech's, AgTech's, Credit bureaus, Rating agencies, etc. as each of these entities complement each other within the lending ecosystem. Therefore, collaboration among banks, financial institutions, and FinTech firms would be pivotal in improving the credit access of the smallholder farmers through a combination of expertise, technology, innovation, and agility.

Improving the digital literacy of these customers can act as icing on the cake for the overall success of the financial inclusion plan in India and the rest of the world. A successful implementation of financial technology in agriculture will help in poverty alleviation and reduction in the financial inequalities within and among the countries thereby achieving United Nation's Sustainable Development Goals (SDG) of "No Poverty" and "Reduced Inequalities".

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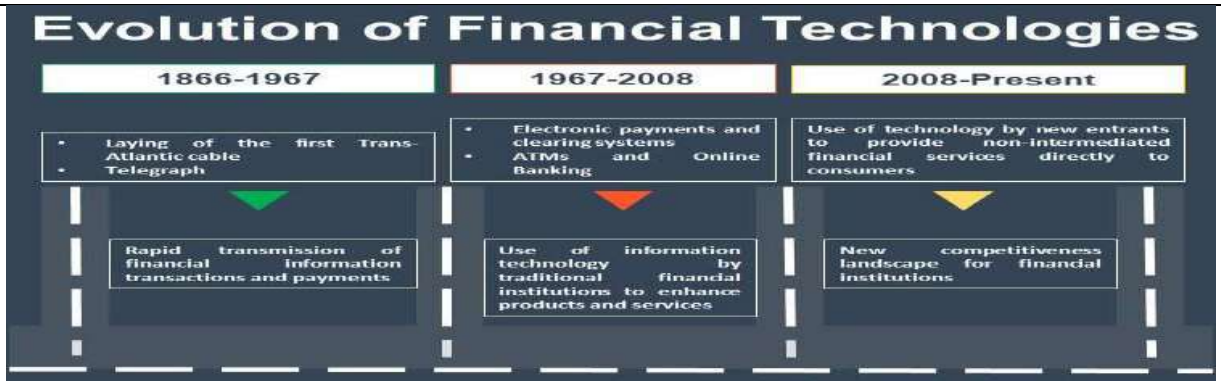
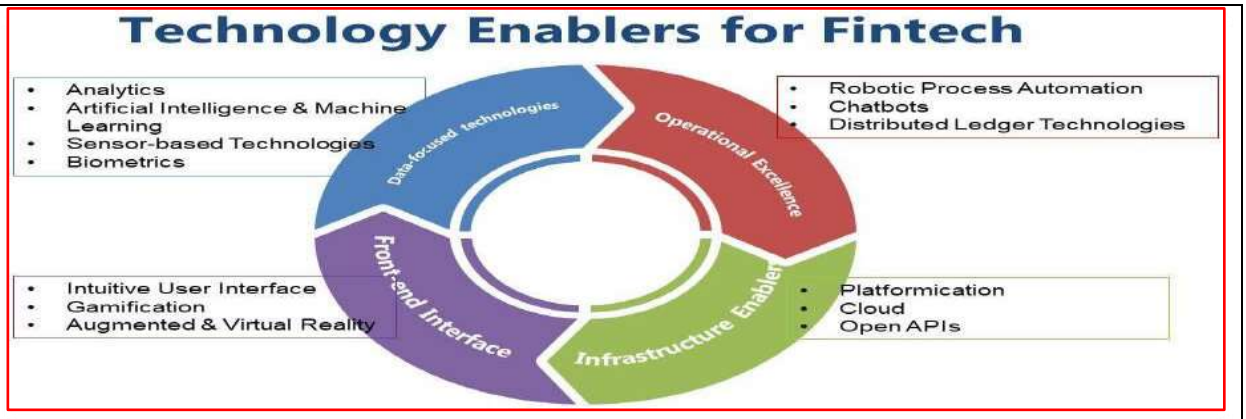


Source: The Three Phases of Fintech. Consumers International (2017), URL: https://doi.org/10.2139/ssrn.3332550

Figure-1: Evolution of Financial Technologies

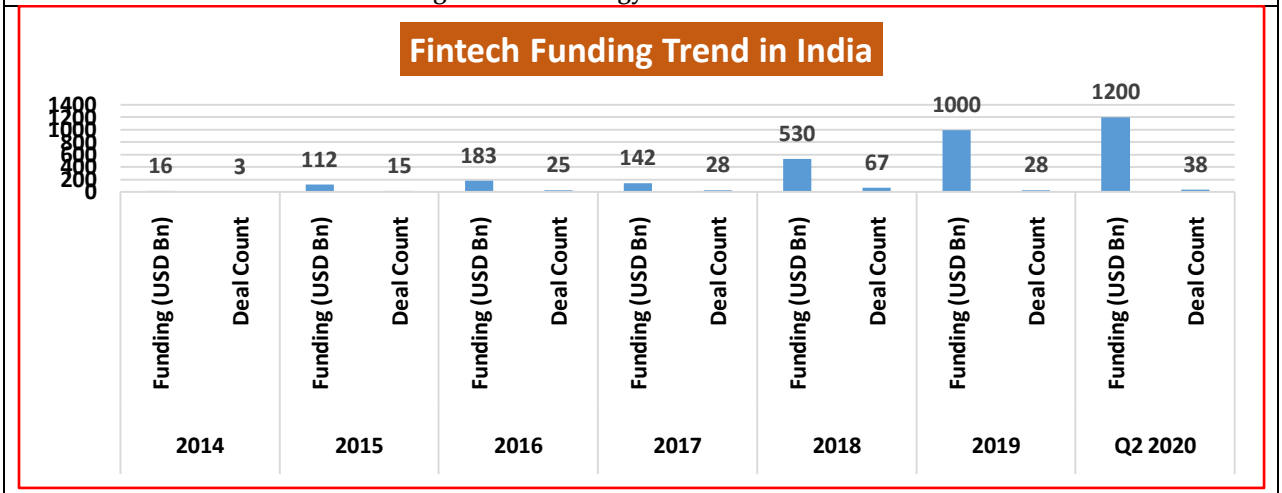
Source: Google URL: https://bit.ly/3onn2D4

Figure-2: Fintech Ecosystem



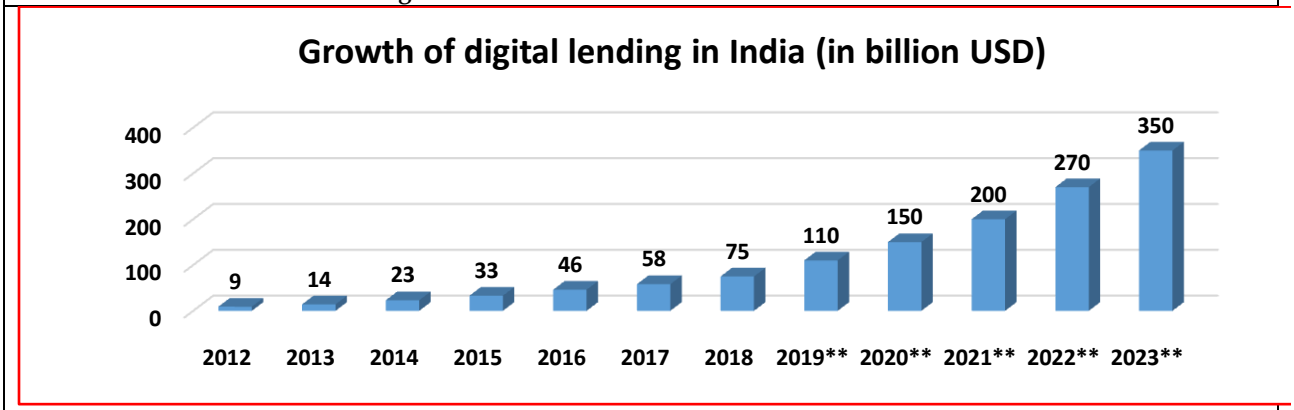
Source: Department of Economic Affairs, G. (2019). URL: https://bit.ly/3HkuPJf

Figure-3: Technology Enablers for Fintech



Source: Ramasubramanian, S. (2019) & Srivastava, R. (2019) URL:https://tinyurl.com/4xs4t53w

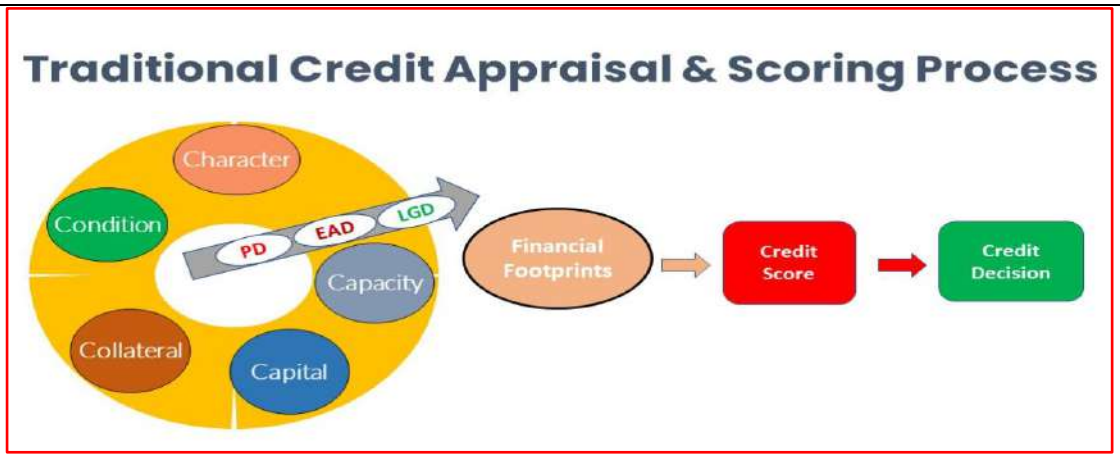
Figure-4. Trends in Fintech Investments in India



Source: CIBIL, BCG Google 2018 Digital Lending Survey URL: https://tinyurl.com/2rkka5j5

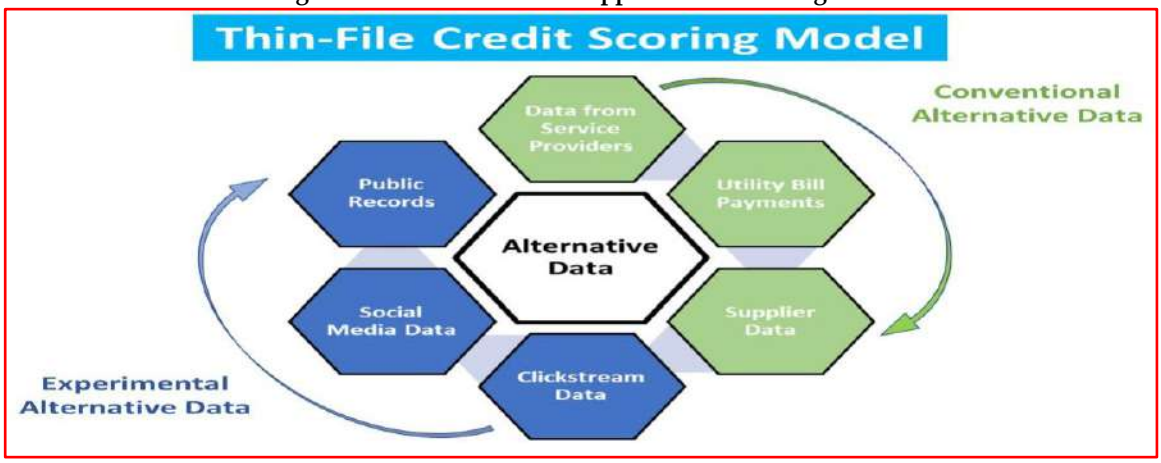
Note: Numbers from 2012 to 2018 are actual and 2019 onwards are forecasted, hence marked as **

Figure-5.Growth of the Digital lending industry in India



Source: Srivastava, A., 2021URL: https://tinyurl.com/bdeydubw
Note: Probability of Default (PD), Exposure at Default (EAD) & Loss Given Default (LGD)

Figure-6: Traditional Credit Appraisal and Scoring Process

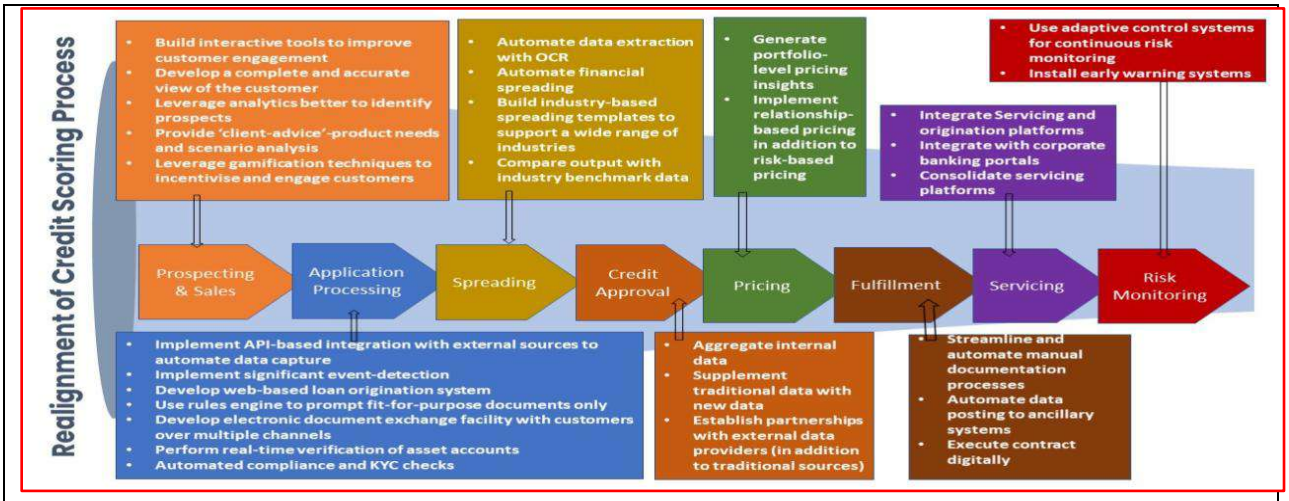


Source: Rethinking Credit Lending by Infosys, 2018 URL: https://infy.com/3Le8zmA

Figure-7: Thin-file Credit Scoring Model

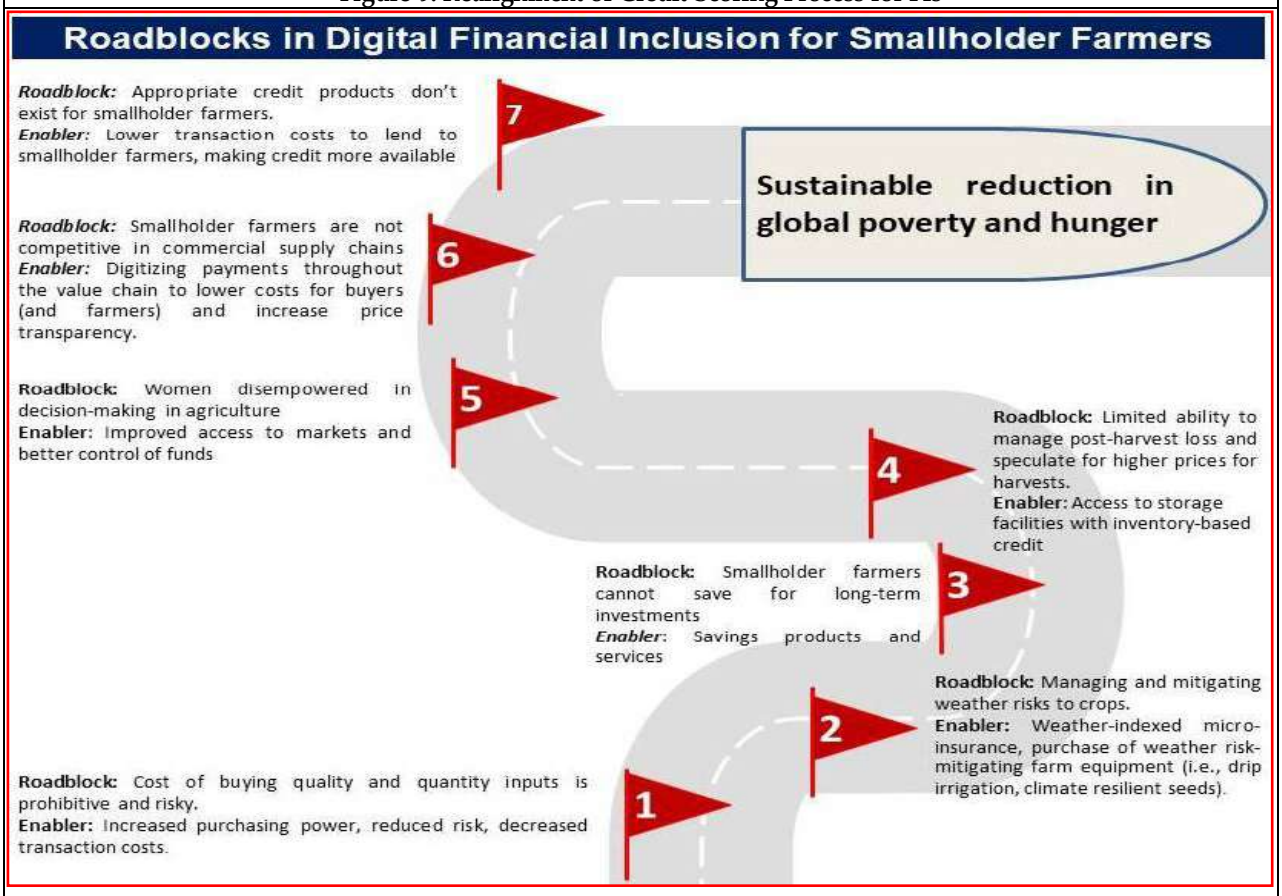
Source: World Bank Group & ICCR, 2019 URL: https://bit.ly/3gp0Q71

Figure-8: Machine Learning for Credit Scoring



Source: Infosys, 2018 URL: https://infy.com/3gshLpf

Figure-9: Realignment of Credit Scoring Process for FIs



Source: USAID & m-STAR, 2016 URL: https://tinyurl.com/2p8afwhw

Figure-10: Roadblocks in Digital Financial Inclusion for Smallholder Farmers

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RESEARCH ARTICLE

Perceived Attributes of Organic Red Gram Farmers in Dry land Areas of Karnataka

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ABSTRACT

Over the past decades, demand on organic farming has been increased rapidly in all over the world. Therefore, people show an interest on cultivation of organic crops at their field level as well as purchasing organic products. This paper studies the perceived attributes of the organic red gram farming in dry land areas of Karnataka. Farmer's perception towards organic red gram farming was measured using six perceived attributes parameters like relative advantages, compatibility, complexity, trialability, observability, predictability. The data were collected from 120 respondents from Gulbarga district. The findings indicated based on the attributes, were assessed by listing appropriate indicators like low cost, time saving, easy to use *etc*., in terms of relative advantage; difficult in learning and maintenance related to complexity; different barriers like cultural, social, language *etc*., related to compatibility; possibility of trying the organic red gram cultivation in terms of trialability; feedback and accuracy of information related to observability and possible impacts related to predictability.

Keywords: Perceived attributes, Organic farming, Natural resource, Red gram grower sand Healthy lives.

INTRODUCTION

Green revolution in India has witnessed a jump in agricultural production with the introduction of High Yielding Varieties (HYVs) of various crops and by following intensive cultivation practices with the use of fertilizers, pesticides and other inputs. It is true that the increasing use of fertilizers and pesticides at high rates has boosted

agricultural production in the country. But it has also caused adverse impact on soil and water, as well as environment. Long term continuous use of high doses of chemical fertilizers alone badly affects the soil physical, chemical and biological properties. In order to overcome this situation, organic farming, which aims at cultivating the land and rising crops in such a way as to keep the soil alive and in good condition. It is a method of farming which excludes the use of compound chemicals such as chemical fertilizers, pesticides and herbicides. Instead of that natural resources such as organic matters, mineral and microbes are used. Organic farming systems rely on large scale application of animal waste or farm yard manure, compost, crop rotations, crop residues, green manuring, vermicompost, bio fertilizers, bio-pesticides and biological control of pest and diseases. In India the use of organic manures in subsistence farming is an age old practice. Organic manures improve physical, chemical and biological properties of the soil. Organic farming is gaining momentum in India and particularly in Karnataka state. In Karnataka state, the journey in organic agriculture started by a small number of innovative and progressive farmers, is now being driven on a huge scale by state and central Governments, food processing industry, exporters, certifiers and domestic supply chain companies.

Pulses play an important role in Indian agricultural economy as they are rich sources of proteins and constitute 10 to 15 per cent of India's food grain diet. Major portion of Indian population belongs to vegetarian group and every person on an average is required to consume 70 to 80 gms of pulses per day in order to maintain good health and physique, according to the recommendations of Indian Council of Medical Research. So in this study the main focus is given on farmers view on organic red gram farming in dry land areas of Karnataka and the six different perceived attributes were used to conduct this research. Attributes refers to the characteristic or qualities possessed by the object. In this study perceived attributes of organic red gram cultivation were studied in terms of relative advantages, compatibility, complexity, trialability, observability, predictability.

METHODOLOGY

The study was conducted in Gulbarga district of Karnataka involving 120 organic red gram growers. This district was purposively selected as it ranks first in area and production of red gram. There are ten mandals in Gulbarga district, among these; three mandals were selected randomly for the study. From each mandal two villages *i.e.* a total of six villages were selected randomly. From the prepared list, 20 farmers were selected by simple random sampling procedure from each village thus the total sample for the study constituted 120 farmers and the data has been analysed using appropriate statistical tools. Scale developed by Shireesha (2015) with suitable modification was used to study the perceived attributes of organic Red gram by the farmers. Since there were variation in the number of statements under each component and the responses were collected on a two point continuum namely agree, and disagree with the scores 2 and 1 respectively.

RESULTS AND DISCUSSION

Based on the obtained scores, the respondents were grouped into low, medium and high perceived attributes categories using exclusive class interval technique. The perceived attributes of organic red gram farming by the respondents such as Relative advantage, Compatibility, Complexity, Trialability, Observability and Predictability were studied. The results pertaining to perception of respondents towards attributes of organic red gram farming were presented in the form of frequencies and percentage. The results in the table 1 indicated that, majority of the respondents had medium perceived attributes (54.10%), followed by high (29.20%) and low perceived attributes on organic Red gram farming (16.70%).

Hence, from the above results, it could be concluded that majority of the respondents had medium perceived attributes. This trend might be due to the fact that the majority of the organic red gram farmers they were received medium training and extension contact on organic farming and the respondents were knew that the organic farming technology is having more beneficial to the soil as well as human beings therefore majority of the young farmers

were having a good attitude on organic farming. This is in line with Kaur (2009). The below table 2 revealed that, the attributes were assessed by listing appropriate indicators like low cost, time saving, easy to use *etc*., in terms of relative advantage; difficult in learning and maintenance related to complexity; different barriers like cultural, social, language *etc*., related to compatibility; possibility of trying the organic Red gram cultivation in terms of trialability; feedback and accuracy of information related to observability and possible impacts related to predictability.Since there were variation in the number of statements under each component and the responses were collected on a two point continuum namely agree, and disagree with the scores 2 and 1 respectively

Relative Advantage

Relative advantage is the degree to which an innovation is perceived as being better than the idea it supersedes. The degree of relative advantage is often expressed as organic red gram cultivation is economic profitability, low cost, saving time, or other benefits. By analysing the table 2with respect to relative advantage, majority of respondents agreed to the statements *viz*., eco-friendly farming system (95.83%), more demand for organic products (83.33%), saving of time (81.66%), net profitability is more (79.16%) and the farmers using this organic farming technology are satisfied (75.00%). This is in line with the findings of Pornpratansombat *et al.* (2011).

Compatibility

Operationalised as the degree to which organic farming is consistent with the existing value, their situation and past experiences of the respondents *i.e*., cultural compatibility, no harm to plants and animals and suitable to all type of soil condition etc. By analysing the table 2with respect to compatibility, majority of the respondents agreed that organic Redgram practices were consistent with the maintain soil fertility and suitable to all type of soil condition (87.50%), no harm to plants and animals (83.33%), cultural compatibility (81.66%) and less labour requirement (66.66%). This is in line with the findings of Nandkumar(2015)

Complexity

Operationalised as the degree to which organic farming is relatively difficult to understand and use *i.e*., initial cost is expensive, application of input is difficult and less availability of resources etc. By analysing the table 2with respect to complexity, majority of the respondents agreed that organic Red gram practices were consistent with the, initial cost is expensive (82.50%), less availability of resources (81.66%), application of input is difficult (75.00%), require more management practice (66.66%) and manual weed control is difficult (58.33%).

Trialability

Operationalised as the degree to which organic farming can be experimentally practiced or verified on a limited basis for assessing the advantage of the organic farming *i.e*., easy to adopt organic farming practices in small quantity.
By analysing the table 2with respect to trialability, majority of respondents agreed to the statements *viz*., easy to use organic inputs for crop production in small scale and (75.00%), easy to adopt organic farming practices in small quantity (66.66%).

Observability

Operationalised as the degree to which results of organic farming are observed practically *i.e*., organic farming technology gives more yield and low incidence of pest and diseases By analysing the table 2with respect to observability, majority of respondents agreed to the statements *viz*., maintain soil fertility (87.50%), market price is high for organic produce (79.16%), and organic farming technology gives more yield (78.83%) and low incidence of pest and diseases (66.66%).

Predictability

Operationalised as the degree to which the progress and consequences of the organic farming can be anticipated *i.e.,* certainty of results and assured income by organic product. By analysing the table 2with respect to predictability,

majority of respondents agreed to the statements *viz*., no harmful residues in organic foods (81.66%), assured income by organic product (75.00%) and certainty of results (66.66%).

CONCLUSION

The study shows that the perceived attributes of the organic red gram farming in Gulbarga district, the main objective is to study the perceived attributes of organic red gram farmers in dryland areas of Karnataka. The results revealing that majority of the respondents had medium perceived attributes (54.10%), followed by high (29.20%) and low on organic red gram farming (16.70%). The complexity in organic red gram cultivation were, it require more management practice, manual weed control is difficult, initial cost is expensive, less availability of resources and application of input is difficult. Hence, the trainings and visits have made them to achieve relevant and timely information about organic inputs and in this study majority of the farmers agreed that organic farming is a good farming practice and it sustain the "health condition". So, by providing trainings on "organic farming" to the respondents they can learn to prepare inputs in their field and skill to apply the "bio fertilizers", seed treatment and learn to save their cost at initial level and the scientists of agricultural university, Krishi Vidyan Kedra sand private personnel should bestow special attention on evaluating new farming practice.

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5.

Table 1: Distribution of respondents according to their perceived attributes (n=120)

Sl. No	Category	Class Interval	Respondents	
			Frequency	Percentage
1.	Low	26-30	20	16.70
2.	Medium	30-34	65	54.10
3.	High	34-38	35	29.20
Total			120	100

Table 2: Perceived attributes of organic Redgram farming (n=120)

Sl. No	Perceived attributes		Components	Agree		Disagree	
				F	%	F	%
1	Relative advantage	A	Market price ishigh for organic produce	90	75.00	30	25.00
		b	Net profitability is more	95	79.16	25	20.83
		c	The farmers using this organic farming technology are satisfied	90	75.00	30	25.00
		d	Saving of time	98	81.66	22	18.33
		e	Eco friendly farming system	115	95.83	05	04.16

2	Compatibility	a	Suitable to all type of soil condition	105	87.50	15	12.50
		b	Cultural compatibility	98	81.66	22	18.33
		c	No harm to plants and animals	110	83.33	10	08.33
		d	Less labor requirement	80	66.66	40	33.33
3	Complexity	a	Require more management practice	80	66.66	40	33.33
		b	Manual Weed control is difficult	70	58.33	50	41.66
		c	Initial cost is expensive	99	82.50	21	17.50
		d	Less availability of resources	98	81.66	22	18.33
		e	Application of input is difficult	90	75.00	30	25.00
4	Trialability	a	Easy to adopt organic farming practices in small quantity	80	66.66	40	33.33
		b	Easy to use organic inputs for crop production in small scale	90	75.00	30	25.00
5	Observability	a	Maintain soil fertility	105	87.50	15	12.50
		b	Organic farming technology gives more yield	85	78.83	35	29.16
		c	Low incidence of pest and diseases	80	66.66	40	33.33
		d	Market price ishigh for organic produce	95	79.16	25	20.83
6	Predictability	a	Certainty of results	80	66.66	40	33.33
		b	Assured income by organic product	90	75.00	30	25.00
		c	No harmful residues in organic foods	98	81.66	22	18.33

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RESEARCH ARTICLE

Design of Plasma Arc Process with Pulse Cable

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ABSTRACT

This article discusses the design of Pulse conductor operation. Pulsed conductor processes are discussed in the context of the specific application of the process used to generate finer particles of copper and copper oxide. Experiments with manual drills and EDM have shown that the current pulse, not DC, creates a more stable process. Also, pulse EDM processing has the benefit of almost zero growth or erosion of the cathode electrode. The almost zero growth of the cathode provides the possibility that you only need one usable electrode. Two-wire experiments show that if two wire electrodes of the same diameter are used, the alignment of the wires must be very good for a stable operation. If the alignment of the wire is not good, only the cross-sectional area of the wire is corroded by the loss of that part of the electrode. This mismatch of wires also creates a situation where the electrodes will touch as they pass through each other, creating a short circuit state. The work satisfied the sustainability development goal Industry innovation and infrastructure and responsible consumption and production.

Keywords: EDM, Diameter, Electrodes, Cathode, Copper

INTRODUCTION

It is clear that operating with a pulsed power supply will likely work better with a wired electrode than with a direct current The power supply of a wired electrode is poorly aligned with the cathode electrode. Because the cathode electrode is larger compared to the anode electrode, the cross section of the anode will still be completely eliminated. Pulse conductor operation using closed loop electrode motion control system. Stable and closed motion control is needed to increase the rate of erosion in the process. Both the EDM process and the stick process show that the stability of the motion controller is the key to increasing the maximum erosion rate. The average voltage drop across

the electrode gap is usually measured to estimate the distance between the electrodes and to close the motion control circuit. The pulse process is defined as a process that uses a pulsed DC power supply to generate a pulse current between the flat electrode and the wire electrode, the position of which is controlled by a closed loop motion control system in which a medium arc voltage is applied as a feedback signal.

Mechanical Design of the Pulsed Wire Process

The mechanical design of the machine in terms of particle production can be split into two parts; the design of thereactor, and the design of the wire feed system. The design of these parts of the mechanical design has changedsignificantly as a result of the information gained during the development of the process.

Some of the key requirements the mechanical design must accomplish are the following:

- The new machine must use an anode in wire form
- The machine must be able to run continuously for long periods of time
- The machine should limit the need for frequent operator adjustment
- Seals in the reactor must be eliminated

The development of the mechanical portion of the process was completed at the same time that the idea of using asingle wire electrode with a flat plate cathode electrode rather than two wires was developed. As a result, the reactorand the wire feed system can use two wires, or a wire anode electrode and a larger cathode electrode.

Reactor Design

Maintenance Requirements One of the most time-consuming maintenance requirements of the rod process is the reassembly of the seals in the reactor. Because the rods rotate and move constantly, the seals and pads used in the reactor often need to be changed. Even when a new seal is installed in the reactor, the dielectric fluid still leaks due to variations in rod diameter and rod mismatch. One of the main goals of a pulse wire machine is to eliminate the need for seals or pads in the reactor. The wires are matched and flexible to bend at an angle in the reactor, unlike rod electrodes. An open top tank is used to allow wires to enter from above without the need for sealing. Wire electrodes into the top of the reactor led by a Teflon tube. Teflon tubes are formed through curved holes in the wire feed plate. Because the wire is routed through a Teflon tube, it bends in a circle while the wire is horizontal and perpendicular to the flat electrode.

Because the electrodes enter from the top of the reactor and then bend inside the reactor, there is no need for sealing. Teflon pipes will wear out over time and will need to be replaced, but pipe replacement is easy and will only be required once or twice a year, not daily. The design shown was developed prior to the decision to use a 0.0625-inch flat cathode electrode. A second wire electrode with a diameter of .25 inches was used as the cathode electrode. The diameter of the cathode electrode is 4 times larger than the diameter of the anode electrode; This makes the cathode electrode more efficient as a flat plate compared to the anode electrode. The cathode electrode is at the terminal and the anode conductor is equipped with a conductor system. The dielectric fluid enters the reactor through a tube that drains the dielectric gap and fills the reactor. Fluid exits the reactor through an overflow pipe (black tube). The fluid flowing through the overflow pipe is discharged into a 10-gallon container. The fluid that enters the reactor through the filling pipe is pumped out of the same storage tank. The water in this closed system is circulated until the concentration of particles in the liquid is high enough. When the particle concentration is high enough, the low-flow peristaltic pump begins to remove the fluid from the storage tank. The float valve in the storage tank keeps the fluid at the same level by adding deionized pure water. Under stationary conditions, the concentration of particles in the fluid is almost constant, and the fluid leaving the system comes out with the same concentration.

Wire Feed System

A good mechanism for feeding raw wire in a continuous process is friction drive roller, like the equipment used in wire feeders. Roller drive is good because it can feed the cable indefinitely without interruption or interruption. A set of U-Groove drive wheels from Miller welding equipment is used in the machine so the rollers are ready-made components. The diameter of these rollers is about 1.6 inches. Because the electrode gap in the process is very small,

ranging from a few tens of thousands to thousands of inches, positioning of high-resolution electrodes is required. Also, the clearance of the positioning system must be small to prevent prolonged delays when changing directions. A micro-stepper motor along with a 10: 1 gearbox to drive the roller is required to provide good solution motion. The stepper motor is powered by a 256 micro stepper controller, resulting in a theoretical output of 102,400 speed steps. The lower 10: 1 rear gearbox has about 200,000 steps per inch or 0.000 005 inches per step. The drive pulley must be electrically disconnected from the stepper motor because an electric current is transmitted to the wire through the drive pulley. To separate the engine from the drive pulley, a timing belt with Kevlar cable is used to transmit torque from the gearbox to the drive pulley. The timing belt protects the motor and pulley, but introduces some flexibility into the system. Because the system has friction, traction, flexibility, rotation, and other effects, the expected resolution of the cable positioning system is expected to be less than 5 million inches per machine step. However, the solution is expected to be less than the electrode gap. It has been experimentally confirmed that the resolution of the system is less than ten thousand inches (.0001 inch).

Power Supply

Pulsing the current across the electrode gap limits the length of the discharge time in the process. When the length ofthe discharge time is limited, the maximum particle size is also limited. Limiting the maximum particle size has asignificant impact on the distribution of particle size. The design chosen for the pulsed wire process power supply isa simple current limiting pulsed DC power supply. The power supply designuses a resistor to limit the current across the electrode gap. The resistor is a passive element so no active feedbackloop is needed to provide a constant current. Ohm's Law is used to determine what resistance is needed for a givenvoltage and current. There are three states that should be considered during the design of this type of power supply.The first state is the short circuited state where the electrodes are touching. Ideally the machine will never be in thisstate, but it is nearly impossible to completely prevent the electrodes from shorting out. Using Ohm's Law thecurrent can easily be determined and is shown in Equation (1). This is the maximum current that can be expected inthe system. Equation (2) shows the power dissipated by the resistor in this shorted state. The power dissipated by theresistor is very significant and is the largest loss in the power supply. This is because the resistor limits the current inthe circuit by converting electrical power to heat. All the components in the current loop should be selected to handlethe shorted current for an indefinite period. Failure to select components that will indefinitely handle the shortedcurrent could result in failure of the power supply, or worse an electrical fire.

$I=V_{source}=R$(1)

$P_{resistor}=IV_{source}$(2)

The second state that needs to be analyzed is the current during a discharge. Typically, once the discharge hasstarted the voltage across the electrodes will be between 18 and 26 volts depending on the electrode gap distance. Forthe design of this power supply the electrode voltage drop, Vgap, will be assumed to have a value of 22 volts.Equations (3), (4), and (5) show the current, power dissipated by the resistor, and the power delivered to theelectrode gap, respectively. The current and power dissipated by the resistor is less in this discharge state comparedto the shorted state. The rate of wire erosion is roughly proportional to the average power delivered to the electrodegap. Because the current in the gap is constantly being switched on and off, the duty cycle of the process must beconsidered. The duty cycle is the ratio of ton=toff , or in other words the percent of the time that the current is flowingthrough the gap. The average power delivered to the electrode gap. The power supply design requires an electronicswitch to handle the high frequency switch-ing of the load. A set of N-channel MOSFET transistors were selected forthe supply.N-channel.

MOSFET transistors were used in the power supply due to their low cost, high switching speed, and low onresistance. A MOSFET gate driver was also selected to improve the switching characteristics and reduced theswitching losses of the transistors. The power supply design requires a constant voltage source of 80 VDC. A custommade toroidal transformer was used to convert three phase 208 VAC power to three phase 55 VAC power. A threephase full bridge rectifier was then used to rectify the power into a DC voltage. An LC input filter was used to

filterthe rectified DC voltage to a nearly constant voltage of 80 VDC. The LC filter acts as a buffer between the erosionprocess and the three phase AC input.

Design of the Control System

Pulse conductor performance control system is very important. The control system uses process measurements to perform corrective actions for the cable position, stabilizing the process. An important note is that breakdowns (when the controllers supply the electrodes are close to each other) should be avoided to prevent short circuits between the two electrodes. In addition, the incremental time or the time required to reach the set point must be kept to a minimum to respond quickly to system interruptions. The outflow of the electrode gap is difficult to model properly. The length of the electrode is constantly changing and the relationship between the distance between the electrode gap and the voltage drop between the electrode intervals is nonlinear. However, a simple model is sufficient to thoroughly determine what type of controller should be used and what the best parameters are to be expected. Two PCI interface cards are used to connect the computer to the machine using a pulse cable. The FPGA (Field Programmable Gate Array) control card is used to provide digital input / output and to output step direction signals to the stepper motor controller. The second interface card provides a variety of analog-to-digital converters. The voltage and current signals are received using an analog digital PCI card operated by a computer controller. This administrator calculates the new location for the machine. EMC software produces smooth movement to new locations with limited speed and acceleration. The FPGA card then generates a step-by-step signal for the stepper motor controller to change the position of the stepper motor. The stepper motor changes the position of the electrodes to adjust the distance between the electrodes.

Voltage and Current Sensing

Great care was taken in disconnecting the power supply of the power supply emitted from all the control systems in the machine. This isolation aims to ensure operator safety and reduce noise and displacement in voltage and current signals. In the original design of the pulse voltage process, the electrode gap was measured, converted to a digital signal, transmitted by optical isolation, converted to an analog signal, and finally converted to a digital signal from analog to digital PCI card in a computer. Unfortunately, with this setting, many filter and alias issues are created due to the conversion of signals from analog to digital twice at two different speeds. The signal must be converted from analog to digital twice, since the analog-to-digital converter in a computer is not disconnected from the output power supply. The way the current is felt through the arc is very different from the way the voltage is received. The current transformer used in the machine uses the Hall effect principle to measure the indirect current in the conductor by measuring the magnetic field caused by the metal ring in the current transformer. Because the inverter only measures the magnetic field produced by the current in the conductor, the signal it generates is now electrically disconnected from the emitted power supply.

Because the power supply uses passive resistance to limit the current in the circuit if the current across the resistor isknown, then the voltage across the resistor is also known. Also, if the voltage across the resistor is known, then thevoltage across the electrode gap is also known. This means that only one of the two parameters of voltage andcurrent really need to be measured. Using Ohm's law for the resistor the voltage drop across the resistor at any giveninstant of time is given in Equation (1) as a function of the instantaneous current i. The only other element in thecircuit is the electrode gap, so the remaining voltage must be across the electrode gap as shown in Equation (2),where the open circuit voltage of the power supply is Vd . The current transducer measures the average current, I over several discharges so the remaining termsmust also be expressed as an average value. The average open circuitvoltage is shown in Vd Equation (3), and the resulting average gap voltage, is shown in Equation (4).

Vr = i R (3)
Gap=VdVr(4)
Vd= Vd (ton=toff) (5)
Vgap=VdRi(6)

The rod process produced a large amount of energy from the arc that was converted directly into heat increasing thetemperature of the dielectric fluid in the system. The change in dielectric fluid temperature was enough to require achiller to be installed in the system to keep the fluid at a reasonable temperature. This same effect was expected withthe wire process, but the pulsed discharges in the pulsing wire process do not add a significant amount of energy tothe fluid, unlike the rod process. Most of the energy in the pulsing wire process is used to create particles, and verylittle is used to heat the dielectric fluid. Because the temperature of the water does not change significantly when thepulsing wire process is used, all the designed experiments were performed with the water at room temperature. Thiseliminated the dielectric temperature as a design variable.

Impact of Motion Control Parameters

The PID motion control parameter clearly affects the response variable. PID parameters affect the stability of the process. If the PID parameter is poorly adjusted, the erosion rate will be reduced and the particle size will change more due to the change in distance between the electrodes. It is possible to set PID parameters for each experiment performed on the machine. However, if the PID parameter is set for each setting, the effects of the project variable and the PID parameter will be confused. It will not be clear whether the resulting change in the given setting is a function of the PID parameter, the design variable, or any combination of the two.To prevent confusion of PID parameters and design variables in the experiment, the PID parameter is kept constant for all experiments performed on the machine. A set of PID parameters was found that allowed for a reasonably stable operation over a range of design variables used in the experiment. After completing the designed experiments and some optimal settings for maximum current, pulse frequency and pulse duty cycle, the PID parameter for this setting can be modified to optimize performance at optimal settings.

Expected Form of the Model

The three remaining design variables are peak current, frequency, and duty cycle. These are the design variablesused in the experiments to create predictive models of the process. From a theoretical standpoint these threeparameters are expected to have the largest effect on the process. The rate of erosion is largely a function of theamount of power delivered to the electrode gap [1]. As more current is delivered to the gap, the rate of erosion isincreased. Peak current, pulse frequency, and pulse duty cycle all will have a large effect on the average powerdelivered to the electrode gap. The average power delivered to the gap, is shown in Equation (5) and is Pgapclearly linear with respect to the average gap current I gap. Equation (6) shows the average gap current as a function ofthe peak current, the function q(w), and the Duty Cycle.The duty cycle and the maximum current of the pulse obviously have a linear effect on the average energy transmitted to the gap. Thus, one can expect that the maximum current and duty cycle will have an almost linear effect on the rate of erosion. The power supply model shows that the resistors and wires in series with the electrode spacing are pure resistors. In fact, the resistors and wires used in the power supply have some inductance and parasitic capacitance. Therefore, the resistor bank used in power supply must be considered as a complex Z barrier that is both resilient and reactive. As the pulse frequency increases, the effective resistance of the resistor group increases, reducing the current supplied to the gap. This means that as the pulse frequency increases, the erosion rate tends to decrease. The average particle size produced in this process is expected to be related to the surface area of the part in the EDM process. Parameters in the EDM process that lead to good surface coating are expected to generate small particles. The surface coating on the EDM process is usually smoother as the current decreases and the frequency increases. This effectively generates more frequent and lower voltages compared to the settings for higher currents and lower frequencies. Low and high frequency pulses will destroy less material for each outflow, reducing the possibility of larger particle formation. Little is known about what may affect the size variation of the particles produced in the process. It can be expected that a dispersion of lower particle size will be expected when the process is more stable. This means that the gap between the electrodes is well controlled and all the outflows are the same. It is difficult to predict how design variables can affect the particle size distribution.

Selection of a Designed Experiment

The objective of performing the designed experiment is to determine the optimal setting for the process to operate at.Because of this a RSM, or response surface methodology, design should be used. One constraint in the design is thatthe power supply can only be set to four equally spaced current settings of 16, 32, 48 and 64 amps. This eliminatesthe possibility of using a full central composite design that requires 5 parameter setting. The remaining two factors ofpulse frequency and duty cycle can be set to any setting in a reasonable range. There are two RSM designs thatwould be possible to use with three factors and the con-straints on the current settings. The first is a faced centeredcentral composite design. This design uses three factor levels in each factor. This design has high variance on theedges of the design space, but has nearly flat variance in the middle of the design space where the optimalparameters are expected.

The second possible experimental design would be and I-optimal design. This design is a computer generated designthat selects treatments from a subset of the full factorial design space. The treatments are selected on the basis of Doptimality,or the determinate of the information matrix composed from the treatments selected. An I-optimal designwas created for the experiment and was compared to the face centered central composite design. Both designs havethe ability to create a quadratic predictive model from the data. The face centered central composite design wasfavored over the I-optimal design because the variance of the design is lower and more constant though the center ofthe design space. The face centered central composite design is more commonly used so more tools are available toanalyze it. Because of this the face centered central composite design was chosen over the I-optimal design.

Factor Levels

The factor levels in the face centered central composite design are linearly coded variables from -1 to 1. For each ofthe design variables, a maximum and minimum value must be selected to map to the coded factor levels. For thecurrent design variable only four settings are possible and the higher settings are expected to be favorable so thehigher three settings were selected. The maximum and minimum settings for the pulse frequency and duty cyclewere selected to give extreme values that still result in a stable process. The process was run at each of the extremesetting to make sure that the process could operate stably at these settings. The resulting designed experiment isshown in Table 4.4. The design has 6 center points shown in the table as treatments 7-14. These six center point areused to estimate the variation in the system.

Experimental Procedure

Great care was taken in the experiments to ensure that the operating conditions were the same for each design implementation. The sequence of treatments was randomized to prevent the interpretation of background noise as an effect of the actual parameters. Before each treatment, the end of the electrode is aligned with a file and cleaned. The reactor was cleaned and filled with 4 liters of pure water. Markers up to 5 cm are then attached to the wire electrodes. The manufacturer is positioned so that the marking scale points to 5 cm. The reaction begins and the wire is rotten until the 0 cm mark on the scale. A stop watch is used to measure the time required to disassemble a 5 cm wire. Care was taken to ensure that the particles in the liquid were well mixed and then one liter of liquid was collected in a bottle to analyze the particle size. The reactor is then cleaned and prepared for further operation. For each treatment in the experiment, the erosion rate was calculated based on the mass of the 5 cm line and the time required to destroy that line length.

The remaining two response variables, particle size and particle size variation, were measured using the Beckmann Coulter LS230 particle analyzer. Based on electron microscopy, the expected particle size ranges from about 50 nm at the lower end to about 50-100 μm at the upper end. The LS230 is a laser particle separation analyzer. Laser particle diffusion analyzers typically have a measuring range between 400 nm and 2000 mm. The laser emission method will easily measure larger particles, but will not be useful for measuring smaller particles produced in the process. The LS230 has an additional PIDS (Polarization Scattering) module for measuring particles from 40 nm to 800 nm.

The used LS230 is equipped with a small volume fluid module that requires only 200 ml of liquid sample. 200 ml of RODI (deionized) water was placed in the LS230 sample module and then the machine was calibrated and prepared for sample measurement. The measuring sample container was shaken to separate the large particles in the sample. A syringe is used to introduce fluid from the sample container into the LS230 sample module until the appropriate PIDS concentration is reached. A bubble removal cycle is then applied on the device to remove air bubbles into the laboratory when particles are introduced. The sample was then analyzed for 3 to 90 seconds. All three series were then averaged to obtain a single particle size histogram (see Appendix A).

After the first design experiment has been performed and the data are analyzed, it is clear that a second experiment will be needed to accurately characterize the rate of erosion in the process. This second experiment is necessary due to the lack of correspondence between the data and the predictive model generated by the data. From the first experiments, it is clear that the pulse current is a very important factor. It is also clear that current has a positive effect on the rate of erosion. Since the current is known to have a positive effect on the erosion rate, the goal is to find a setting that will increase the maximum erosion rate, the current being set to the maximum value for the second designed experiment. The cycle parameters of the remaining two frequencies and duties can be set to any reasonable value, as opposed to the current setting, which can only be set to 16, 32, 48 or 64 amperes. With greater flexibility, a new design was selected for the second experiment. For the second design, a complete central composite design with alpha dots was selected. The design has 5 levels for each factor. In addition to the design changes for the second experiment, the new design focuses on the maximum expected given by the first experiment.

RESULTS

As was explained, two designed experiments were performed to create a predictive model of the rate of erosion,mean particle diameter, and particle diameter variance for the proposed pulsed wire process. The raw data from thefirst experiment (current included as a factor) is found in Table 3. This data is shown in the randomized order thatthe runs were performed. For each of the three response variables (erosion rate, mean particle diameter, particle sizevariance) a predictive model was created using statistical tools commonly used in designed experiments. The factoreffects were calculated using least squares regression and a t-test was used to determine the significance of each ofthe effects. The designed experiments used are capable of creating, at most, a quadratic predictive model. Twodesigned experiments were performed for this research. The first designed experiment was created to create modelsfor the erosion rate, mean particle diameter, and particle diameter variance. A second experiment was required toproperly model the rate of erosion. These two experiments will be referred to as the first and second designedexperiments, respectively.It includes sustainability development goal responsible consumption and production.

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Table 1: Required Resistance Values and Related Power Dissipation.

PeakCurrent(Amps)	Resistance(W)	PowerDissipated(Watts)
16	3.5	896
32	1.75	1792
48	1.17	2688
64	0.875	3584

Table 2: Mapping to the Coded Factor Levels.

CodedValue	Current(Amps)	PulseFrequency(kHz)	PulseDutyCycle(%)
-1	32	5	30
0	48	12.5	50
1	64	20	70

Table 3: Face Centered Central Composite Design.

Treatment	Current(Amps)	PulseFrequency(kHz)	PulseDutyCycle(%)
1	32	5	30
2	32	5	30
3	32	5	30
4	32	5	30
5	32	5	30
6	32	5	30
7	48	12.5	30
8	48	12.5	50
9	48	12.5	50
10	48	12.5	50
11	48	12.5	50
12	48	12.5	50
13	48	12.5	50
14	48	12.5	50
15	48	20	50
16	64	5	30
17	64	5	70
18	64	12.5	50
19	64	20	30
20	64	20	70

Table 4: Second Composite Design (with Alpha points).

Treatment	PulseFrequency (kHz)	PulseDutyCycle (%)
1	3.2	32.9
2	6.8	32.9
3	3.2	47.1
4	6.8	47.1
5	5.0	40.0
6	5.0	40.0
7	2.5	40.0
8	7.5	40.0
9	5.0	30.0
10	5.0	50.0
11	5.0	40.0
12	5.0	40.0
13	5.0	40.0

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RESEARCH ARTICLE

Genetic Estimation of Heterobeltiosis and Standard Heterosis in CGMS hybrids of Pigeon Pea [*Cajanus Cajan* (L.) Millsp.]

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ABSTRACT

Heterosis is the most important phenomenon for breaking yield barrier level of crops. Hence an experiment was undertaken to identify the best heterotic cross combinations for exploitation of heterosis. In this context 10 lines and 3 restorers of pigeon pea were exploited through line tester mating design. Thus, the resultant 30 hybrids along with 13 parents and standard checks (GTH 1) were evaluated for better parent and standard heterosis. So, percent estimation of heterosis over better parent showed that 22 CGMS hybrids out of 30 were manifested heterotic effect significantly in desirable direction. It's heterotic ranged from 12.84 to 146.56 per cent. As against with standard check, 7 CGMS hybrids achieved highest per cent of heterosis and out of that 3 most high yielding CGMS hybrids in terms of standard heterosis were, CMS GT 1008 A X GTR 3 (56.63 %), CMS GT 712 A X GTR 3 (53.80 %) and CMS GT 712 A X GTR 50 (41.91 %) performed better. Its heterotic percentage ranged from -29. to 56.63 %. Therefore, these hybrids can be exploited further through heterosis breeding method that may help plant breeder to develop high yielding hybrids.

Keywords: Cytoplasmic genic male sterility (CGMS), Crop production, climate change, sustainability, consumption, Heterosis.

INTRODUCTION

In this current era, drastic "changes in climate" (climate action) affecting the "crop production and its productivity" which results in lower economic yield of pigeon pea. In the same way, world population is also increasing. So, to achieve "sustainability in food consumption", we need to increase productivity of any crop through development of a greater number of hybrids and varieties. So, Pigeon pea [*Cajanus cajan* (L.) Millsp.] is a major crop among the pulse crops of India and ranks next to chickpea in area and production which is commonly known as Arhar or Tur. It belong to family leguminaceae and sub family of *Papilionaceae*. Moreover, pigeon pea is differed from other legume crops in terms of adaptation and growth habits and classified as an 'often cross-pollinated crop' with 25-70 % natural out-crossing (Saxena *et al.* 1990). The chromosome number of pigeon pea is 2n=22(diploid species) and its centre of origin is East Indies . According to Linnaeus (1937), the East Indies is the primary centre of origin for pigeon pea.

It ranks 4th in the world among legume crops and its cultivation is predominant especially in India and other developing countries of tropics and sub-tropics. Enhancement of food security is achieved through increasing of an agricultural productivity by exploiting heterosis is prime objective of a Plant Breeder. Pigeonpea is an often-cross pollinated crop, and its resultant F_1 hybrids express strong heterosis. So, pigeonpea hybrids with high per cent of heterosis, which might be commercially exploited by developing F_1 hybrids. ICRISAT initiated the development of commercial hybrids of pigeon pea in collaboration with ICAR (Indian Council of Agricultural Research). In 1974, male sterile source of genetic male-sterility (GMS) was identified and its GMS based hybrids could not be commercialized because of labour intensive in seed production and difficult to maintain seed purity as it requires rouging of about 50 per cent fertile plant from the female plot resulted into decreased population (Reddy and Faris, 1981).

In order to achieve a breakthrough in productivity of pigeon pea, the first CGMS based pigeon pea hybrid, GTH-1 was developed by Sardarkrushinagar Dantiwada Agricultural University, Sardarkrushinagar in Gujarat state during 2004. Parents of this hybridare GT 288 A (CMS line developed from *C. scarabaeoides* cytoplasm) and GTR-11 (restorer/male). Morphological characterization of stable and diversified CGMS (A) and restorer (R) lines of pigeon pea for good heterotic combinations has been developed by Acharya and Patel (2010). Sardarkrushinagar Dantiwada Agricultural University has done extensive work to diversify both A & R lines for successful hybrid programme against the background of GT-288A having A_2 cytoplasm (Tikka *et al*. 1997; Chauhan *et al*. 2004 and Acharya and Patel, 2010). The first stable CMS line for commercial exploitation could be developed by (Tikka *et al*. 1997), GT-288A with its maintainer, GT-288B utilizing as A_2 cytoplasm source. This cytoplasmic-genic male sterility system contains A line with S (rr), B line with F (rr) and R line with S/F (RR) and consequently, first CGMS based hybrid SKNPH10 (GTH-1) has been released for cultivation in Gujarat (Majumder, 2004).Generally, Heterosis is expressed its superiority in term of phenotypic performance in F1 crosses over heterobeltiosis and standard check and these crosses can be exploited by the development of a commercially viable and acceptable male-sterility (CMS) system involving a 3 line breeding system, A-, B- and R-lines (Srivastava *et al.,* 2020).Thus, main objective of this investigation was to estimate the extent of heterosis for seed yield and its component characters including restoring capacities of R- lines for better yield potential by using CGMS lines.

MATERIALS AND METHODS

The experiment was conducted to investigate the heterosis consisted of 10CMS lines female lines and 3 testers as restorers (Table 2)were crossed in line x tester mating design during *Kharif,*2015-16. The resulted 30 hybrid combinations along with 13 parents (10 B lines and 3 R lines) and 2 checks (GTH 1) were evaluated during *Kharif,*2016-17 using RBD design. The parental materials for the study were obtained from the Pulses Research Station, Sardarkrushinagar Dantiwada Agricultural University, Sardarkrushinagar. The complete set of 44 genotypes was sown in a single row of 3.0 m length keeping inter row and intra row distance of 60 cm, and 20 cm, respectively. The recommended packages of practices were followed as per the recommendation to raise a healthy

crop. The latitude and longitude were 240 12' N and 720 12' E, respectively. The altitude of 154.5 m above Mean Sea level and soil type was sandy loam with pH 7.5 for this location (Table 1)

The observations were recorded on plot basis for days to flowering (DF) and days to maturity (DM), and as well on individual plants basis for number of branches per plant(BPP), number of pods per plant (PPP), 100-seed weight (SW) (g), seed yield per plant SYPP(g), Protein content and Leaf area. The Protein content was estimated in percentage by using Nuclear Magnetic Resonance Technique (Tiwari *et al.,* 1974).Leaf area was measured by leaf area meter (Model LI-3000, LI-COR, USA) and expressed by (cm^2).The recorded data of all traits were allowed for statistical analysis using INDOSTAT Ver. 9.2.

RESULTS AND DISCUSSION

The most important reason to get highest heterosis is presence of an enormous amount of variability between the parents utilized in hybridisation. So, experiment was conducted to identify the superior parent and as well as superior CGMS hybrid. Thus, results of ANOVA for all the characters presented in Table 3 and revealed that there is presence of significant differences among the parents for all the characters. This showed that presence of enormous amount of variability between parents (lines and testers) for most of the characters under studied. Meanwhile in hybrids also significant differences were observed for all the characters which they were specified that there is presence of enormous heterosis for these traits. Mean sum of squares due to line *vs* tester significant for most of the traits except for 100 seed weight, harvest index and protein content.

In practical plant breeding, the heterosis measured over better parent and standard check is more realistic and is of more practical importance. Hence, in the present investigation, heterosis has been estimated over the better parent (heterobeltiosis) and as well as standard check (GTH 1) The results of Earliness in flowering and maturity is very important parameter of increasing yield of any research work. So, the results of early flowering (Table 4) was observed in 6 hybrids out of 30 against better parent heterosis in desirable direction (negative) & it ranged from -8.04 (CMS GT 712 A X GTR 50) to 0.58 per cent (CMS GT 1011 A X GTR 3). Simultaneously, three most desirable standard heterotic crosses for days to flowering were placed in ascending order *i.e.,* CMS GT 712 A X GTR 50 (-10.06 %), CMS GT 712 A X GTR 3 (-8.81 %) and CMS GT 712 A X GTR 52 (-8.18 %) over standard check GTH. Heterosis in both negative and positive direction for days to 50% flowering had also been reported by Sekhar *et al*. (2004), Wankhade *et al*. (2005), Soni *et al.* (2017),

The perusal of the results of days to 75 % maturity (Table 4) in respect to heterobeltiosis exhibited that, 5 out of 30 hybrids were matured early than better parent and significantly performed in desirable direction. Rather, none of the hybrids were matured earlier than standard check. However, all hybrids were exhibited significant results in positive direction. So, Heterosis in both negative and positive direction for days to maturity had also evident by Wankhade *et al*. (2005), Vaghela *et al*. (2011), Patel and Tikka (2014a) and Patel and Tikka (2014b). Plant with higher number of primary branches,are closely associated with higher seed yield. The results of number of branches per plant (Table 5), 6 hybrids showed better parent heterosis for highest number of branches in comparison with superior parent. Its heterotic value ranged from -15.63 (CMS GT 703 A X GTR 52 and CMS GT 1006 A X GTR 52) to 38.10 per cent (CMS GT 712 A X GTR 50). In the other way, standard heterosis was manifested in 5 hybrids in significant and positive direction. The three most heterotic crosses among 30found superior against standard check GTH 1 were, CMS GT 1008 A X GTR 3 (26.45 %), CMS GT 712 A X GTR 3 (23.97 %) and CMS GT 712 A X GTR 50 (19.83 %).These results were similar with findings of Acharya *et al.* (2009), Shoba and Balan (2010a), Patel and Tikka (2014a), Patel and Tikka (2014b), Mhasal*et al*. (2015) and Soni*et al.* (2017) for number of branches per plant.

The results of pods per plant showed (Table 5) that 28 hybrids evinced significant and positive heterosis over better parent. The heterobeltiosis ranged from 11.55 (CMS GT 1006 A X GTR 52) to 93.42 per cent (CMS GT 712 A X GTR 3). It was observed that 2 crosses among 30 found significant in positive direction and its heterotic range from -32.58

(CMS GT 1006 A X GTR 50) to 16.93 per cent (CMS GT 712 A X GTR 3) for this trait. Results were in agreement with Chandirakala *et al*. (2010), Shoba and Balan (2010a), Gupta *et al.* (2011), Patel and Tikka (2014a), Patel and Tikka (2014b), Ajay *et al.* (2015) and Soni*et al.* (2017).

For 100 seed weight (gm), 3 hybrids *viz.,* CMS GT 712 A X GTR 3, CMS GT 1006 A X GTR 3 and CMS GT 1008 A X GTR 50) showed highest per cent of heterosis over better parent and standard check in significant and positive direction (Table 6). The range of heterobeltiosis from -6.87 (CMS GT 1011 A x GTR 50) to 9.18 per cent (CMS GT 1008 A X GTR 50) and similarly, Standard heterosis for GTH 1 ranged from -7.08 (CMS GT 1011 A x GTR 52) to 7.70 per cent (CMS GT 712 A x GTR 3). The findings were in accordance with results of Chandirakala *et al*. (2010), Gupta *et al.* (2011), Patel and Tikka (2014a), Patel and Tikka (2014b), Ajay *et al.* (2015) and Soni*et al.* (2017). For this trait.

The main objective of any plant breeder is to develop high yielding hybrids and varieties. So, in our experiment, the perusal results of seed yield per plant revealed (Table 6) that 22CGMS hybrids manifested heterotic effect over its better parent with significant difference in desirable direction. It's heterotic range from 12.84 (CMS GT 705 A X GTR 3) to 146.56 per cent (CMS GT 712 A X GTR 3). As against with standard check, 7 out of30CGMS hybrids achieved highest per cent of heterosis in desirable direction and thus the three most high yielding CGMS hybrids in terms of per centage were, CMS GT 1008 A X GTR 3 (56.63 %), CMS GT 712 A X GTR 3 (53.80 %) and CMS GT 712 A X GTR 50 (41.91 %). However, its standard heterotic range from -29.61 (CMS GT 705 A X GTR 3) to 56.63 per cent (CMS GT 1008 A X GTR 3).The above cited findings are similar with results of Shoba and Balan (2010a), Gupta *et al.* (2011), Lay *et al*. (2011), Patel and Tikka (2014a), Patel and Tikka (2014b), and Soni *et al.* (2017), Salama *et al.* (2019).

The perusal results of protein content revealed (Table 7) that 8CGMS hybrids out of 30 exhibited significant and positive heterosis over better parent. Its heterotic range was observed from -6.72 (CMS GT 703 A X GTR 50) to 9.31 per cent (CMS GT 1014 A X GTR 3).Two hybrids such as, CMS GT 1008 A X GTR 52 and CMS GT 1014 A X GTR 3exhibited high per cent of heterosis was observed against standard check significantly in desirable direction. The standard heterosis for GTH 1 ranged from -6.67 (CMS GT 710 A X GTR 50) to 4.05 per cent (CMS GT 1008 A X GTR 52). The results were coinciding with the findings of Baskaran and Muthiah (2006) and Patel and Tikka (2008), Shoba and Balan (2010a), Patel and Tikka (2014a) and Patel and Tikka (2014b) for protein content.

The important trait leaf area revealed (Table 7) that 22 hybrids showed heterobeltiosis with range of -7.00 (CMS GT 1013 A X GTR 50) to 53.47 per cent (CMS GT 712 A X GTR 3). Similarly, 20 hybrids exploited standard heterosis against GTH 1 significantly in positive direction. With range of f -11.05 (CMS GT 1013 A X GTR 52) to 50.99 per cent (CMSGT 712 A X GTR 3). Present findings were similar with Saritha *et al.* (2012) and Soni *et al*. (2017).

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Table 1: Geographic and edaphic detail of Sardarkrushinagar

Sr. No.	Details	Sardarkrushinagar
1.	Latitude	24^0 12' N
2.	Longitude	72^0 12' E
3.	Altitude	154.5 m above MSL
4.	Soil type	Sandy Loam with pH 7.5

Table 2: Pedigree of parental lines

Genotypes			
Sr. No.	**Name of the parents**	**Pedigree**	**Source/Origin**
Lines:			
1.	CMS GT 703 A	ICP-13175	SDAU, S. K. NAGAR
2.	CMS GT 705 A	ICP-15352	SDAU, S. K. NAGAR
3.	CMS GT 710 A	AGS-85	SDAU, S. K. NAGAR
4.	CMS GT 712 A	AGS-113	SDAU, S. K. NAGAR
5.	CMS GT 1006 A	ICP-7250	SDAU, S. K. NAGAR
6.	CMS GT 1008 A	ICP-10897	SDAU, S. K. NAGAR
7.	CMS GT 1009 A	ICP-11887	SDAU, S. K. NAGAR
8.	CMS GT 1011 A	ICP-13189	SDAU, S. K. NAGAR
9.	CMS GT 1013 A	ICP-13560	SDAU, S. K. NAGAR
10.	CMS GT 1014 A	ICP-13804	SDAU, S. K. NAGAR
Testers:			
11.	GTR 3	CMS 17–II F_2 (Fertile)-1 derivative of *C. scaraboides* × *C. cajan*	SDAU, S. K. NAGAR
12.	GTR 50	F_4 derivatives of SKNPCH-8-1-1-3	SDAU, S. K. NAGAR
13.	GTR 52	F_4 derivatives of SKNPCH-3-3-4-1	SDAU, S. K. NAGAR

Table 3: Analysis of variance showing mean sum of squares for different characters in pigeon pea.

Sources of variation	d.f	Days to Flowering	Days to Maturity	Number of branches per plant	Number of pods per plant	100 Seed Weight (g)	Seed Yield per Plant (g)	Protein Content (%)	Leaf Area (Cm^2)
Replications	2	5.59	0.33	0.99	376.09	0.00	103.37	0.31	14802.91
Parents	12	165.42**	154.03**	4.97**	1357.17**	0.37*	270.74**	0.61**	233650.70**
Lines	9	134.46**	149.57**	3.92**	1280.38**	0.42*	172.60**	0.76**	226850.30**
Testers	2	21.78	30.78	2.46**	219.26	0.05	78.70	0.03	158435.44**
Lines *vs* Testers	1	731.30**	440.62**	19.49**	11524.18**	0.59	1178.03**	0.46	445284.84**
Parents *vs* Hybrids	1	11.91	86.33*	48.50**	308732.63**	1.85**	136694.04**	2.59**	11966515.0**
Hybrids	29	126.68**	120.87**	2.01**	3070.03**	0.37*	1354.70**	0.92**	332444.25**
Error	84	8.01	19.54	0.45	427.40	0.19	87.85	0.12	20616.92

*, ** Significant at 5 per cent and 1 per cent levels, respectively

Sr. No.	Cross/ Hybrids	% Heterosis			
		DF		DM	
		BP	GTH 1	BP	GTH 1
1	CMS GT 703 A X GTR 3	-2.65	3.77	-2.83	3.44
2	CMS GT 703 A X GTR 50	-2.36	4.09	-3.23	3.01
3	CMS GT 703 A X GTR 52	-1.77	4.72 *	-2.83	3.44
4	CMS GT 705 A X GTR 3	-1.47	5.35 *	-2.61	4.30
5	CMS GT 705 A X GTR 50	-2.65	4.09	-1.61	5.38 *
6	CMS GT 705 A X GTR 52	-2.35	4.40 *	-1.00	6.02 *
7	CMS GT 710 A X GTR 3	-2.62	5.03 *	-1.43	3.44
8	CMS GT 710 A X GTR 50	-2.92	4.72 *	-1.43	3.44
9	CMS GT 710 A X GTR 52	-1.46	6.29 **	-0.20	4.73 *
10	CMS GT 712 A X GTR 3	-4.29	-8.81 **	-1.73	-2.37
11	CMS GT 712 A X GTR 50	-8.04**	-10.06 **	-5.45 *	-3.01
12	CMS GT 712 A X GTR 52	-4.26	-8.18 **	-3.23	-3.23
13	CMS GT 1006 A X GTR 3	-2.02	6.60 **	-2.58	5.38 *
14	CMS GT 1006 A X GTR 50	-2.89	5.66 *	-1.79	6.24 **
15	CMS GT 1006 A X GTR 52	0.00	8.81 **	-2.78	5.16 *
16	CMS GT 1008 A X GTR 3	-3.92	-7.55 **	-2.37	-2.37
17	CMS GT 1008 A X GTR 50	-4.50 *	-6.60 **	-4.61 *	-2.15
18	CMS GT 1008 A X GTR 52	-0.65	-4.40 *	-2.37	-2.37
19	CMS GT 1009 A X GTR 3	-1.71	8.18 **	-4.78 *	2.80
20	CMS GT 1009 A X GTR 50	-5.71**	3.77	-5.98 **	1.51
21	CMS GT 1009 A X GTR 52	-4.57 *	5.03 *	-4.58 *	3.01
22	CMS GT 1011 A X GTR 3	0.58	8.18 **	-3.01	4.09
23	CMS GT 1011 A X GTR 50	-0.88	6.60 **	-3.81	3.23
24	CMS GT 1011 A X GTR 52	-4.09 *	3.14	-1.60	5.59 *
25	CMS GT 1013 A X GTR 3	-6.34**	6.92 **	-3.21	10.11 **
26	CMS GT 1013 A X GTR 50	-3.31	10.38 **	-3.40	9.89 **
27	CMS GT 1013 A X GTR 52	-3.31	10.38 **	-3.21	10.11 **
28	CMS GT 1014 A X GTR 3	-2.56	-4.09	10.11 **	10.11 **
29	CMS GT 1014 A X GTR 50	-1.92	-3.46	-3.98	-1.51
30	CMS GT 1014 A X GTR 52	-1.60	-3.14	-2.37	-2.37
Range		-.804 to 0.58	-10.06 to 10.38	-5.98 to 10.30	-3.23 to 10.11
No. of crosses showing significant desirable heterosis		6	6	5	0

Table 4: Estimation of heterobeltiosis (Better parent Heterosis) and standard heterosis for Days to 50 % Flowering and Days to 75 % Maturity

Sr. No.	Cross/ Hybrids	% Heterosis			
		DF		DM	
		BP	GTH 1	BP	GTH 1
1	CMS GT 703 A X GTR 3	-2.65	3.77	-2.83	3.44
2	CMS GT 703 A X GTR 50	-2.36	4.09	-3.23	3.01
3	CMS GT 703 A X GTR 52	-1.77	4.72 *	-2.83	3.44
4	CMS GT 705 A X GTR 3	-1.47	5.35 *	-2.61	4.30
5	CMS GT 705 A X GTR 50	-2.65	4.09	-1.61	5.38 *

6	CMS GT 705 A X GTR 52	-2.35	4.40 *	-1.00	6.02 *
7	CMS GT 710 A X GTR 3	-2.62	5.03 *	-1.43	3.44
8	CMS GT 710 A X GTR 50	-2.92	4.72 *	-1.43	3.44
9	CMS GT 710 A X GTR 52	-1.46	6.29 **	-0.20	4.73 *
10	CMS GT 712 A X GTR 3	-4.29	-8.81 **	-1.73	-2.37
11	CMS GT 712 A X GTR 50	-8.04**	-10.06 **	-5.45 *	-3.01
12	CMS GT 712 A X GTR 52	-4.26	-8.18 **	-3.23	-3.23
13	CMS GT 1006 A X GTR 3	-2.02	6.60 **	-2.58	5.38 *
14	CMS GT 1006 A X GTR 50	-2.89	5.66 *	-1.79	6.24 **
15	CMS GT 1006 A X GTR 52	0.00	8.81 **	-2.78	5.16 *
16	CMS GT 1008 A X GTR 3	-3.92	-7.55 **	-2.37	-2.37
17	CMS GT 1008 A X GTR 50	-4.50 *	-6.60 **	-4.61 *	-2.15
18	CMS GT 1008 A X GTR 52	-0.65	-4.40 *	-2.37	-2.37
19	CMS GT 1009 A X GTR 3	-1.71	8.18 **	-4.78 *	2.80
20	CMS GT 1009 A X GTR 50	-5.71**	3.77	-5.98 **	1.51
21	CMS GT 1009 A X GTR 52	-4.57 *	5.03 *	-4.58 *	3.01
22	CMS GT 1011 A X GTR 3	0.58	8.18 **	-3.01	4.09
23	CMS GT 1011 A X GTR 50	-0.88	6.60 **	-3.81	3.23
24	CMS GT 1011 A X GTR 52	-4.09 *	3.14	-1.60	5.59 *
25	CMS GT 1013 A X GTR 3	-6.34**	6.92 **	-3.21	10.11 **
26	CMS GT 1013 A X GTR 50	-3.31	10.38 **	-3.40	9.89 **
27	CMS GT 1013 A X GTR 52	-3.31	10.38 **	-3.21	10.11 **
28	CMS GT 1014 A X GTR 3	-2.56	-4.09	10.11 **	10.11 **
29	CMS GT 1014 A X GTR 50	-1.92	-3.46	-3.98	-1.51
30	CMS GT 1014 A X GTR 52	-1.60	-3.14	-2.37	-2.37
Range		-.804 to 0.58	-10.06 to 10.38	-5.98 to 10.30	-3.23 to 10.11
No. of crosses showing significant desirable heterosis		6	6	5	0

*, ** Indicates significant at 5 per cent and 1 per cent levels, respectively.

Table 5: Estimation of heterobeltiosis (Better parent Heterosis) and standard heterosis for For Number of Branches Per Plant (NBPP) and Number of Pods Per Plant (NPPP)

Sr. No.	Cross/ Hybrids	% Heterosis			
		Number of Branches Per Plant		Number of Pods Per Plant	
		BP	**GTH 1**	**BP**	**GTH 1**
1	CMS GT 703 A X GTR 3	-13.18 *	-7.44	47.83 **	-10.63
2	CMS GT 703 A X GTR 50	11.43	-3.31	66.03 **	-3.60
3	CMS GT 703 A X GTR 52	-15.63 *	-10.74	57.06 **	-1.78
4	CMS GT 705 A X GTR 3	-10.08	-4.13	56.01 **	-5.68
5	CMS GT 705 A X GTR 50	20.95 **	4.96	42.13 **	-17.48 **
6	CMS GT 705 A X GTR 52	-12.50	-7.44	38.85 **	-13.17 *
7	CMS GT 710 A X GTR 3	-4.65	1.65	54.60 **	-6.54
8	CMS GT 710 A X GTR 50	1.63	3.31	60.52 **	-6.80
9	CMS GT 710 A X GTR 52	-10.16	-4.96	30.56 **	-18.35 **
10	CMS GT 712 A X GTR 3	16.28 *	23.97 **	93.42 **	16.93 **
11	CMS GT 712 A X GTR 50	38.10 **	19.83 **	89.57 **	10.16
12	CMS GT 712 A X GTR 52	7.03	13.22	71.49 **	7.25
13	CMS GT 1006 A X GTR 3	-11.63	-5.79	26.87 **	-23.30 **

14	CMS GT 1006 A X GTR 50	16.19 *	0.83	16.11	-32.58 **
15	CMS GT 1006 A X GTR 52	-15.63 *	-10.74	11.55	-30.24 **
16	CMS GT 1008 A X GTR 3	18.60 **	26.45 **	93.18 **	16.79 **
17	CMS GT 1008 A X GTR 50	11.02	16.53 *	80.67 **	4.90
18	CMS GT 1008 A X GTR 52	-0.78	4.96	66.11 **	3.88
19	CMS GT 1009 A X GTR 3	-13.18 *	-7.44	55.66 **	-5.90
20	CMS GT 1009 A X GTR 50	5.71	-8.26	57.83 **	-8.36
21	CMS GT 1009 A X GTR 52	-14.06 *	-9.09	46.42 **	-8.43
22	CMS GT 1011 A X GTR 3	-12.40	-6.61	54.17 **	-6.80
23	CMS GT 1011 A X GTR 50	16.19 *	0.83	65.86 **	-3.69
24	CMS GT 1011 A X GTR 52	-4.69	0.83	55.93 **	-2.49
25	CMS GT 1013 A X GTR 3	-14.73 *	-9.09	57.42 **	-4.83
26	CMS GT 1013 A X GTR 50	12.38	-2.48	60.11 **	-7.03
27	CMS GT 1013 A X GTR 52	-7.03	-1.65	57.55 **	-1.47
28	CMS GT 1014 A X GTR 3	-6.98	-0.83	50.45 **	-9.05
29	CMS GT 1014 A X GTR 50	10.48	-4.13	64.82 **	-4.03
30	CMS GT 1014 A X GTR 52	-10.16	-4.96	53.99 **	-3.69
Range		-15.63 to 38.10	-10.74 to 26.45	11.55 to 93.42	-32.58 to 16.93
No. of crosses showing significant desirable heterosis		6	4	28	2

* ** Indicates significant at 5 per cent and 1 per cent levels, respectively

Table 6: Estimation of heterobeltiosis (Better parent Heterosis) and standard heterosis For 100 Seed Weight (100 SW) and Seed Yield Per Plant (SYPP)

Sr. No.	Cross/ Hybrids	% Heterosis			
		100 Seed Weight		Seed Yield Per Plant	
		BP	GTH 1	BP	GTH 1
1	CMS GT 703 A X GTR 3	1.10	2.01	69.00 **	5.42
2	CMS GT 703 A X GTR 50	0.80	0.73	29.56	-23.06 *
3	CMS GT 703 A X GTR 52	1.52	-0.28	46.30 **	-12.06
4	CMS GT 705 A X GTR 3	2.41	3.33	12.84	-29.61 **
5	CMS GT 705 A X GTR 50	-2.46	-2.53	125.69 **	31.47 **
6	CMS GT 705 A X GTR 52	1.69	-0.10	49.93 **	-9.87
7	CMS GT 710 A X GTR 3	0.72	1.63	120.10 **	37.30 **
8	CMS GT 710 A X GTR 50	3.40	3.33	50.42 **	-12.38
9	CMS GT 710 A X GTR 52	3.85	2.01	31.49	-20.95 *
10	CMS GT 712 A X GTR 3	5.94*	7.70 *	146.56 **	53.80 **
11	CMS GT 712 A X GTR 50	1.64	3.33	136.07 **	41.91 **
12	CMS GT 712 A X GTR 52	-2.70	-1.08	107.27 **	24.60 *
13	CMS GT 1006 A X GTR 3	*5.43	4.58*	18.68	-25.97 *
14	CMS GT 1006 A X GTR 50	0.31	0.24	32.78	-22.65 *
15	CMS GT 1006 A X GTR 52	-0.71	-2.46	40.38 *	-15.61
16	CMS GT 1008 A X GTR 3	0.34	3.68	139.90 **	56.63 **
17	CMS GT 1008 A X GTR 50	9.18*	7.39*	75.71 **	14.72
18	CMS GT 1008 A X GTR 52	-1.98	1.28	110.16 **	37.22 **

19	CMS GT 1009 A X GTR 3	2.10	3.02	36.45 *	-14.89
20	CMS GT 1009 A X GTR 50	-0.03	-0.10	58.61 **	-7.61
21	CMS GT 1009 A X GTR 52	0.04	-1.73	25.84	-24.35 *
22	CMS GT 1011 A X GTR 3	-5.81	-4.96	46.43 **	-8.66
23	CMS GT 1011 A X GTR 50	-6.87	-6.94	35.14 *	-21.28 *
24	CMS GT 1011 A X GTR 52	-5.40	-7.08	64.74 **	-0.97
25	CMS GT 1013 A X GTR 3	-4.40	-3.54	19.97	-25.16 *
26	CMS GT 1013 A X GTR 50	3.09	3.02	48.61 **	-13.43
27	CMS GT 1013 A X GTR 52	-3.25	-4.96	50.47 **	-9.55
28	CMS GT 1014 A X GTR 3	-0.65	0.24	82.23 **	13.67
29	CMS GT 1014 A X GTR 50	-0.35	-0.42	30.28	-24.11 *
30	CMS GT 1014 A X GTR 52	1.45	-0.35	79.41 **	7.85
Range		-6.87 to 5.94	-7.08 to 7.70	12.84 to 146.56	-29.61 to 56.63
No. of crosses showing significant desirable heterosis		3	3	22	7

* ** Indicates significant at 5 per cent and 1 per cent levels, respectively

Table 7: Estimation of heterobeltiosis (Better parent Heterosis) and standard heterosis for For Protein Content (%) and Leaf Area (cm2)

Sr. No.	Cross/ Hybrids	% Of Heterosis			
		Protein Content (%)		Leaf Area (cm^2)	
		BP	GTH 1	BP	GTH 1
1	CMS GT 703 A X GTR 3	-6.57 **	-5.40 **	21.02 **	19.06 **
2	CMS GT 703 A X GTR 50	-6.72 **	-5.56 **	0.92	9.12
3	CMS GT 703 A X GTR 52	-6.64 **	-5.47 **	31.92 **	11.97 *
4	CMS GT 705 A X GTR 3	-4.22 **	-5.25 **	16.90 **	15.01 *
5	CMS GT 705 A X GTR 50	-1.83	-2.89	-2.07	5.88
6	CMS GT 705 A X GTR 52	-4.49 **	-5.52 **	29.31 **	9.76
7	CMS GT 710 A X GTR 3	1.01	-3.92 **	22.84 **	26.04 **
8	CMS GT 710 A X GTR 50	-2.06	-6.67 **	11.51 *	20.57 **
9	CMS GT 710 A X GTR 52	2.89	-2.55	44.00 **	47.76 **
10	CMS GT 712 A X GTR 3	4.13 **	-0.85	53.47 **	50.99 **
11	CMS GT 712 A X GTR 50	4.40 **	-0.51	35.43 **	46.44 **
12	CMS GT 712 A X GTR 52	2.78	-2.14	42.91 **	39.35 **
13	CMS GT 1006 A X GTR 3	-0.67	-5.51 **	1.14	-0.49
14	CMS GT 1006 A X GTR 50	7.25 **	2.21	-7.64	-0.14
15	CMS GT 1006 A X GTR 52	4.82 **	-1.09	21.32 **	2.98
16	CMS GT 1008 A X GTR 3	-1.24	-4.38 **	52.37 **	49.91 **
17	CMS GT 1008 A X GTR 50	0.30	-2.89	32.01 **	42.74 **
18	CMS GT 1008 A X GTR 52	7.47 **	4.05 **	49.44 **	44.11 **
19	CMS GT 1009 A X GTR 3	1.49	-3.45 *	22.71 **	20.73 **
20	CMS GT 1009 A X GTR 50	3.05	-1.80	3.15	11.53

21	CMS GT 1009 A X GTR 52	1.28	-3.66 *	47.55 **	25.25 **
22	CMS GT 1011 A X GTR 3	-0.43	-4.05 **	20.61 **	18.66 **
23	CMS GT 1011 A X GTR 50	6.16 **	2.29	12.38 *	21.51 **
24	CMS GT 1011 A X GTR 52	-0.09	-3.73 *	30.38 **	18.54 **
25	CMS GT 1013 A X GTR 3	0.47	-1.74	4.92	3.22
26	CMS GT 1013 A X GTR 50	-0.58	-2.77	-7.00	0.55
27	CMS GT 1013 A X GTR 52	1.75	-0.50	4.80	-11.05
28	CMS GT 1014 A X GTR 3	9.31 **	3.98 **	31.70 **	29.57 **
29	CMS GT 1014 A X GTR 50	0.29	-4.43 **	15.57 **	24.96 **
30	CMS GT 1014 A X GTR 52	5.84 **	-0.14	29.96 **	22.57 **
Range		-6.72 to 9.31	-6.67 to 4.05	-7.00 to 53.47	-11.05 to 50.99
No. of crosses showing significant desirable heterosis		8	2	22	20

RESEARCH ARTICLE

Evaluation of Gerbera (*Gerbera jamesonii L.*) Hybrids Based on Morphological Characteristics under Controlled Environment Conditions

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ABSTRACT

Gerbera (*Gerbera jamesonii*), a high value cut flower can be grown in tropical and subtropical climate under controlled environment conditions in greenhouse. The flower has a stedy demand in domestic as well as in international market. Considering the above, an experiment was carried out to assess the performance of nine gerbera hybrids, namely, Ankur, Pre-intenzz, Sunway, Silvester, Artist, Dune, Intense, Stanza and Dana-ellen for growth and floral quality under controlled environment conditions. The present investigation was conducted in the Protected Cultivation Unit of Research Centre for Smart Agriculture, Centurion University of Technology and Management, Paralakhemundi campus, Odisha. The experiment was planned in randomised block design and replicated thrice. Amongst the nine hybrids, Artist exhibited superior performance in terms growth and floral characters of gerbera,*viz.*, number of suckers per plant (5.3), number of leaves per plant (38.3), stalk length (52.3 cm), basal girth of the stalk (2.4 cm) and capitulum diameter (9.7 cm) at eighteen months after planting.

Keywords: Gerbera hybrids, controlled environment condition, growth parameters, floral characteristics, quality.

INTRODUCTION

Gerbera (*Gerbera jamesonii*) is a high value cut flower widely gaining popularity because of its beautiful inflorescence and its growing demand in domestic as well as in export market (Maitra *et al*.2020a, 2020b). As it is a high value crop, it offers ample scope for enhancing income from the unit area. Also, it addresses the issues of SDG1 and SDG 2 as more income can ameliorate the problems of poverty and hunger, respectively (UN, 2022). Gerbera belongs to the family *Asteraceae* and commonly known as Transverse daisy too (Elomaa *et al*., 2018). Gerbera is a diploid plant widely distributed in South Africa, Africa, Madagascar, and tropical Asia. It is a stem less perennial herb, leaves are petiolate, coarse or sometimes leathery (Goldblatt *et al*.,2019). In general, it can continue commercial flowering for three years or more. The major producing states of gerbera in India are Karnataka, Maharashtra, West Bengal, Tamil Nadu, Himachal Pradesh, Jammu and Kashmir and Gujarat. They thrive in partial shade conditions in tropical and subtropical climates (Xiwen *et al*.,1986).

Keeping in view, the growing market for cut flowers, selection of hybrids of gerbera is gaining importance. As performance of any cultivar varies with agroecology and growing conditions,an evaluation study of gerbera for growth and floral characters under controlled conditions of southern Odisha is necessary. However, the research carried out on gerbera cultivars under controlled environment conditions at southern Odisha condition is meagre. Therefore, nine commercial hybrids of gerbera were considered for this location to study.

MATERIALS AND METHODS

The present investigation was laid out in randomized in block design with three replications at Protected Cultivation Unint under Centre of Smart Agriculture, Centurion University of Technology and Management, Parlakhemundi, Odisha. This experimental material comprised of nine hybrids, *viz*.,Ankur, Pre-intenzz, Sunway, Silvester, Artist, Dune, Intense, Stanza and Dana-ellen. Standard package of practices was adopted for last eighteen months to raise a healthy crop. Five plants from each cultivar in each replication were used for recording observations. The data were recorded for six characters, *viz*., plant height (cm), number of suckers per plant, number of leaves per plant, basal girth of the stalk (cm), stalk length (cm) and capitulum diameter (cm) in eighteen months old gerbera hybrids cultivated under poly house conditions.

Plant height (cm)
In each treatment of every replication five plants of gerbera were randomly selected and the plant height (cm) was measured with a scale in centimeters

Number of suckers per plant
In each treatment of every replication, five plants of gerbera were randomly selected and the numbers of suckers were counted.

Number of leaves per plant
In each treatment of every replication, five plants of gerbera were randomly selected and the leaves per plant were recorded.

Stalk length (cm)
In each treatment of every replication, five fully opened flowers of gerbera were randomly selected and the stalk length was measured with a scale from the base of the stalk to the base of capitulum in centimeters.

Basal girth of the stalk (cm)

In each treatment of every replication, five fully opened flowers of gerbera were randomly selected and the basal girth of the stalk was measured using a thread and scale. The selected stalk was wrapped with the thread to know the circumference of the stalk and further the length of the wrapped portion of the thread was measured with a scale in centimeters.

Capitulum diameter (cm)

In each treatment of every replication, five fully opened flowers of gerbera were randomly selected and the diameter was measured with a scale in centimeters.

Statistical analysis

Observations recorded were analysed using single factor randomized block design through OPSTAT online (http://14.139.232.166/opstat/onefactor.htm?flavor=One+Factor+Analysis) at 5% level of significance.

RESULTS AND DISCUSSION

Plant height (cm)

The data on plant height showed significant differences among hybrids (Table 1). Among the hybrids, Dana-ellen was found to betallest (49.8 cm) which is at par with Stanza (49.4 cm) and Artist (48.4 cm).In comparison, Silvester was found to record shortest plant height (36.9 cm).This might be due to the genotypic variation among the hybrids. Similar findings were observed by Ahlawat *et al*. (2012) and Sil *et al*. (2017).

Number of suckers per plant

The hybrids recorded significant differences in number of suckers per plant and presented in the Table 1. Among the gerbera hybrids, Artist was found to record the highest suckers per plant (5.3) followed by Dune (4.7) and the minimum number of suckers per plant was recorded by Silvester (2.7). This might be attributed due to the ability of the cultivar in accumulation of photo synthates. Higher the ability results in increased production of suckers. The results corroborate with the findings of Sarmah *et al*. (2014).

Number of leaves per plant

The hybrids recorded significant differences in number of leaves per plant and presented in the Table 1. Among the gerbera hybrids, Artist was found to record highest leaves per plant (38.3) and it was closely followed by Dune (34.3).But the fewer leaves amongst hybrids was noted with Stanza (23.0). This might be attributed due to increased photosynthetic efficiency which is ought to depend upon the genetic makeup of a hybrid. The results are in conformation with Singh *et al*. (2014) and Barooah and Talukdar (2009).

Stalk length (cm)

The gerbera hybrids recorded significant differences in stalk length and presented in the Table 1. Among the gerbera hybrids, the significantly maximum stalk length was recorded by the hybrid Artist (52.3 cm) which is at par with Ankur (51.7 cm) and the minimum stalk length was recorded by Intense (40.0 cm). The quality of cut flowers is mainly attributed by stalk length. The hybrid with longer stalk length supply reserved food to flower for an extended period of time which may attribute to increase the shelf life of the flower (Biswal *et al*., 2017).

Basal girth of the stalk(cm)

Among, the gerbera hybrids, Artist recorded maximum basal girth of the stalk (2.4 cm) which was significantly superior over Pre-intenzz, Silvester, Ankur in the tune of 2.1 cm, 1.9 cm, 1.7 cm, respectively. However, the minimum basal girth of the stalk was recorded by Ankur (1.9 cm). Similar findings were observed by Thangam *et al*. (2009).

Capitulum diameter(cm)

The gerbera hybrids recorded significant differences in capitulum diameter and presented in the Table 1. Among the gerbera hybrids, Artist was found to record maximum capitulum diameter (9.5 cm) which is at par with Dana-ellen (9.1 cm). However, significantly lowest caputulum diameter was recorded by the hybrid Intense (7.2 cm) which is statistically at par with Pre-intenzz (7.6 cm). Similar observations on difference in capitulum diameter wasearlier reported by Singh et al. (2014).

CONCLUSION

Based on the present study, it can be mentioned that gerbera hybrid Artist was found to perform superior over other cultivars. However, Ankur and Dana-ellen were in close proximity in terms of floral quality. Henceforth it can be concluded that Artist, Ankur and Dana-ellen may be chosen under polyhouse conditions in southern Odisha condition for commercial cultivation of gerbera.

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Table 1: Morphological characteristics of different Gerbera hybrids

Hybrids	Plant height (cm)	Suckers per plant	Leaves per plant	Stalk length (cm)	Basal girth of the stalk (cm)	Capitulum diameter (cm)
Ankur	43.1	3.1	31.3	51.7	1.7	8.8
Pre-intenzz	41.9	4.2	28.7	42.3	2.1	7.6
Sunway	41.4	4.5	23.3	45.7	2.2	8.3
Silvester	36.9	2.7	31.3	46.3	1.9	8.3
Artist	48.4	5.3	38.3	52.3	2.4	9.5
Dune	37.7	4.7	34.3	44.1	2.3	8.1
Intense	40.9	3.7	24.7	40.0	2.0	7.2
Stanza	49.4	4.4	23.0z	44.4	2.2	8.5
Dana-ellen	49.8	4.5	30.7	49.0	2.3	9.1
SEm (±)	3.3	0.3	3.2	2.6	0.1	0.5
CD (p=0.05)	8.1	0.7	8.0	6.5	0.3	1.2

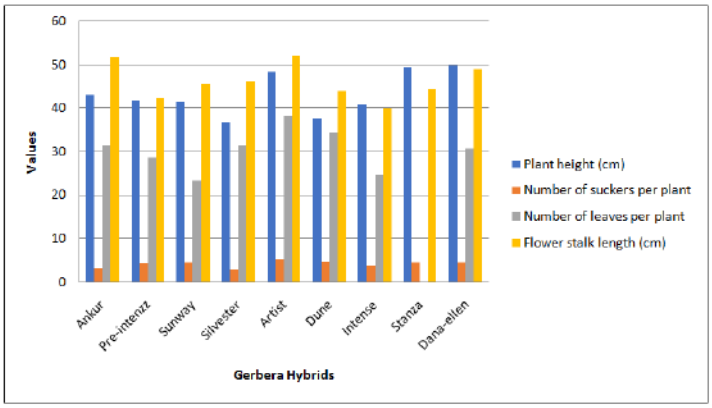

Fig. 1: Morphological characteristics of different Gerbera hybrids

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RESEARCH ARTICLE

Seed Processing: A Step towards Better Seed Quality

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ABSTRACT

Getting higher yield is highly dependent on the supply of high quality seed as carriers of specific and requested varietal characteristics. Seed production of the crops is highly dependent on season. Optimal conditions for seed production are mainly found during Rabi season (October-November to April-May). For quality seed production post-harvest processing steps and techniques are well integrated to select seed lot fractions with the best quality and the highest field emergence potential. This encourages more sustainable consumption and production. One of the major constraints of getting higher amount of seed yield is the losses during seed processing. To overcome this problem the harvested seed lot should go through a proper seed processing channel.

Keywords: Seed processing, SDG goal 12, Seed quality.

INTRODUCTION

Seed processing is defined as to comprise all the operations after harvest that aim at maximizing seed viability, vigour and health. In agriculture seed processing includes drying, cleaning, seed treatment, packaging and storage.

Principle and Objective

- The quality of seed is improved during processing in two ways

1. Separation of other tree seeds or inert matter and
2. Upgrading or the elimination of Poor quality seeds.

- The ultimate goal of seed processing is to obtain the maximum percentage of pure seed with maximum germination potential.
- The threshed produce is heterogeneous in nature.
- Processing brings homogeneity in the produce.
- This homogeneity helps in obtaining uniformity in the field.

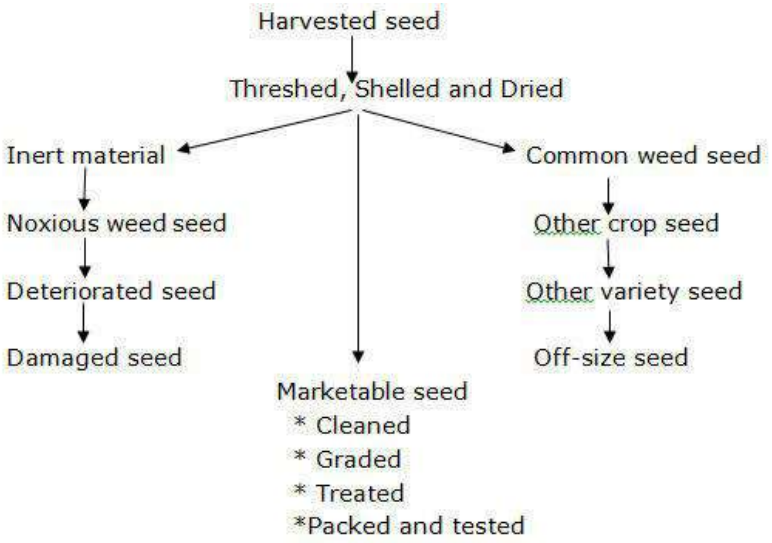
Requirement in Seed Processing

- There should be complete separation.
- There should be minimum seed loss.
- Upgrading should be possible for any particular quality.
- There should be have more efficiency.
- It should have only minimum requirement.

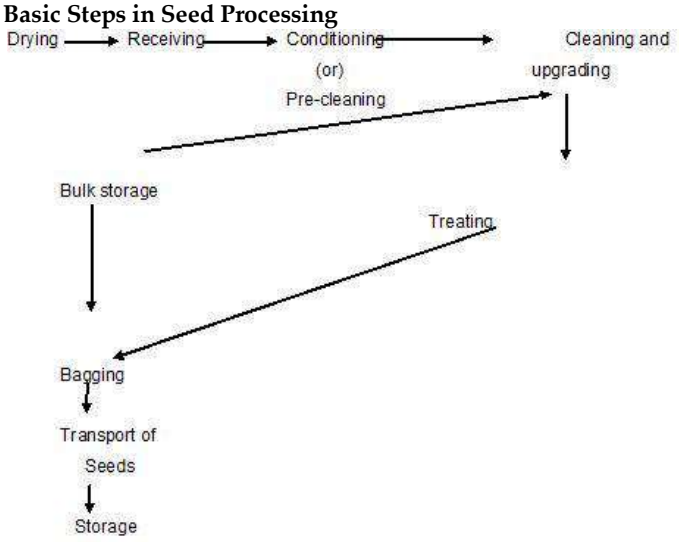
Types of Materials Removed During Seed Processing

- Inert materials.
- Common weed seeds.
- Noxious weed seeds.
- Deteriorated seeds.
- Damaged seeds.
- Other crop seeds.
- Other variety seeds.

Off-size seeds.



Basic Steps in Seed Processing



Pre-cleaning and Conditioning

This is the operation that prepares a seed lot for basic cleaning. The equipment required for preconditioning is generally specific for individual crop.

Some important preconditioning equipment are:

Sheller: This is equipment is used for shelling of corn seeds from its cob.

Huller: It is equipment which removers tightly fixed husk from seeds of grasses to facilitate in the process of sowing and germination (Hulling).

Debearder: This is equipment removes the awns and other appendages from the seed of oat and barley that create problems in the seed processing (Debearding).

Scarification: This is equipment scratches the hard seed coat to improve the process of germination by increasing exchange of water and oxygen in crops like lucern, fababean, ricebean etc.

Advantages of Pre-cleaning

- ✓ Removal of large trash improves the flow ability of seed mass through elevators, hoppers and conveyors.
- ✓ Better separation can be made with air screen cleaner when large trashes have been removed.
- ✓ Increase the capacity of air-screen cleaner
- ✓ Removes high moisture unwanted material which would otherwise increase time and cost of drying.
- ✓ Reduced storage volume

Basic Cleaning

This step of seed processing removes the larger, smaller and thicker adulterants as compares to the crop seed from the seed lots. Basic cleaning is done based on weight, size and density using cleaner with air screen.

This process involves following equipment

Grader: It separates the undersized seeds from the normal desirable seeds based on seed density and size with the help of screen and its vibrations.

Scalper: It is top most screen of seed cleaner/grader with larger holes than the desirable seed size to remove the inert matter of larger size than the seed (Scalping).

Aspirator: It removes lighter inert matter and adulterant than the crop seed from the seed lot with the help of pressure.

Air Screen Cleaner: It is generally made up of 2-3 screen of deferent mesh sizes, which are agitated to provide proper speed and place for separation. Air operation removes light and inert matter.

Seed Grading

Classification of seed lot based on commercial usage viz.,size shape, density and colour is known as grading. It is done further improvement of seed lots as finishing operation. It improves the seed lot by removal of cracked, damaged, shriveled and other defective seeds apart frominert matter.

Air Screen Cleaner

- This is the most important machine of every cleaning plant.
- It uses screens and aspiration (air blow) for two separations.
- A coarse upper screen removes larger material, a lower fine screen stops the seeds and lets through fine matter and then the seed fraction passes through a transverse or nearly vertical air stream which can separate light impurities such as empty or partly filled seeds, husks and glumes from the seed.
- In most cases a number of sieves with different sized perforations are used and the cleaning is a process of gradually shifting out smaller particles.

Specific Gravity Separation

- This method makes use of a combination of weight and surface characteristics of the seed to be separated.
- The principle of floatation is employed here.
- A mixture of seeds is fed onto the lower end of a sloping perforated table.
- Air is forced up through the porous deck surface and the bed of seeds by a fan, which stratifies the seeds in layers according to density with the lightest seeds and particles of inert matter at the top and the heaviest at the bottom.
- An oscillating movement of the table causes the seeds to move at different rates across the deck.
- The lightest seeds float down under gravity and are discharged at the lower end, while the heaviest ones are kicked up the slope by contact with the oscillating deck and are discharged at the upper end.
- This machine separates seeds of the same density but of different size and seeds of the same size but of different densities.

Indented Cylinder

- This helps to separate seeds according to the length.
- The equipment consists of a slightly inclined horizontal rotating cylinder and a movable separating trough.
- The inside surface has small closely spaced hemispherical indentations.
- Small seeds are pressed into the indents by centrifugal force and can be removed.
- The larger seeds flow in the centre of the cylinder and is discharged by gravity.

Magnetic Separator

- The magnetic separator separates seed according to its surface texture or related seed characteristics.
- First, seed is treated with iron filings, which adhere to rough surface alone.
- The treated seed lot is passed over a revolving magnetic drum and separated from smooth, uncoated seed.
- It may help to add varied amounts of water while mixing seed and powder, depending on the seed type.
- At any rate, the effectiveness of magnetic separation depends on the components of the seed lot and on the powder and water used in the treating operation.
- The greater the difference between surface textures of the seed lot's components, more effective will be the separation.

Colour Separator

- The colour separator is used to separate discoloured seed, greatly of lower quality.

- Separation based on colour is necessary because the density and dimensions of discoloured seed are the same as those of sound seed, so other machines are not effective for separation.
- Electronic colour separation uses photocells to compare the seed colour with "background" which are selected to reflect the same light as the good seed.
- Seed that differs in colour is detected by the photo cells, which generate an electric impulse.
- The impulse activates an air jet to blow away the discoloured seed.

Friction Separator

- The air-screen combinations cannot remove debris that has a size and density similar to the seeds.
- However, if the debris has a different surface texture, it may be possible to remove by friction cleaning.
- Any object rolling or sliding over a sloping surface encounters a certain friction depending on the texture of itself and that of the sloping surface.
- Separation is made on a velvet cloth or rubber belt with variable inclination, which ensures that the slope necessary for the run off of the seed is different from the slope necessary for run -off of the debris.
- The belt continuously moves upwards and removes the debris while the seeds roll down the slope.

Spiral Separator

- The separator, which classifies seed according to its shape and rolling ability, consists of sheet metal strips fitted around a central axis in the form of a spiral.
- The unit resembles an open screw conveyor standing in a vertical position.
- The seed is introduced at the top of the inner spiral.
- Round seeds roll faster down the incline than flat or irregularly shaped seeds, which tend to slide or tumble.
- The orbit of round seed increases with speed on its flight around the axis, until it rolls over the edge of the inner flight into the outer flight where it is collected separately.
- The slower moving seed does not build up enough speed to escape from the inner flight. Most spirals have multiple inner flights arranged one above the other to increase the capacity.

Liquid flotation

- Cleaning by flotation relies on the Principle that the density of the seed of a given species is specific both for filled and ill filled seed. In this method, liquids with a density or specific gravity between that of the full and empty seed are used.
- The specific gravity of the liquids used is such that the full seed sinks and the empty seed and light debris float.

The following factors to be taken in to consideration when designing a seed – cleaning plant:

1. Handling and cleaning of the seeds should be possible without mixing or damaging seed with a minimum of equipment, personnel and time.
2. Seed separators, elevators, conveyors and storage bins should be arranged so that seeds can flow continuously from beginning to end, yet be flexible enough to bypass a machine or return part for recleaning.
3. Other factors to be considered are kinds of crop seeds to be cleaned, nature of contaminants and weed seeds, volume of seed to be handled, method of handling, type of conveying system and location of shipping and receiving facilities.

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Table 1. Physical Characteristics of Seed and the Processing Equipment available for Grading.

Sl.no.	Characters	Processing Equipment
1	Size	Based on size it can be separated with air screen cleaner cum grader
2	Length	Disc or indented cylinder separator
3	Weight	Specific gravity separator
4	Shape	Spiral separator draper separator for round and flat seeds.
5	Surface texture	Rough from smooth surface seed-dodder mill
6	Colour	Electronic colour separator
7	Electronic Conductivity	Seed differing in their ability to conduct electrical image can be separated with electronic separator

Fig. 1: Maize Thresher

Fig.2 : Rice Huller

Fig.3: Debearder

Fig. 4: Sclper

Fig. 5: Huller

Fig. 6.Sieve Stand

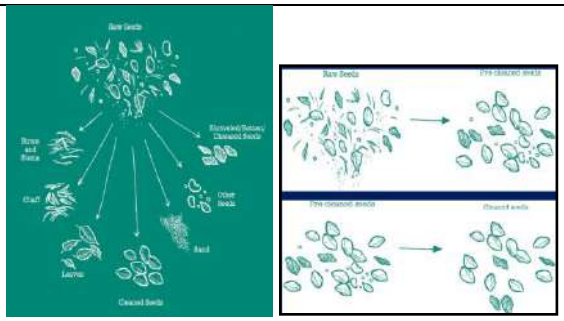

Fig. 7. Seeds Cleaning

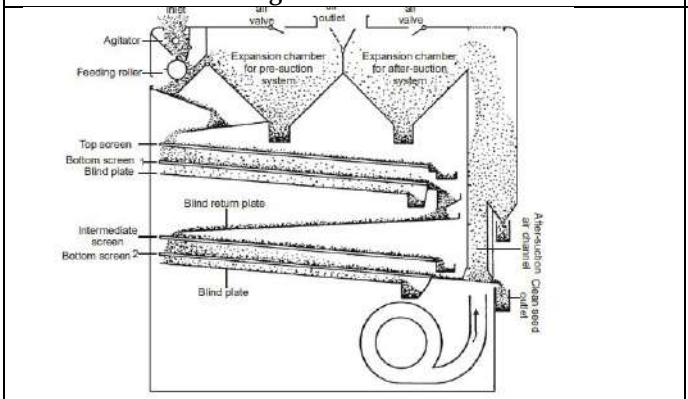

Fig.8: Air screen cleaner

Fig.9: Specific gravity separator

Fig.10: Indent Cylinder

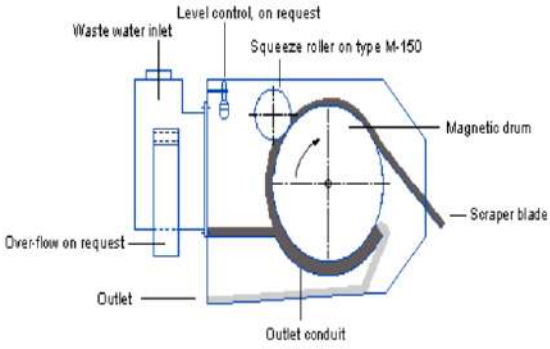

Fig.11: Magnetic separator

Fig.12: Colour separator

Fig.13: Spiral Separator

RESEARCH ARTICLE

Effects of Aging and Exercises on Fine Motor Skills

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ABSTRACT

Aging is the natural degeneration process, which impacts the brain's ability to perform the fine motor skill as it requires high cognitive and multi segmental synchronous activities. As there is little evidence in relation to aging and lifestyle together with respect to fine motor skills, we intended to conduct a study and find the relationship between the two on fine motor skills. Cross sectional study design was conducted and 120 participants of age 35-75, both gender were recruited for it without any past history of neurological conditions and injuries to the upper limb. Participants were categorized into 4 groups based on the age and their lifestyles. Each participant Hand Fine motor skills was assessed by Jebsen Taylor Hand Function Test Data analysis by Pearson correlation($r=0.268$ with p value = <0.003) and Two Way ANOVA ($F=27.801$ with p value of 0.00) indicates that there is a significant relationship between the ageing and lifestyle on fine motor skills. There is a positive correlation between the ageing and lifestyle in fine motor skills. From this study, we can state Ageing has direct relation to decline Fine motor skills, but it can be controlled if one follows health and active lifestyle.

Keywords: Ageing, Fine Motor Skills, Jebsen Taylor Hand Function Test, Aerobic exercises, Active Lifestyle.

INTRODUCTION

Function of the Upper Limb whether dominant or non-dominant side is foundational basis for the Fine Motor skills, which help individual to perform day to day activities freely and in synchronously. Fine Motor skills is the ability of

a person activities which required precise and accurate movements which includes, ability to discern the dimensions of the objects, distance between the hand and the objects and ability to plan and execute the task. This requires a series of coordinated events occurring at each joint (multi segmental activity) and which can perform the task smoothly. Central nervous system plays a vital role in this by organizing the available degree of freedom of the multiple joints for the better functional units, which is known as motor synergies to effectively control the limb movement to achieve the desired outcome [1]. Generally, motor synergies have an important role to stabilize the performance variable against internal and external perturbations. The main task of the CNS is to move the multi-segment unit—including shoulder, elbow and wrist towards the target to complete the task with low end-effector position variability and the motor synergy re shapes accordingly to the moving target to maximize end-effector accuracy. According to the Motor abundance theory, CNS plays a crucial role in adjustments occur in response to changing environmental and task demands by motor variability.

On the other hand, healthy ageing is the natural process of degeneration to one owns body and Central Nervous system is no exception to it. Neural ageing is a process of degeneration by changing the structural properties and the neurochemical properties of the brain. Which results in decline of the cognitive and motor performance and negatively impacts on the quality of their respective life. These age related neural impairments are observed at the behavioral level that is, slow reaction time (RT), reduced motor control and coordination while processing and performing any motor task. Many studies stated that increase in cerebral O2 levels enhances the cognitive function. However, it seems that O2 itself may not play the only role in this improvement but, by an association with other processes, its role is fundamental. Physical exercise has been described as an efficient modulator of the health status through increased mitochondrial bioenergetics such as adenosine triphosphate synthesis and reduced lipo genesis, reactive oxygen species (ROS) production, endoplasmic reticulum stress, and proinflammatory cytokine production such as tumour necrosis factor- alpha (TNF-α) Physical exercise has been shown to promote neuroprotection [2]. Aerobic training, according to Colcombe et al., is associated with less brain tissue loss in elderly people [3]. It has been reported that when healthy elderly people performed aerobic exercises, their cardiopulmonary functions improved and cognitive capacity improved, which in turn improved functions such as motor skills, cognitive speed, delayed recall functions, and visual attentions.[4]ensuring the lifes of one individual healthy and independent promoting well being for all the ages is the motto of SDG - 3, which is good health and well being [6]. Unfortunately there is not enough literature evidence in supporting to the influence of the ageing on fine motor skills, which is why we intended to look into it. We hypothesized that fine motor skills in aged is depends on the life styles that individual follows. For this purpose, we intended to conduct a study to evaluate the effect of ageing on fine motor skills by using the Jebsen Taylor Hand Function Test (JTHFT) among an aged population (adults and old people) with respect to different lifestyles.

MATERIALS AND METHOD

Figure 1 depicts theCross sectional study which was conducted with an aim to find the relation between aging and exercise on Fine motor skills in adults. Purpose of the study and method of testing was well explained to all participant, to prevent fear and apprehension, after obtaining informed consent from them individually, 120 subjects both gender of age between 35-75 without any History of Neural Disorders or Diseases (Stroke, Parkinson's, Nerve Injuries etc.) and Fractures or injuries related to Upper extremity and good visual acuity (with/Without eye wear) were recruited. Based on the age and daily lifestyle (Participant who are having sedentary lifestyle and Active Life style (at least of 30 mins of Any Kind of Exercises other than Daily activities). Participants were grouped into 4 different categories:

- Group AS (Adult Sedentary life style) – Adults of age (35-60) with sedentary life style
- Group AA (Adult Active Life style) – Adults of age (35-60) with Active life style
- Group OS (Old Sedentary Life style) – Older age of 60+ with sedentary life style
- Group OA (Old Active Life style) – Older age of 60+ with Active life style

Outcome Measure: Each subject was assessed by using Jebsen-Taylor Hand Function Test (JTHFT) on the dominant hand only and the value was noted accordingly among the subjects, the test was conducted in a sitting position on a chair with back and forearm supported. The Jebsen-Taylor Hand Function Test (JTHFT) is a standardized and objective measure of fine and gross motor hand function using simulated activities of daily living (ADL) with moderate to high test–retest reliability and excellent intra rate reliability (r=0.84 and 0.85, P<0.05) with absent practice effect (P<0.05).[5] The JTHFT includes a series of seven subtests representing fine motor, non-weighted and weighted hand function in ADL, which includes:

1. Printing a 24-letter, third-grade reading difficulty sentence
2. Turning over 7.6×12.7 cm (3×5-inch) cards (simulated page turning)
3. Picking up small, common objects (e.g. pennies, paper clips, bottle caps) and placing them in a container
4. Stacking checkers (test of eye-hand co-ordination)
5. Simulated feeding
6. Moving large empty cans
7. Moving large weighted [0.45 kg (1 lb)] cans.

Time required to perform each task is noted and summed. 15-45 minutes is the approximate time required to complete entire test. Data analysis is one by using SPSS 20.0 version was used for statistical analysis with significance level at 5% (i.e. $\alpha = 0.05$). Following statistical techniques were used: 1. Pearson Correlation was used to find out the correlation between the data of JTHFT (Jebsen Taylor Hand Function Test) with relation categorical variables and 2. Two Way- ANOVA (Analysis of Variance) was used to find an association between categorical variables were used and MS-EXCEL spreadsheet was used to generate the tables and graphs suitably.

RESULTS AND DISCUSSION

From the descriptive data represented in Table 1, shows that JTHFT value is higher in older adults with Sedentary life style compared to older adults with active lifestyle and in young adults though the scores are very near, Adults with sedentary life style having higher JTHFT value compared to Active Adults, the data is clearly represented in Figure 1 too. Results of the task in JTHFT are purely dependent on the motor performance, which is directly related to Instrumental Behavior formed by combination of Habitual and Goal directed systems. Habitual system is the tendency of an individuals to repeat past behaviors without considering the casual relationship of action and outcomes with the selected action, whereas Goal-directed system is an organized actions with respect to the properties of the object such as size, shape, location and also future task demands. Figure 2 shows the relation of age and lifestyle with respective to JTHFT Fine motor skill scores. Both, Pearson correlation(r=0.268 with p value = <0.003) and Two Way ANOVA (F=27.801 with p value of 0.00) shows that there is a significant relation between the ageing and fine motor skills. Neuroplasticity is the capacity of the brain in promoting the neurogenesis and neural connections due to psychophysiological and environmental factors, which can be achieved only through Active lifestyle. The above findings from the statistical analysis by Pearson correlation and ANOVA studies are similar to the statement of Colcombe et al.[3] that is, exercises/ active lifestyle specifically aerobic training helps in protecting brain tissue from ageing and also improves in cognitive capacity which helps in better visual attentions, cognitive speed, delayed recall functions and motor skills.

Results of the study shows that there is a significant influence of ageing and lifestyle on fine motor skills (based on JTHFT values). Better in Active Adults followed by Sedentary Adults, Active Old aged and Sedentary Old aged participants. As study have a positive correlation between the ageing and lifestyle in fine motor skills. we can conclude that, Aging has direct relation to decline Fine motor skills, but it can be controlled if one follows health and active lifestyle. Not only that, results from this study will help in bringing the awareness about active lifestyles and effects on the brain and also helps in better planning of geriatric physiotherapy management.

Limitation:

Non-dominated Hand scores aren't considered. There wasn't any emphasis on different type of Active Lifestyle

Recommendation

Further studies can be performed in regards to different lifestyle activities and also by including the non-dominant hand.

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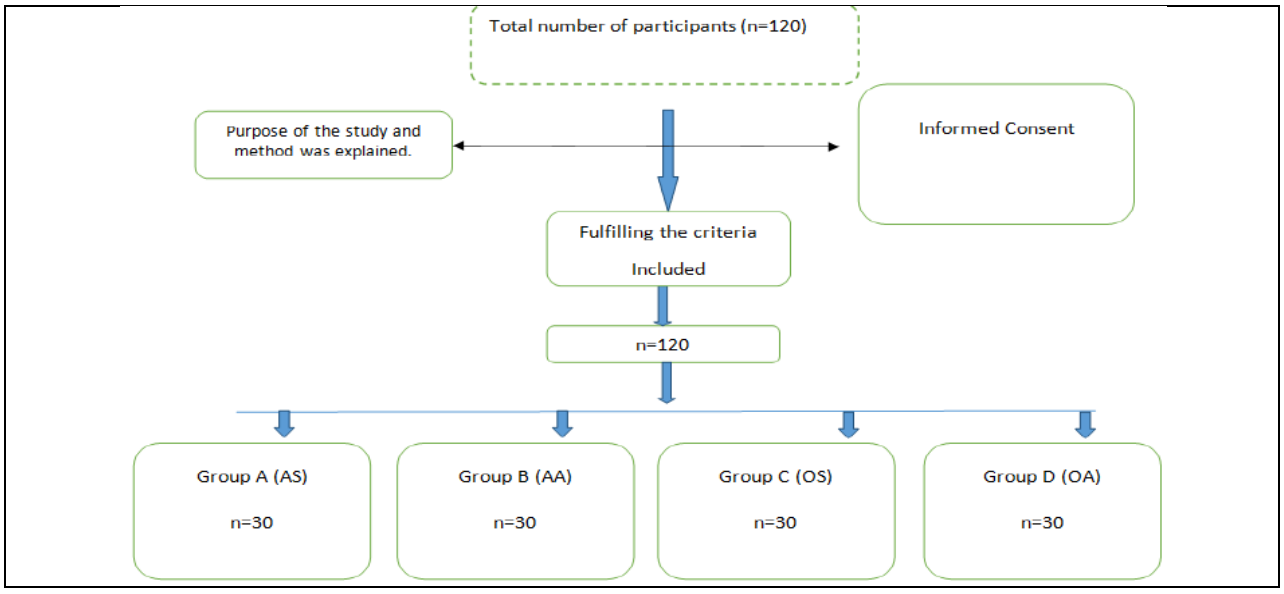
Table 1: Results of JTHFT scores (Jebsen Taylor Hand Function Test)

Groups	N	Age		JTHFT score
		Range	Mean +/_ S.D	Mean +/- S.D
AA	30	20.0	44.53 +/_ 6.08	37.26 +/_ 3.49
AS	30	20.0	46.13 +/_ 6.38	38.03 +/_ 2.93
OA	30	14.0	68.53 +/_ 4.11	49.06 +/_ 5.68
OS	30	15.0	67.90 +/_ 4.62	59.20 +/_ 6.45



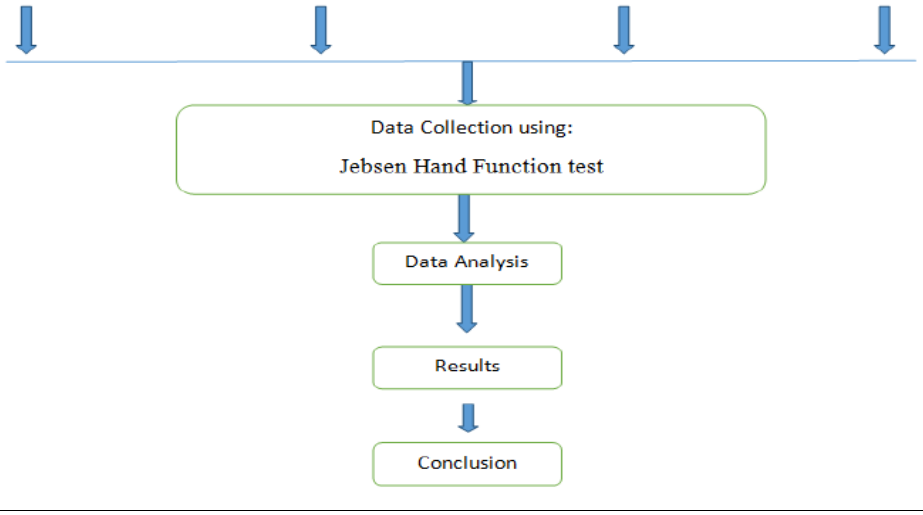


Figure 1: Flow Chart

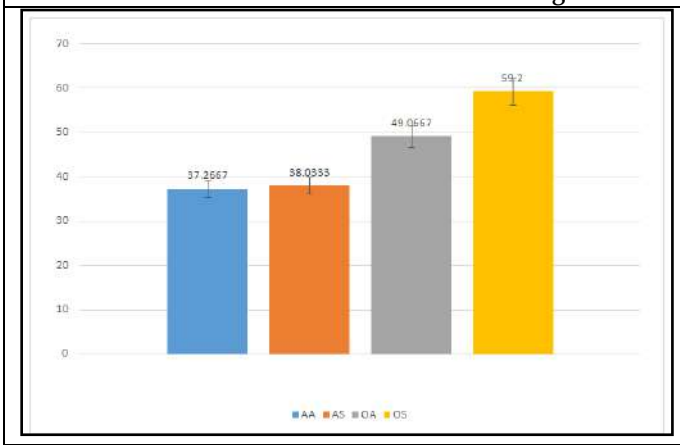


Figure 2: JTHFT Mean Scores of Each Group

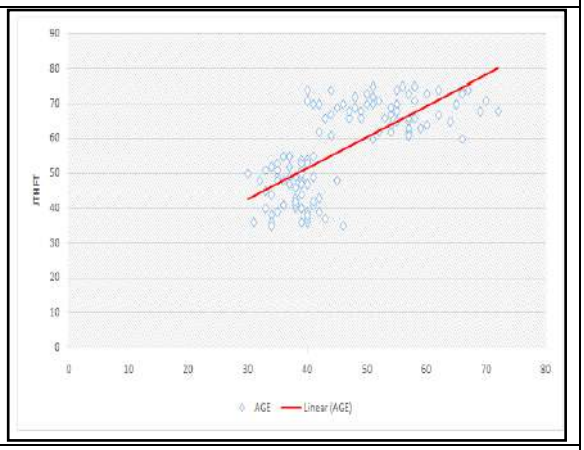


Figure 3: Correlation Plot Chart of JTHFT versus AGE and Lifestyle

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RESEARCH ARTICLE

A Novel Hybrid Approach to Data classification using Cuckoo Search Algorithm

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ABSTRACT

This paper proposes a cuckoo search based hybrid approach to classify data sets with varying number of classes. The objective of the work is to maximize accuracy and minimize the time complexity. For each of the input dataset an optimized target was determined by using Cuckoo search technique. The targets are used in Extreme Learning machine to classify the dataset. We have used some of the bench mark datasets from UCI learning repository and performed classification using the proposed approach. The proposed work can be used in disease diagnosis to achieve good health and well-being

Keywords: Extreme Learning Machine, Normalization, Cuckoo Search , Neural Network, Classification, Accuracy, Input, Target, Time complexity, Good health and Well-being

INTRODUCTION

Data classification is one of the most important areas of data science. Various tasks like pattern classification, data filtering, financial analysis, stock market predictions, weather forecasting, disease predictions, bioinformatics, image processing are using data classification in common. [1] Classification is the task of dividing different data from their known features to a particular group. The classifier can either be a binary or a multinomial classifier. Classifiers applied to data sets with two classes are said to be binary classifiers whereas multinomial classifiers are used for datasets containing more than two classes. This paper proposes an algorithm that uses the Cuckoo search algorithm and extreme learning machine (ELM) to classify multinomial data sets. Here the cuckoo search is used to find optimal target from the input s and the ELM performs the classification using the optimal targets.

Motivations

The major areas of concern in classification through neural networks are:

- Classification accuracy
- Training time

- Assumptions of target

To address the above issues the proposed work tries to use a combination of cuckoo search and ELM. The purpose of ELM is to bypass the training process of conventional neural networks thereby enhancing the time complexity. The use of cuckoo search is to optimize the target to be used by the ELM. The motive to use optimized target is for avoiding extensive mathematical computation involved to map input into assumed target.

The flow of the paper is as follows:

Section 2 describes about data sets used and pre processing. Section 3 deals with the working of Cuckoo search algorithm. Section 4 gives an idea about Extreme Learning Machine. The sections 5 and 6 deals with result analysis and conclusion respectively.

Datasets and Preprocessing

We have used 3 bench mark datasets from UCI learning repository for training and testing purposes. [9]The description of the datasets are given below

Iris Flower

The dataset consists of 150 samples which consists of a set of Iris flowers, where the goal is to predict three classes setosa, versicolor and virginica based on sepal (green covering) length and width, and petal (the flower part) length and width.

Seed

This dataset consist of experimental high quality visualization of the internal kernel structure produced by a soft X-ray technique. The images were recorded on 13x18 cm X-ray KODAK plates. Studies were conducted using combine harvested wheat grain originating from experimental fields, explored at the Institute of Agro physics of the Polish academy of science Lubin. The data set can be used for the tasks of classification and cluster analysis. The dataset contains the following feature attributes, 1) area A, 2) perimeter P,3) compactness C, 4) length of kernel, 5) width of kernel, 6) asymmetry coefficient 7) length of kernel groove. All of these parameters were real-valued continuous.

Diabetes

This dataset contains the Pima Indian women diabetes dataset to differentiate the normal persons and diabetic patients. This dataset has 768 instances 8-feature attributes and one class attribute. Attribute information which is clinically found are: 1. Number of times pregnant 2. Plasma glucose concentration a 2 hours in an oral glucose tolerance test 3. Diastolic blood pressure (mm Hg) 4.Triceps skin fold thickness (mm) 5. 2-Hour serum insulin (mu U /ml) 6. Body mass index (weight in kg/(height in m)^2) 7. Diabetes pedigree function 8. Age (years) 9. Class variable (0 or 1) The data set was selected from a larger data set held by the National Institutes of Diabetes and Digestive and Kidney Diseases. There are 268 (34.9%) cases in class '1' and 500 (65.1%) cases in class '0'.

Data Preprocessing

Prior to training the above data sets are normalized [1]. Normalization is essential to map the datasets into an acceptable range for better handling. Here all inputs are mapped to a range between 0-1 which is the primary requirement of a neural network.

Working of Cuckoo Search Algorithm The Cuckoo Search Algorithm (CSA) is one of the most popular optimization techniques. it was developed by Xin-she Yang and Suash Deb in 2009. In this approach we have used the Cuckoo search via levy flights.

The standard Cuckoo Search algorithm is as follows

Assumptions

Each cuckoo lays one egg at a time and dumps it in a randomly chosen nest.

The best nests with the high quality of eggs will carry to the next generations.
The number of available host nest is fixed and if a host bird identifies the cuckoo egg with the probability of pa = [0,1] then the host bird can either throw them away or abandon them and build a new nest.
The Levy flight refers to a random walk which is exhibited by certain animals. The walk depends on step lengths with random directions. The next movement depends on the current position and mathematically represented by
$Xi\ (t+1)=Xi(t)+\alpha \circledcirc Levy(\lambda)$
Where Xi(t+1) is the New nest position
Xi(T) is the current nest position
$\alpha >0$ is the step length
Levy(λ) is the random flight with random step size λ
$\oplus$refers to XOR operation
The pseudo code for cuckoo search is given by
Begin
Objective function f(x), x = (x1 , x2 , … , xd) T ;
Generate initial population of n host nests xi i = [1,2, … n]
While (t< Max Generation) or (stop criterion)
Get a cuckoo randomly by Levy Flights
Evaluate its fitness Fi
Choose a nest among n (say j) randomly
If (Fi> Fj)
Replace j by the new solution;
End If
A fraction (pa) of worse nests is abandoned and new ones are built;
Keep the best solutions (or nest with quality solutions)
Rank the solution and find the solution and find the current best
End while
Post process results and visualization
End Begin

Extreme Learning Machine: An Overview

The Extreme Learning Machine (ELM) is one of the popular approaches used for patter classification. It is proposed by Huang at el [13] that uses Single Layer Feed forward Neural Network (SLFN) Architecture. The ELM works on the principle of single layer feed forward network. Instead of finding the trained weight set through learning process, the ELM uses mathematical model to find the trained weight set directly from input and target. It makes use of the Moore Penrose generalized inverse to find the weight set. Mathematically it is represented as
W= H+.T
Where W is the trained weight set
T is the target
H+ is the generalized Moore-Penrose inverse
The advantages of using ELM over BPNN are as follows
Direct computation of weight sets there by reduced time complexity.
Simple architecture.

Promising Accuracy

One of the disadvantages of the Neural Network is the learning time. But ELM overcomes the problems caused by gradient descent based algorithms such as Back propagation applied in ANNs [15]. ELM can significantly reduce the amount of time needed to train a Neural Network.

ELM learning Algorithm

The standard ELM algorithm has three steps as follows [8]

Given a training set X= {(xi, ti) | xi∈ Rn and ti∈ Rm, i = 1, 2,⋯ ,N}activation function g(x), and the number of hidden nodes L, Assign randomly input weight vectors ai and hidden node bias or impact factor bi, i = 1, 2, ⋯ , L.

Calculate the hidden layer output matrix H, where H=$\sum_{i=1}^{N} ai.xi$+ bi

Calculate the output weight β: β = H†T. where H† is the Moore-Penrose generalized inverse of hidden layer output matrix H.

Proposed Approach

Our Proposed approach is an attempt touse CSA along with ELM to classify certain bench mark data sets. Here 3 different data sets are chosen and divided into training and testing groups. (2/3 for training and 1/3 for testing). The algorithm for the proposed work is given below

Algorithm

Initialize D1, D2 and D3 with given values, where D1, D2 and D3, represent the datasets.

For a=1 to n, where n =the number of instances present in the datasets

Do Normalize the D1, D2 and D3 by column normalization.

Partition each of the Ds to two parts; one part containing, 2/3rd and the next part containing 1/3rd of the data instances. The first part is used for training whereas the second part is used for testing purpose

On each of the Ds CSA algorithm is applied to find a target.

The output, i.e. the optimized targets are used as targets in ELM

Using the input and target the weight matrix is calculated

The found weight matrix was operated on the test dataset to produce the outputs.

The accuracy of the classifier is measured; a k cross validation scheme is used to validate the outputs.

RESULTS AND OBSERVATIONS

The proposed work compares the classification accuracy and time complexity of normal BPNN and CSA-ELM approach. The table1 shows the overall accuracy comparison.

Analysis of Time Complexity

The time complexity in conventional BPNN approach is the sum of training and testing time. The training time becomes an overhead in case of BPNN approach. As the proposed approach uses ELM , direct calculation of the weight matrix drastically reduces the training time .The following bar chart depicts the training time comparison for BPNN and CSA-ELM approach.

CONCLUSION AND FUTURE WORK

The target plays an important role in classification problems. Conventional BPNN tries to map the inputs into assumed targets which at times become a computational overhead. From the result analysis part it is very much clear that choosing optimal target through CSA gives promising outcomes both in terms of both classification accuracy and training time.

The future scope of the work is to address the following areas

- To use other optimization techniques for target optimization
- To use other forms of neural network and support vector machine for classification
- To use additional bench mark datasets .

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Table 1- Performance comparison of Back propagation neural network, PSO-BPNN and the proposed approach

Dataset	Number of classes	Number of Samples	Number of features	Number of Training samples	Number of testing samples	Number of misclassifications		Classification Accuracy	
						BPNN	CSA-ELM	BPNN	CSA-ELM
Iris	3	150	4	120	30	11	1	78%	97%
Seed	3	210	7	150	60	17	6	72%	90%
Diabetes	2	768	7	500	268	64	38	76%	86%

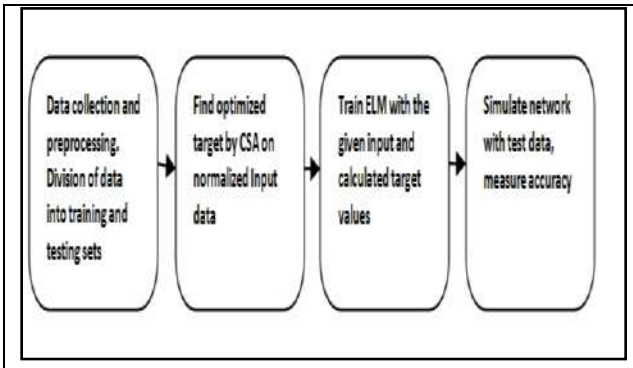

Figure 1Proposed Model of CSA-ELM

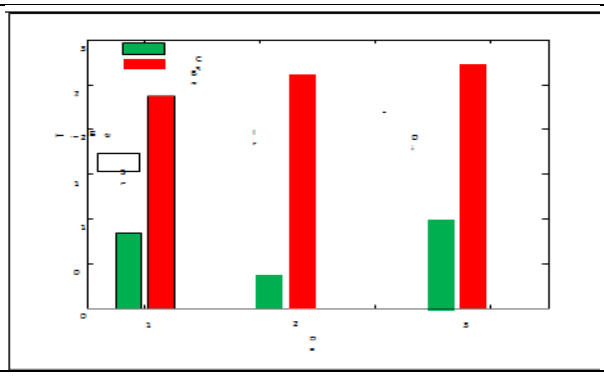

Figure 2 Training time Comparison of PSO-ELM and PSO-BPNN

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RESEARCH ARTICLE

Estimation of Crop Water Requirement in Maize and Chickpea for Different Patterns of Intercropping

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ABSTRACT

Intercropping is a type of crop intensification where more than two or more crops are cultivated simultaneously for efficient resource utilization and more productivity from unit area. Maize (*Zea mays* L.) is considered as an important staple and versatile crop that offers ample scope for adoption of intercropping. Legumes are suitable crops that fit well as components in intercropping to achieve multifaceted benefits of the cropping system. Among different legumes, chickpea (*Cicer arietinum* L.) is a winter pulse widely grown under various agroclimatic regions and it is considered as a suitable crop species grown as intercrop in winter maize. The present study aimed to estimate crop water requirement of maize, chickpea and different intercropping combinations of these two components. The study used a descriptive method to establish water requirement of maize and chickpea with different row proportions of intercropping using Modified Penman-Montieth equation. The results showed that crop water required to grow sole maize for whole season is about 3434.9 m^3/ha and for sole chickpea it is about 2060 m^3/ha. Water requirement of different crops varies when it grows with different plant population and intercropping proportions. The seasonal crop water requirement of maize intercropped with different percentage of chickpea population is found as 3452.95 m^3/ha, 3467.35 m^3/ha, 3479.14 m^3/ha and 3488.96 m^3/ha for 25%, 50%, 75% and 100% chickpea populations, respectively. The crop water required to grow chickpea as intercrop along with the maize will be 0.53% to 1.57% more in comparison to the crop water requirement to grow maize in pure stand.

Keywords: Maize, chickpea, reference evapo transpiration, crop coefficient, irrigation schedule

INTRODUCTION

Currently, Indian agriculture is in search of solution for several challenging tasks such as feeding exponentially growing population, combatting climate change, maximising the productivity from declining farmland and other natural resources. Increasing the productivity with maximizing input resources (water, fertilizers, and land) use efficiency may be achieved by adoption of the intercropping system. Intercropping is one of the agricultural methods adopted to increase the input use efficiency with a reduced the dependency on external inputs to attain agricultural sustainability (Maitra *et al*., 2020; 2021). In this system, two or more crops having different height, duration and morphological characters are grown simultaneously in the same land (Maitra *et al*., 2001). Intercropping system offers a several benefits including maximizing water use efficiency and improved nitrogen fixation in soil through legumes that may be used by cereals in association (Gitari *et al*. 2020). The UN in September 2015, adopted 17 Sustainable Development Goals (SDGs) which were ambitious agenda targeting to end poverty and secure world, for people, planet and prosperity and these goals are to be achieved by 2030. Intercropping has enough potential for poverty alleviation, reduction of hunger, provisioning of healthy foods and biodiversity enhancement covering directly or indirectly some SDGs, such as "SDG 2 (end hunger, achieve food security and improved nutrition and promote sustainable agriculture), SDG 13 (take urgent action to combat climate change and its impacts) and SDG 15 (protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss)" (UN, 2022).

Maize (*Zea mays* L.) is one of the important cereal crops belonging to *Poaceae* family. It is considered as major grain crop and feeding billions of people in the world with the third position after rice and wheat (Maitra *et al*., 2019a; Manasa *et al*., 2020). India holds fourth position for the cultivation area under maize and seventh position for production. Maize is comparatively widely spaced crops and offer abundant opportunity to grow along with legume crops as an intercrop with advantages of increasing inputs use efficiency (Maitra *et al*., 2019b). Chickpea is a very common pulse grown in India and it is anenormous source of nutrition for human being. In addition to health benefits, chickpea cultivation may improve the soil health especially in arid and semi-arid areas (Banik *et. al*., 2006). Chickpea is most suitable legume crop may grow along with the maize during winter.

Precise scheduling of irrigation water including determination of crop water requirement may be the primary step in crop production (Santosh and Maitra, 2021; 2022). Information on the crop water requirement of maize and chickpea as sole crop is available, but water requirement information of intercropping chickpea and maize is not available. Therefore, current study has been conducted to estimate the crop water requirement of both maize and chickpea grown as intercrop using FAO-56 Modified Penman equation.

MATERIALS AND METHODS

The study was conducted at the Experimental Farm of Centurion University of Technology and Management (CUTM), Odisha. Chickpea (variety '*Rachana*') was intercropped with maize (hybrid *NMH 450-Ganga*) with various combination of plant population and row arrangement. Primarily, Maize sowed with 60 cm x 25 cm (plant to plant and row to row) spacing. In between the maize rows chickpea was planted in single or double row to maintain the required percentage of plant population. The different combination chickpea plant population intercropped with maize given in the Table 1. Irrigation was provided ten days once through furrow irrigation method. The daily irrigation water requirement of both the crops were estimated by using the following relationship

$IR = ET_0 \times K_c \times A$

Where, IR=irrigation water requirement, ET_0 = Reference evapo transpiration, K_c = crop coefficient of the crop, A = area occupied by the crop.

The Modified Penaman Montieth equation (Allen *et al*., 1998) has been used to determine the ET_0 on daily basis from the January to April. The combined crop coefficient (K_c) for the chickpea intercropping with maize was determined using following equation.

$$K_c = \frac{f_1 h_1 K_{c1} + f_2 h_2 K_{c2}}{f_1 h_1 + f_2 h_2}$$

Where,

f_1 and f_2 = land fractions occupied by crop 1 and crop 2
h_1 and h_2 = height of crop 1 and crop 2
K_{c1} and K_{c2} = crop coefficient values for crop 1 and crop 2

Area occupied by each plant is multiplied with the ET_0 and combined K_c values gave irrigation water requirement (IR) of crops.

RESULTS AND DISCUSSION

The irrigation water requirement of maize, chickpea as sole crop and different combination chickpea plant population with maize as intercrop were determined using Modified Penman-Montieth equation. The Modified Penman-Montieth equation used ten years climatological data recorded at CUTM campus. Reference evapo transpiration was determined and the average of ten days ET_0 values from January to April months were presented in Table 2. As the irrigation schedule was maintained once in ten days interval, average of ten days daily data were presented in Table 2. Combined crop coefficient (K_c) for intercropping of chickpea with the maize was calculated using equation and presented in Table 3. Table 3 shows the K_c values of maize, chickpea, maize and different population of chickpea combination as intercropping for different crop stages.

The irrigation requirement of maizeas sole crop was estimated and presented in Table 4. The Table 4 presents the results such as depth of water required for maize in each irrigation (ten days interval), irrigation water requirement (IR) of maize plant and irrigation water requirement of maize in one hectare. The daily water requirement of maize was ranging in between 1.25 l/day/plant and 9.01 l/day/plant. The peak irrigation water requirement (IR) of crop was found during 9th irrigation (after 90 days of sowing) as480.70 m^3/ha. Gross irrigation water requirement of maize as sole crop for whole season was estimated as 3434.9 m^3/ha (343.9 mm).Similar results were found from other studies as maize may require 395.8 mm (Bhat *et al*., 2017), 423 mm (Abirdew *et al*., 2018) and 456.9 mm (Baseey *et al*., 2019) depth of water for whole season. The IR for the chickpea was estimated on daily basis and presented as ten days average in Table 5. The Table 5 presents information such as ET_c of chickpea for every irrigation (ten days), ten day average of daily IR of a chickpea plant and gross IR required for chickpea in one ha area. The ET_c of the chickpea for each irrigation (ten days interval)was ranging between11.07 mm and 35.83 mm, IR of each chick pea plant was ranging between 0.33 L/plant/day and 1.07 L/plant/day and gross IR of chickpea in one hectare was ranging between 110.68 m^3/ha and 358.28 m^3/ha. Total gross IR of chickpea was found to be 2060.66 m^3/ha (206 mm).Similar results were found from other studies as chickpea may require 436.7 mm (Desta *et al*., 2015) and323 (Kirnak *et al*., 2017)depth of water for whole season.

The IR for maize and chickpea alone for one hectare and IR for different combination chickpea population as intercrop with maize in one hectare area were presented in the Table 6. The IR found for the combination C_1 (maize (100%) and chickpea (25%)) in one hectare and presented as ten days average values in Table 6. The IR for C_1 combination in one irrigation schedule (10 Days) was ranging between 68.87 m^3/ha (initially during showing) and 480.70 m^3/ha (during the ninth irrigation schedule). Total gross IR for the C_1 combination was estimated as 3452.95 m^3/ha. The total IR required to grow maize with C_1 combination requires 0.5% more IR in comparison to the IR required to grow maize alone. The IR found for the combination C_2 (maize (100%) and chickpea (50%)) in one hectare and presented as ten days average values in Table 6. Total gross IR for the C_2 combination was estimated as 3467.35 m^3/ha. The total IR required to grow maize with C_2 combination requires 0.94% more IR in comparison to the IR

required to grow maize alone. The IR found for the combination C_3 (maize (100%) and chickpea (75%)) in one hectare and presented as ten days average values in Table 6. Total gross IR for the C_3 combination was estimated as 3479.14 m^3/ha. The total IR required to grow maize with C_3 combination requires 1.29% more IR in comparison to the IR required to grow maize alone. The total gross estimated IR for the C_4 combination (maize (100%) and chickpea (100%)) found to be 3488.96 m^3/ha. The total IR required to grow maize with C_4 combination requires 1.57% more IR in comparison to the IR required to grow maize alone. The IR of maize and chickpea as sole crop in different piece of land may found as 5495 m^3/ha. The results of study shows that by adding merely small quantity of more IR(0.5%, 0.94%, 1.29% and 1.57% for C_1, C_2, C_3 and C_4 combination of maize with chickpea intercropping respectively) to maize IR may be sufficient for both maize and chickpea as intercrop grown in single piece of land. As in evapotranspiration maximum amount of water lost through evaporation least amount water lost through transpiration. Therefore IR provided to maize is just enough to satisfy the evaporation from soil supplementary IR may provide to satisfy the transpiration requirements of chickpea as intercropping.

CONCLUSION

The study concluded that the irrigation water requirement of maize and chickpea as sole crops and in intercropping in an additive series of experiment with varying chickpea population where standard population of maize was maintained. Study revealed that a slight quantity of supplement water is sufficient to grow chickpea under maize as intercrop. Crop water requirement will be huge and different, if maize and chickpea were grown at different lands in their pure stands, but as intercrop in the same piece of land a negligible change in water requirement can fulfill the requirement of water for both the crops. Input resources such water may be used with higher use efficiency by adopting the intercropping method for production of yield output and in additive series it can be easily adopted. Current study is only based on estimation, but this study has to get approval through conducting research on response of yield for different combination of chickpea population intercropping with maize.

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Table 1. Different combination of different percentage of chickpea intercropping with maize

SI.No	Crop combination	Percentage of crop stand	Plant population / ha
1.	Maize sole	100 % maize	Maize: 66,666
2.	Chickpea sole	100 % chickpea	Chickpea: 3,33,333
3.	C_1	Maize (100%) + Chickpea (25%)	Maize: 66,666 Chickpea: 83,333
4.	C_2	Maize (100%) + Chickpea (50%)	Maize: 66,666 Chickpea: 1,66,666
5.	C_3	Maize (100%) + Chickpea (75%)	Maize: 66,666 Chickpea: 3,33,333
6.	C_4	Maize (100%) + Chickpea (100%)	Maize: 66,666 Chickpea: 2,49,999

Table 2. Ten days average of daily reference evapotranspiration (ET_0) from 1st Jan to 30th April for ten years (2011-2021)

Year	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Mean
Irrigation Schedule												
1st	2.03	2.13	2.37	2.28	2.19	2.27	2.30	2.07	2.30	2.18	2.23	2.21
2nd	2.18	2.56	2.38	2.47	2.17	2.52	2.49	2.72	2.23	2.08	2.32	2.37
3rd	2.31	2.48	2.39	2.48	2.27	2.37	2.56	2.39	2.47	2.32	2.42	2.41

4th	2.80	2.65	2.68	3.03	2.63	2.31	2.79	2.38	2.80	2.65	2.75	2.68
5th	2.84	3.34	3.62	3.54	2.57	2.74	3.27	3.13	3.38	2.90	2.94	3.12
6th	2.92	3.31	3.28	3.58	2.77	2.74	3.29	3.18	3.16	3.90	3.03	3.20
7th	3.43	4.21	4.15	3.87	3.25	3.43	3.54	4.10	3.97	3.84	4.00	3.80
8th	4.32	4.58	3.77	3.95	3.48	4.27	3.88	4.38	3.90	4.50	4.37	4.13
9th	4.05	4.70	4.10	4.31	3.59	4.00	3.87	4.57	4.19	4.17	4.43	4.18
10th	4.27	4.88	4.59	4.83	4.83	4.40	4.15	5.32	4.28	4.60	5.05	4.65
11th	5.91	6.04	4.75	4.74	4.49	4.62	3.84	5.76	5.16	4.51	5.14	5.00
12th	5.26	5.51	4.96	4.91	4.29	4.68	4.49	5.68	4.85	4.76	5.20	4.96

Table 3. K_c values of Maize and Chickpea under different intercropping practices

Kc values for different crop Stages	Maize	Chickpea	C_1Maize (100%) + Chickpea (25%)	C_2Maize (100%) + Chickpea (50%)	C_3Maize (100%) + Chickpea (75%)	C_4Maize (100%) + Chickpea (100%)
$K_{c\ ini}$	0.30	0.40	0.31	0.32	0.33	0.33
$K_{c\ mid}$	1.15	1.00	1.08	1.02	0.97	0.93
$K_{c\ dev}$	0.60	0.30	0.60	0.60	0.60	0.60

Table 4. Crop water requirement of Maize

Irrigation schedule	ET_c per irrigation (mm)	Crop water requirement per plant per day (L/plant/day)	Crop water requirement per ha per irrigation (m^3/ha)
1st	6.64	1.25	66.41
2nd	11.87	2.23	118.73
3rd	14.43	2.71	144.33
4th	18.75	3.52	187.53
5th	24.92	4.67	249.23
6th	28.77	5.39	287.67
7th	37.99	7.12	379.91
8th	45.40	8.51	454.00
9th	48.07	9.01	480.70
10th	41.89	7.85	418.90
11th	34.97	6.56	349.74
12th	29.78	5.58	297.76
Total	343.49		3434.90

Table 5. Crop water requirement of Chickpea

Irrigation schedule	ET_c per irrigation (mm)	Crop water requirement per plant per day (L/plant/day)	Crop water requirement per ha per irrigation (m^3/ha)
1st	11.07	0.33	110.68
2nd	19.00	0.57	189.96
3rd	21.65	0.65	216.49
4th	26.79	0.80	267.91
5th	35.83	1.07	358.28
6th	31.96	0.96	319.64
7th	26.59	0.80	265.94
8th	20.64	0.62	206.36
9th	12.54	0.38	125.40
Total	206.07		2060.66

Table 6. Crop water requirement of maize and chickpea under different combination of intercropping

Irrigation Schedule	Maize (m^3/ha)	Chickpea (m^3/ha)	C_1 Maize (100%) + Chickpea (25%)	C_2 Maize (100%) + Chickpea (50%)	C_3 Maize (100%) + Chickpea (75%)	C_4 Maize (100%) + Chickpea (100%)
1	66.41	110.68	68.87	70.84	72.45	73.79
2	118.73	189.96	118.73	118.73	118.73	118.73
3	144.33	216.49	147.00	149.14	150.89	152.35
4	187.53	267.91	193.49	198.25	202.15	205.40
5	249.23	358.28	256.16	261.70	266.23	270.01
6	287.67	319.64	287.67	287.67	287.67	287.67
7	379.91	265.94	379.91	379.91	379.91	379.91
8	454.00	206.36	454.00	454.00	454.00	454.00
9	480.70	125.40	480.70	480.70	480.70	480.70
10	418.90	-	418.91	418.91	418.91	418.91
11	349.74	-	349.75	349.75	349.75	349.75
12	297.76	-	297.76	297.76	297.76	297.76
Total	**3434.90**	**1813.69**	**3452.95**	**3467.35**	**3479.14**	**3488.96**

RESEARCH ARTICLE

Test Evaluation of TIG Welding Process Parameters Based on Energy Consumption and Maximum Strength

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ABSTRACT

The choice of the parameters of the welding process is an important step to achieve stability in the production of parts. Welding is an energy-intensive process that is consumed worldwide. Stimulating the growth and progress of society provides an increasing demand for marketing. Tungsten inert gas (TIG) welding is a widely practiced and energy-intensive process in the industry with a number of options. Various parameters affect the quality of the joint, in which gap and welding current are the main factors affecting the strength of the joint. The manufacturing sector is the dominant energy consumer. The step towards resilience is highly dependent on the energy profile of the welding process. The current study focuses on the selection of optimal process parameters (clearance and welding current) to reduce the energy consumed in the bonding process without sacrificing quality aspects such as joint strength. The proposed method was performed using a case study involving TIG welding of the butt joint on Al-Mn-Si alloy wheels.

Keywords: Energy efficiency, TIG, optimization, Tensile strength.

INTRODUCTION

Welding is a permanent welding process used to attach various materials such as metals, alloys or plastics together to their contact surfaces by applying heat and / or pressure. During welding, the part to be welded will melt to the surface and a permanent bond can be achieved after repair. Sometimes fillers are added to form weld pools of the alloy, which after processing provide a strong bond between the elements. The feasibility of welding depends on various factors such as metal changes that occur during welding, changes in hardness in the welding area due to

rapid hardening, oxidation levels due to the reaction of the material with atmospheric oxygen and the tendency to crack at the joints location. Welding is the most important welding technology, which requires high energy consumption and production costs. Sustainable production has become the ultimate destination for industries worldwide due to the growing awareness around the world [1]. Sustainability emphasizes the theory of triple completion with three main components: economic and social environment [1, 2]. Environmental and social aspects are often not assessed with the weights necessary for production operations. Therefore, the welding process requires a lot of capital and has a significant impact on the environment. Few researchers report focusing on environmental considerations in market operations [3, 4]. Due to its energy intensity, the recent welding process has attracted a lot of attention to achieve durability. Therefore, selecting the most appropriate welding parameters is important to achieve durability. Lack of proper planning can lead to increased processing costs.

Tungsten Inert Gas Welding (TIG) falls into the category of a welding process that produces a combination of metals by heating them with tungsten electrodes, which are unusable in an inert atmosphere using inert gases such as argon. This process is typically used for welding aluminum and its alloys [5, 6]. In this study, the optimized parameters for TIG welding based on Taguchi and artificial neural network (ANN) were selected. Taguchi was used to design the experiment. ANN is used to select the best welding parameters up to the minimum power and the highest UTS value. The study was performed on Al-Mn-Si alloy wheels at 410 watts, ESAB AB, SE-69581, U4000iw, TIG welding machine. The alloy wheels are similar to the AA3103 alloy wheels used in the aerospace and automotive industries [7].

TIG Welding

TIG welding is an arc welding process that uses unusable tungsten electrodes to create welding. The welding area is protected from the atmosphere with inert gas (argon or helium) and fillers are usually used. The power supply is supplied from the power supply (rectifier) via a hand or welding torch and is supplied to a tungsten electrode mounted in the element manually. An electric arc is then formed between the tungsten electrode and the work piece using a DC power supply that produces energy and is conducted through an arc through a column of highly ionized gas and steam [1]. The tungsten electrodes and the welding area are protected from the surrounding air by inert gas. Electric arcs can generate temperatures up to 20,000oC and this heat can be focused on melting and joining two different parts of the material. Welding baths can be used to connect base metals with or without filler material. Schematic diagram of TIG welding and mechanism of TIG welding is shown in Fig. 1

Basic TIG Welding Mechanism

Tungsten electrodes are commonly available from 0.5 mm to 6.4 mm diameter and 150 - 200 mm length. The current carrying capacity of each size of electrode depends on whether it is connected to negative or positive terminal of DC power source. The power source required to maintain the TIG arc has a drooping or constant current characteristic which provides an essentially constant current output when the arc length is varied over several millimeters. Hence, the natural variations in the arc length which occur in manual welding have little effect on welding current. The capacity to limit the current to the set value is equally crucial when the lectrode is short circuited to the work piece, otherwise excessively high current will flow, damaging the electrode.

Properties and Advantages of Aluminium

Aluminum is a very light metal. The use of aluminum in the automotive and aerospace industries reduces weight and energy consumption. The strength of aluminum can be improved according to the properties required for different applications by modifying the composition of its alloy wheels. Aluminum is a highly corrosion resistant material. Different types of surface treatment can further improve its corrosion resistance. Aluminum is a good source of heat and electricity, and in terms of weight it is almost twice as good as copper. This has made aluminum the most commonly used material in large power lines. Aluminum has good adhesion and low melting point. In the melting state, it can be processed in several ways. Its flexibility allows the aluminum product to be shaped primarily near the end of the product design [3]. Aluminum can be connected in many ways such as bolts, rivets (temporary

connections) and welding (permanent method). Aluminum and its alloys are bonded in industry by various methods. The thermal conductivity of aluminum is very high; So the heat easily melts away from the market place. It is important that the heat source has sufficient power to reach the melting point of 565 / 650ºC aluminum rapidly. The coefficient of thermal expansion of aluminum is also high compared to steel, so it is prone to deformation and stress if proper welding procedure is not carried out. Aluminum is a reactive metal that rapidly forms an oxide layer on the surface and the strength of the weld zone decreases. Therefore, welding aluminum using a conventional arc welding process becomes difficult.

By understanding the nature of welding and using the right procedures, aluminum and its alloys can be easily welded. The most common commercial methods for welding aluminum and aluminum alloys use a continuous supply arc or wire electrode [DC with and without pulse current] or a fixed tungsten electrode plus an AC charging cable. To ensure acceptable welding quality, there are two important factors to keep in mind - loosening and removing the oxide film and preventing the formation of new oxides during the welding process. It is important to prepare and be careful before starting welding. The area to be connected and the area around the welding area [~ 50 mm]. The surface must be clean and completely dry as grease and moisture can form gases and cause pores in the weld.

TAGUCHI Method

Dr. Taguchi of Nippon Telephones and Telegraph Company, Japan has developed a method based on "ORTHOGONAL ARRAY" experiments which gives much reduced "variance" for the experiment with "optimum settings" of control parameters. Thus the marriage of Design of Experiments with optimization of control parameters to obtain BEST results is achieved in the Taguchi Method. "Orthogonal Arrays" (OA) provide a set of well balanced (minimum) experiments and Dr. Taguchi's Signal-to-Noise ratios(S/N), which are log functions of desired output, serve as objective functions for optimization, help in data analysis and prediction of optimum results.

Artificial Neural Network(ANN)

ANN is also known as **A**rtificial Neural Network and it is a tool of MATLAB. An artificial neuron network (ANN) is a computational model based on the structure and functions of biological neural networks. Information that flows through the network affects the structure of the ANN because a neural network changes-or learns, in a sense-based on that input and output.

Electric Energy Consumption

Electric energy consumption is the form of energy consumption that uses electric energy. Electric energy consumption is the actual energy demand made on existing electricity supply. Electric energy is most of ten measured either in joules(J),or in watt hours(W·h) representing a constant power over a period of time.

1 W·s=1J

1 W·h=3600W·s=3600J

Electric and electronic devices consume electric energy to generate desired output (i.e., light, heat, motion, etc.). During operation,somepartoftheenergy—dependingontheelectricalefficiency—isconsumed in unintended output, such as waste heat. Electricity has been generated in power stations since 1882.[2]The invention of the steam turbine in 1883 to drive the electric generator started a strong increase of world electricity consumption. In 2008,theworldtotal of electricity production was 20.279 petawatt -hours(PWh). This Number Corresponds To Average Power of 2.31 TW continuously during the year. The total energy needed to produce this power is roughly a factor 2 to 3 higher because a power plant's efficiency of generating electricity is roughly 30–50%. The generated power is thus in the order of 5 TW. This is approximately a third of the total energyconsumptionof15TW.

LITERATURE SURVEY

Recently, there has been increasing interest in energy consumption and environmental issues facing the manufacturing industry. The welding sector also has a preference for sustainability, as evidenced by the increase in jobs reported in this direction. The following subsections describe the methods of energy efficiency in welding and the approved methods for optimizing the welding parameters.

Energy Efficiency in Welding

Despite the weakness, there have been few reports of energy efficiency in the market. The environmental characteristics of the welding process were analyzed by [8] by introducing a model for health hazard assessment. The authors also emphasize the growing importance of analyzing the impact of welding on the environment. The components of resistance for different welding operations are discussed by [9]. Emphasis is placed on energy savings, waste materials, resources and parameters, environmental benefits and saving opportunities in various welding processes. Several welding methods were included in the study. In another study,[10] The authors developed a mathematical model for energy efficiency in hot laser welding. The developed method is applied to the high-strength double-strength DP800 steel in the automotive industry. It is hypothesized that the developed techniques can be used to achieve a maximum energy saving of 16% in cold wire laser welding [11] setting process parameters for maximum energy efficiency. It is concluded that high laser power and high pulsating frequency lead to improved energy efficiency. Energy consumption and related environmental impacts for GMAW have been studied by [12]. Friction resistance (FSW) was studied by [13] welded joints were evaluated for health, environmental and economic purposes. The authors also try to link the tensile properties of welded joints, heat input with FSW resistance.

Welding Parameter Optimization

Sustainability in the context of manufacturing organizations aims at, increasing the proportion of SMEs around the world, promising profitability, and resilience; positive social and environmental impacts [13]. Adapting to environment-friendly operations is the in evitable solution. Implementation of this is dependent on various factors and SMEs are often late tore spond to the change[14]. As a result, there remains in adequate penetration of Green Technologies (GT) in India [15]. Sustainable manufacturing has gained higher attention recently for its benefits directed at the Triple Bottom Line (TBL) factors (social, environmental, financial). Characteristics of SMEs have been studied by [16]. Some authors have also proposed strategies for implementing the GT in the Indian manufacturing sector [17], [18], [19]. Still, no reliable guideline exists, to guarantee the successful implementation of sustainable manufacturing[20].

RESEARCH AND METHODOLOGY

Material Selection

In this current experiment, the aluminium alloy (3mm thickness) is considered as the base material. These are widely used in automobile sector and also used for manufacturing a variety of products including cans, foils, kitchen utensils, window frames, beerkegs and airplane parts. This is because of its particular properties. The spark test is carried out to investgate and analyzes the chemical composition of both the base metal and weld metal.

XRF & Hardness Specimen

The chemical composition and Hardness of the base metal Aluminium alloy was obtained by conducting, ROCKWELL Hardness test and XRF test for raw materials size (25mmx25mmx3mm)made with the help of Hand cutter. The Filler metal(ER4043)was used for the welding purpose.

UTM Test Specimen

Strength of the base material (aluminium alloy) was experimentally found out prior to welding operation performed. The specimen was tested for finding the strength of the base metal after comparing with the welding operation of the material. For this tensile strength make the test specimen for UTM.

Hardness RESULTS

UTM Test Result

Tensile test was caring on a computer controlled universal testing machine which has the maximum capacity of 1000KN. Before welding operation the specimen was failed at the point of 146Mpa. Ultimate tensile strength (Mpa) was measured. After welding the strength result will be compare post welding test.

TIG Welding

The bead on plates of size 150mmx100mmx3mm were prepared from the Al alloy. Aluminum alloy (Al-Mn-Si) plates were cut tosize of 200mm x 100mm x 3 mm. The plates dipped in Nitric acid (HNO_3) which was used as etchant followed by washing with hot water. The filler rod was utilized in as-it-is condition. The chemical composition for both base material and filler material are in table-2.ER4043 was used as the filler material in the experiment by considering its resistance to cracking and comparing with the base material composition. The filler material having diameter 1.6 mm was utilized in the experiment along with argon as shielding gas for conducting the TIG welding. The TIG welding process adopted has taken into consideration a number of process parameters like, joint gap, welding current, welding speed and shielding gas flow rate. Two factors have been considered, (i) weld joint UTS, as the joint quality indicator and (ii) energy consumed during the process, as the process cost indicator related to the sustainability aspect; both of these are ultimately dependent on the selection of process parameter. The current study involved the following parameters:

All other parameters were constant during the experiment. The welding joints were tested for finding Ultimate Tensile Strength on aUniversalTestingMachineofmakeBlueStarBSUT-100-JD having maximum capacity of 1000KN, and energy consumed by the help of the power analyzer of make Uma Electronics,modelDPATT-3Bi. Joint preparation: In this experiment a two factor (joint gap and welding current), 3-level process parameter was used for the design. The design of experiment was conducted using Minitab statistical analysis software v.16.1 was used. L9 (3**2) was used and corresponding process parameters for the individual experiments are listed in the table. The degrees of freedom for the process parameters and theirinteractionsare5.Buttjoints were prepared using the parameters defined in the experiment design. The tensile testing specimens were prepared by cutting the sample transverse to the direction of weldment. The tensile test was conducted in a Blue star computer controlled UTM of 1000KN capacity. The UTS values from the results obtained are represented in the table below

The welding process was carried out on the aluminum alloy plates

The tensile test and energy consumption values obtained along with the process parameters for individual experiment were fed into a neural network modeled in Matlab v-15. The network uses the experimental values in the above table to train itself. The input parameters like joint gap and welding current are mapped with corresponding UTS and energy consumed values. After training, for a given UTS and energy consumption values, a set of joint gap and welding current can be obtained as the optimum value.

CONCLUSION AND FUTURE SCOPE

This paper presents the methodology for TIG welding process parameter selection based on Ultimate Tensile Strength and energy consumed in the process. Taguchi has been used for designing the experiments and Artificial Neural Network has been deployed to find optimized welding parameters i.e. joint gap and welding current based on desired UTS and energy consumed values. Al-Si-Mn-Fe alloy was used with ER4043 filler rod for conducting the

experiments to perform butt joints. Conformation tests have been conducted and compared with the results obtained from ANN. The experimental values were found to be closer to the predicted values. Energy efficiency being the need of the hour, the current work may be extended to cover other welding methods like MIG, LBW & EBW. The work satisfied the sustainability development goal Industry innovation and infrastructure.

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Table No.1 Composition of Raw Material

Aluminium Alloy Sample													
Ref No. CUTM/04XRF/ATC/19-28/0240													
Application	<Omnian>			**Normalisation Factor**		1.155							
Sequence	1 of 1												
Position	Large sample												
Measurement Time	05-02-2019 17:28												
Compound	Al	Si	P	S	Cl	K	Ca	Ti	V	Cr	Mn	Fe	Ni
conc. Unit	96.72%	1.04%	0.02%	0.04%	0.40%	0.08%	0.04%	0.03%	0.01%	0.02%	0.41%	0.79%	0.01%
Compound	Cu	Zn	Ga	As	Zr	Sn	Te	Eu	Yb	Os	Ir	Tl	Pb
conc. Unit	0.17%	0.17%	0.01%	0.00%	0.00%	0.01%	0.01%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Compound	Th												
conc. Unit	0.00%												

Table No-2 Composition of Filler Material

SAMPLE RESULT													
Alumium Filler Metal ER4043													
Ref No.													
Application	<Omnian>			**Normalisation Factor**		7.308							
Sequence	1 of 1												
Position	Large sample												
Measurement Time	20-02-2019 17:12												
Compound	Al	Si	P	S	Cl	K	Ca	Ti	V	Cr	Mn	Fe	Co
conc. Unit	86.76%	7.94%	0.74%	0.38%	0.94%	0.25%	0.68%	0.15%	0.03%	0.08%	0.06%	1.11%	0.17%
Compound	Ni	Cu	Zn	Ga	As	Sr	Zr	Eu	Er	Yb	Lu	Os	Ir
conc. Unit	0.01%	0.22%	0.14%	0.00%	0.00%	0.03%	0.00%	0.07%	0.23%	0.00%	0.00%	0.00%	0.00%
Compound	Tl	Pb	Bi	Th									
conc. Unit	0.00%	0.00%	0.01%	0.00%									

Table No-3 Hardness(Rockwell) Test Result On Al Alloy Before Welding

Hardness Test Result			
Types of Indenter:		**BallIndenter1/8**	
Total Load:		**60 KN**	
Material:AluminiumSample1			
SL.NO.	HRA	HRB	HRF
1	22.2	20.4	68.7
2	20.5	15.9	66
3	24.6	26.2	72.1

4	24.9	26.8	72.4
5	22.4	20.7	68.9
Material:AluminiumSample2			
SL.NO.	HRA	HRB	HRF
1	24.5	25.9	71.9
2	24.2	24.8	70.9
3	24.9	26.7	72.4
4	24.4	25.6	71.6
5	25	26.9	72.5
Material:AluminiumSample3			
SL.NO.	HRA	HRB	HRF
1	25.2	27.4	72.7
2	24.1	24.4	70.7
3	24.4	25.6	71.8
4	22.8	21.6	69.3
5	24.4	25.7	71.7

Table No-4 Chemical Composition Compare Is On Between Base And Filler Materials

	Si	Mn	Fe	Cr	Ti	Cu	Zn	Al
Basematerial (Al-Mn-Si)	0.46	0.91	0.69	0.02	0.03	0.07	0.17	Balance
Filler material(ER4043)	7.94	0.06	1.11	0.08	0.15	0.22	0.14	Balance

Table No-5 Experimental Parameters Used

Sl.No.	Parameter	Valuerange
1	**Joint gap**	**0,0.5,1 mm**
2	Welding current	80,90,100ampere
3	Welding voltage	18-22voltapprox.
4	Welding speed	50-60mm/min
5	Shielding gas flow rate	7-8l/min

Table No-6 Input And Output Variables

Expt. No.	Joint gap (in mm)	Welding current (in A)	UTS (in MPa)	Energy consumed
1	0	80	163	1520
2	0	90	180	1800
3	0	100	169	2100
4	0.5	80	171	1520
5	0.5	90	198	1800
6	0.5	100	178	2100
7	1	80	183	1520
8	1	90	205	1800
9	1	100	192	2100

Table No-7 Factors and levels for TAGUCHI orthogonal array design

Symbol	Parameter	Level1	Level2	Level3
A	Joint gap	0	0.5	1
B	current	80	90	100

Table No-8 S-N Ratio And Means For The Strength With The Input Parameters

SlNo	joint gap	current	UTS	SNRA1	MEAN1
1	0.0	80	163	44.2438	163
2	0.0	90	180	45.1055	180
3	0.0	100	169	44.5577	169
4	0.5	80	171	44.6599	171
5	0.5	90	198	45.9333	198
6	0.5	100	178	45.0084	178
7	1.0	80	183	45.2490	183
8	1.0	90	205	46.2351	205
9	1.0	100	192	45.6660	192

Table No-9 S-N Ratio And Means For The Power With The Input Parameters

Sl.No	Joint gap	Current	Power	SNRA2	MEAN2
1	0.0	80	1520	-63.6369	1520
2	0.0	90	1800	-65.1055	1800
3	0.0	100	2100	-66.4444	2100
4	0.5	80	1520	-63.6369	1520
5	0.5	90	1800	-65.1055	1800
6	0.5	100	2100	-66.4444	2100
7	1.0	80	1520	-63.6369	1520
8	1.0	90	1800	-65.1055	1800
9	1.0	100	2100	-66.4444	2100

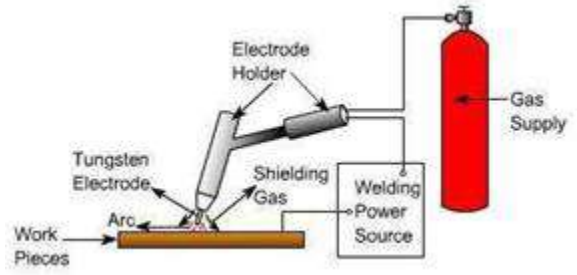


Figure1:Schematic Diagram of TIG Welding System.

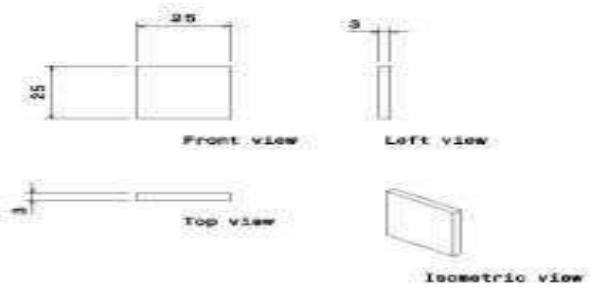


Figure No.2 Dimension Of Sample Specimen

Figure no.3 XRF and Rock Well Test Sample

Figure no. 4 TIG filler material

Figure no.5 Tensile Test Specimen (base material)

Figureno.7 Tensile Testing on UTM

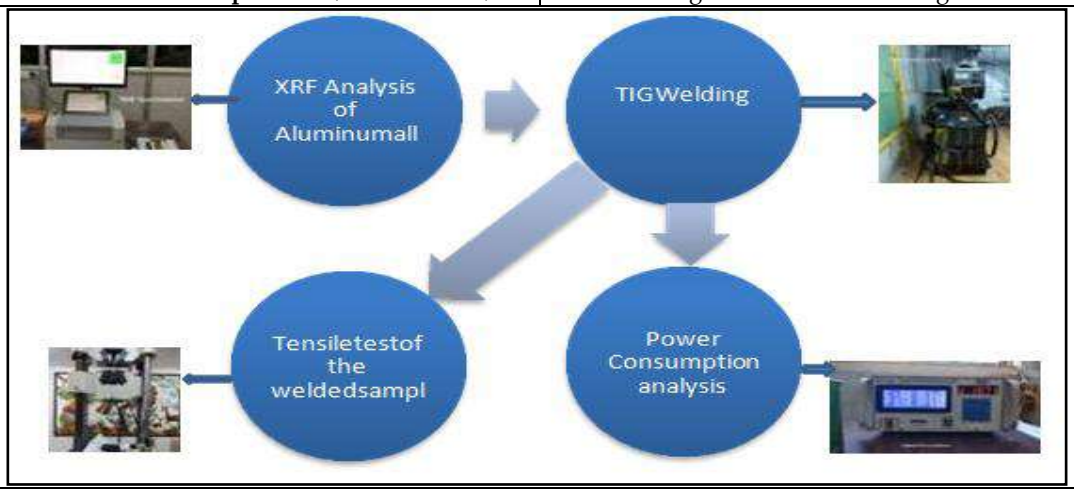


Figure No.8 The Experimental Design Architecture

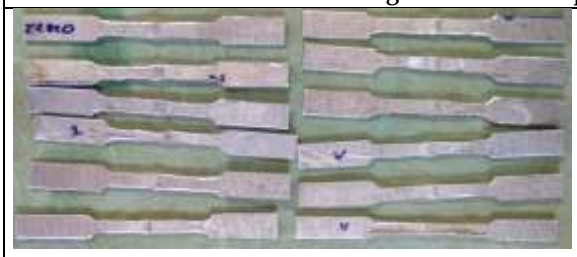


Figure No.9 Welded Specimen For Strength Test

Figure No.10 Fractured Sample After Strength Test

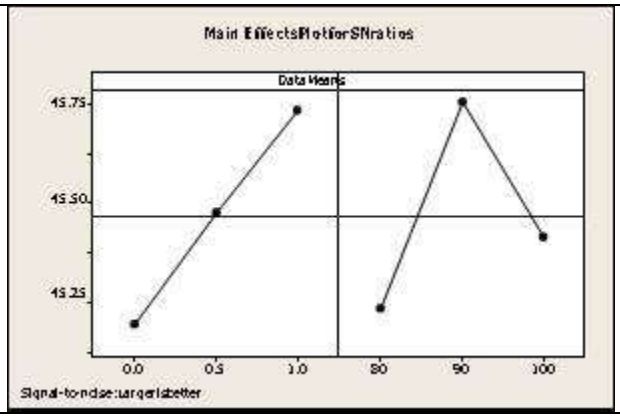
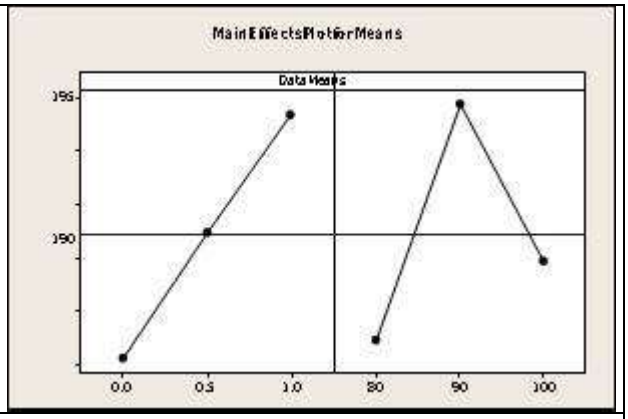


Figure no.11 S-N ratio comparison with UTS value



Figureno.12 Means comparison with UTS value

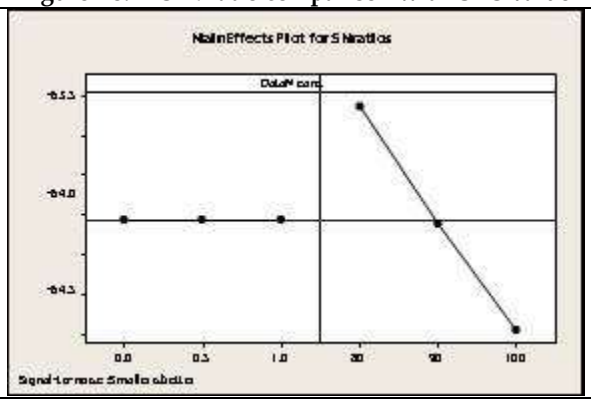


Figure no.14 S-N ratio comparison with power data

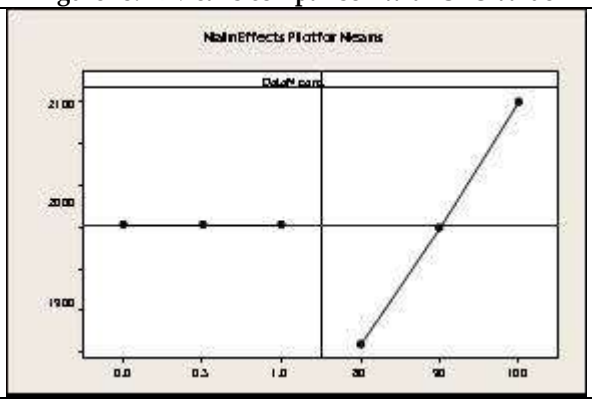


Figure no.15 S-N ratio comparison with power data

RESEARCH ARTICLE

A Study on the Effect of Organochlorine Pesticide on Morphology of Haematological Parameters of *Cyprinus carpio*

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ABSTRACT

Gammaxene is a organo chlorine pesticides used in India. It is used as insecticides and also lice and scabies are also treated with it. They are chlorinated hydrocarbon derivatives which have a wide range of application in chemical and agricultural industry. It is carcinogenic and neurotoxin in nature. The sever toxicity and bioaccumulation of gammaxene is well known. The objective of present study is to analyse the haematological parameters of Amur carp exposed to stress condition by incorporating pesticide. In the present studies morphology of haematological parameters like number of red blood corpuscles, white blood corpuscles, platelets, were analyzed after the fishes were exposed to different concentrations of gammaxene like 2ppm,4ppm,6ppm, 8ppm.The haematological investigation include total of 6 fishes. 2 fishes were kept in controlin the aquarium and 4 fishes were subjected to experiment in centurion university of technology and management BBSR. When the fishes were exposed to different concentration of organochlorine pesticide were kept in that water for study period of 30 days. 2 fishes were kept in the aquarium and feed daily and were observed. 4 fishes were kept at different places and were treated with organochlorine pesticides and were feed daily and observed. As blood was the excellent indicator of stress. So, Blood was collected from the fishes by doing cardiac puncture. The change in morphology of haematological parameters was observed. The morphology of haematological parameters was compared with the control fishes and the results were obtained. These data may help us for understanding haematological parameters of fish if it is treated with gammaxene to estimate the healthstatus.

Keywords: Amurcarp, Gammaxene, Organochlorine pesticides, Haematological parameters, health status.

INTRODUCTION

Pollutants of many types have been found in the natural environment that contaminant it. Pollution of the environment is one of the most important is suescofronting humanity and other life forms of earth. Some of these contaminants are linked with acute and chronic illness. Insecticide are the pollutants that can harm aquatic ecosystem. Insecticide is useful in agricultural industry and forestry but their role in the destruction of aquatic ecology cannot be ignored. Pesticides are agrochemical used in agriculture to manage pests. The rising in Indian population needs to be self-sufficiency in food production through new tools, techniques and chemicals.PesticidesareusednotonlyindevelopingcountrybutdevelopedcountieslikeIndia. Pesticides are chemicals that used to manage pest on agricultural product but when they come in contact with water resources through agricultural land, they have an impact on river and organisms and ecosystem. Gammaxene are chlorinated hydrocarbon derivatives which have a wide range of applications in chemical and agricultural industries. The IUPAC name of the insecticides gammaxene is Benzene hexachloride which is an insecticide. The chemical formula is $C_6H_6Cl_6$. The light induced addition of chlorine to benzene produces stereoisomers of 1,2 ,3,4,5,6, hexachloro cyclohexane. the insecticides lindane also known as gammaxene is also one of these isomers. The insecticidal capabilities of benzene hexachloride were discovered in 1944 after using gamma isomers which is synthesis in1825.Amur carp belongs to class Osteichthyes, order cypriniformes family cyprinidae. The. The Cyprinuscarpio sometimes known as common carp or koi is an exotic carp that is tame for domesticated purposes. Wild form of amur carp is also koi. Fish are poikilothermic animal that live in water as a result quality of their surrounding predict their existence and performance. Insecticides are causing changes in haematological parameters of fishes. For a long time, haematological measure has been frequently utilized to describe the general health of fish. The purpose of this work was to see how gammaxene affect the morphology of RBC in amur carp a fresh water fish and also. The conservation of life under water is absolutely intertwined with SDG 14 which justifies about the impacts of ocean acidification, as its focus includes the protection and restoration of ecosystems, sustainable fishing, protection of coastal and marine areas and protecting the economic benefits derived from marine resources

MATERIALS REQUIRED

Collection of fishes

A total of 6 Live Amur carp were collected from Aquarium house jatani. The experimental fishes were taken to the zoology laboratory where the experiment was conducted.

Acclimatization

For one-month experimental fishes were acclimatized to aquaria filled with normal tap water in a laboratory setting. Before acclimatization the aquarium water is added with methylene blue. This blue solution prevents any fungal infection to the fishes. During acclimatization the same temperature (28$\pm$1C) was maintained. To avoid contamination the water in the aquarium was carefully aerated. It was fitted with filter that helps inaeration. The fishes in the experiment were feed twice a day at 9.30 am and 4.00pm.

Experimental procedure

After 1 month now the fishes were stress free and they have increased in weight and length. 4 plastic tubs were taken set to carryout the experiment. Detergentwasusedtocleanthe4-plastic tubs. The tubs were sun dried and by using measuring cylinder it was filled with 3 liters of tap water. A identification mark was made on the outer side of the tubs marking the level of water that is 3 liters as well as the concentration of the gammaxene that should be added to it. It was provided with air bubble to complete the demand of oxygen of the fishes. The air bubble was joined with plastic pipes and the plastic pipes were connected with T connector and plus connector one main pipe was connected with the air pump and it was plugged in. It meets the demand of oxygen. A control group and a treatment group were formed from the fishes that were collected. The control group fishes were kept in the aquarium and feed normally in the constant temperature. 4 different fishes were placed individually in the plastic tub provided with oxygen and was kept in the tub for 24 hours for better acclimatization of the fish. Gammaxene was obtained from the

botanical garden of centurion university of technology and management. By using weigh machine gammaxene was weight, for a concentration of 2 ppm 0.0057 grams of gammaxene was weighed and securely kept in a place. For 3 ppm 0.0087 grams of gammaxene was weighed. For 4 ppm 0.0117 grams of gammaxene was weighed. For 5ppm 0.0147 grams of gammaxene was weighed. These were keptinse cured placed so that the powder of gammaxene were not to be disturbed. After that 0.0057 grams of gammaxene were taken and it was mixed with normal tap water by using spatula and beaker .Now the solution of gammaxene and water was added to the plastic tub having identification mark 2ppm.Similarly 0.0087 gram, 0.0117 grams , 0.0147 grams were mixed with tap water and added to the plastic tub having identification mark 3ppm 4ppm 5ppm accordingly for a period of 25 days. Both the control and the treatment fishes were fed with commercial diets while the experiment was being conducted. The control group was appropriately maintained in this case.

Blood collection

During each sampling, blood sample were acquired via direct cardiac puncture of the fishes. For this sample collection 31Gx15/64" (0.25x6mm) dispovan insulin syringe were used. A5 unit of blood was drawn measuring in the syringe. As blood samples were collected from cardiac puncture blood was transferred to append of tube containing EDTA an anticoagulant toavoidbloodcoagulationduringeachcollection.Forthepreparationofhaematologicalslides blood samples were smeared on cleaned slides

Preparation of blood smear

A microscopic slide was thoroughly cleaned. Then one drop of blood was placed on the slide at a distance of 2cm from end. An extra glass slide was touch to the blood drop at 45-degree angle and then slide until drop is fully spread. The slide was then air dried. Then slide was treated with methanol until the methanol was left to get dried. After that the slides are stained with giemsa in coupling jar in such a manner that the slides were not touched.

Microscopic examination of haematological slides

The haematological slides were examined under a microscope and blood cells were correctly identified. The red blood cells as well as their morphological modifications were observed.

RESULTS

The nucleus of the mature erythrocytes in the blood of amur crap in the control group is oval and centrally placed. The morphological modifications of red blood cells in amur carp were seen at 2, 3, 4, 5 ppm gammaxene concentration in the treated group. At 2ppm cells are little swollen up. Same happens with 3ppm cells they are little bit swollen up than normal erythrocytes. When the experimental fish is exposed to 4ppm erythrocytes are more swollen up. When the fish is exposed to 5ppm erythrocytes show enlargement and cell wall distortion. If it is observed for more time then the RBC cell membrane are disrupted and their cytoplasm expands and cytoplasmic content eventually leaks out.

DISCUSSION

Red blood cells formed from haemocyto blast precursor cells and mature after they reached the blood streams. Erythrocytes are most abundant cells in fish blood because they contain haemoglobin which aids in the transport of oxygen from gills to various parts of the body. The mature erythrocytes of amur carp are elliptical in shapes and nucleus is positioned centrally. By the treatment of agrochemical pesticides, the erythrocytes show different shapes. Blood physiological job is to carry oxygen and nutrients to cell while removing metabolites from the cells. The degree of toxic stress generated by gammaxene might be linked to four primary reasons:-aberrant erythropoiesis, in adequate haemoglobin production, damage of red cell after they leave bone marrow or enhanced erythropoies is by bone marrow to compensate for anemic condition. It is clear that gammaxene can cause physiological dysfunction as are sult of cellular damage which can impair a fish normal physiological state.

CONCLUSION

The toxic effect of Gammaxene causes change in the morphological features of red bloodcells of amur carp as well as the movement of amur carp. Gammaxene cause direct impact on the movements of fishes as after pouring of gammaxene solution the movement of fishes are slowed down as compare to normal fishes are it is a pesticide and it made the environment stress condition so to cope up with stress condition fish movement are slowed downed

ACKNOWLEDGEMENT

First and fore most, I want to thank my supervisor Dr.Yashaswi Nayak. It is my great pleasure to express my sincere thanks for her guidance and advice for successful completion. I express my sincere thanks to Mr. Soumen Mohanty for the unfailing suggestions and continuous encouragement throughout this course.

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RESEARCH ARTICLE

Analysis of Thermo Acoustic Parameters of Various Milk at Different Temperatures

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ABSTRACT

The physical properties of milk components affect the functional properties and quality attributes of foods in which they are used. Hence, knowledge of the basic physical properties of milk components is critical in determining the usefulness of milk components in food formulations and in determining quality attributes and acceptability of foods containing these components. Although much is known about the chemistry of milk components, fundamental data are limited regarding the physical properties that govern functionality and quality. This lack of information may limit potential uses of milk ingredients in the food processing industry. The densities viscosity and ultrasonic velocities of different milk have been measured at 303K, 308K, 313K and 318K respectively, by using an ultrasonic interferometer at frequency 3MHz.From the experimental data acoustic and thermo dynamical parameters have been calculated. In this present work the parameter acoustic Impedance, and adiabatic compressibility have been computed using the standard relations. The results have been analyzed on the basis of variation in thermodynamic parameters. These parameters are found to be very sensitive in exploring the interaction between the component molecules, which enable to have better understanding of the milk.

Keywords: Densities, Viscosity, ultrasonic velocities, acoustic Impedance, and adiabatic compressibility.

INTRODUCTION

Milk is a translucent white liquid produced by the mammary glands of mammals. It provides the primary source of nutrition for young mammals before they are able to digest other types of food. The early lactation milk is known as colostrum, and carries the mother's antibodies to the baby. It can reduce the risk of many diseases in the baby. The

exact components of raw milk vary by species, but it contains significant amounts of fat, protein and calcium. The major constituents of milk are: water, fat, protein, lactose, ash or mineral matter. The minor constituents are: phospholipids, sterols, vitamins, enzymes, pigments, etc. Thermoacoustics is the combination of thermodynamics and acoustics. It involves the study of transfer of heat by using sound waves. Sound waves, of high intensity are used for the purpose of analysis which fulfills sustainability of dairy farm. The present work deals with the study of acoustical and thermo dynamical parameters of different milk (Cow milk-pure, Pragati, Milkmoo and Omfed) at different temperature. In order to investigate and compare different characteristics property of different milk samples were collected from Bhubaneswar market Odisha.

Experimental Details

Measurement Of Density

The densities of different milk were estimated using a 25 ml Pycnometer bottle. The Pycnometer bottle with the oil was submerged in a temperature-controlled water bath. The density was estimated using the equation

$$\varrho_2 = \frac{w_2}{w_1}\varrho_1 \text{---------- (1)}$$

Where, w_1 = weight of distilled water, w_2 = Weight of milk, ϱ_1 = Density of water, ϱ_2 = Density of milk.

Measurement of viscosity

The viscosities of different milk were estimated using Ostwald's viscometer standardized with distilled water. The Ostwald's viscometer with the milk was submerged in a temperature-governed water shower. The time of flow was estimated by using an advanced stopwatch with an accuracy of 0.01 s. The viscosity was calculated using the equation,

$$\eta_2 = \eta_1 \left(\frac{t_2}{t_1}\right)\left(\frac{\varrho_2}{\varrho_1}\right) \text{---------- (2)}$$

Where, η_1 = Viscosity of distilled water, η_2 = Viscosity of milk, ϱ_1 = Density of distilled water, ϱ_2 = Density of milk. t_1 = Time of flow of water, t_2 = Time of flow milk.

Measurement of velocity

The expression used to determine the ultrasonic velocity is

$U = 2d/T$ (m/s)

Or. $U = 2d \times v$

Or, $U = \lambda \times v$ ---------- (3)

(Here-$2d=\lambda$)

Where, v is the frequency of the generator which is used to excite the crystal; (In the present investigation, the frequency 3MHz interferometer was taken) d- Separation between the reflector and crystal; T. Travel time of the ultrasonic wave.

Theoretical Aspect

The "density, viscosity and ultrasonic velocity" were measured and the following thermo-acoustic parameters were determined using the standard formula using these experimental results.

"Acoustic impedance" $Z = U.\rho$ ---------- (4)

"Adiabatic Compressibility" $\beta = \frac{1}{\rho U^2}$ ---------- (5)

RESULTS AND DISCUSSIONS

The experimental and calculated values of acoustic and thermo dynamical parameters of the milk are listed at different temperatures in table–1 to 4.The variations of the above parameters with respect to temperature are shown in the figurers. Density decrease with increase in temperature indicates decrease in inter molecular forces due to increase in thermal energy of the system. This causes an increase in volume and hence decrease in density. It is observed that, Ultrasonic velocity increases with increase in temperature at a particular all temperature. This is due to the structural changes occurring in the milk solution resulting in increase of intermolecular forces. For a given temperature, ultrasonic velocity increases with increase in temperature. Such an increase in velocity is an indication of existence of strong molecular association between the components molecules. Acoustic impedance is a measure of the resistance offered by the solution to the propagation of ultrasonic wave. In a particular concentration of the milk with increase in temperature, velocity increases and hence acoustic impedance increases. This factor is governed by inertia and elastic properties of the medium and hence supports the possibility of molecular interactions. Adiabatic compressibility decreases with increase in concentration (Fig.13) and temperature (Fig.14), because this depends on electron donor and acceptor capacity. Water and urea are polar solvents, when urea is added, the association of solute and solvent molecules occurs resulting in close packing of molecules. The decreased values of adiabatic compressibility indicate strong intermolecular association between dextran and urea molecules.

CONCLUSION

- The parameters like density, and ultrasonic velocity of dextran solution were measured.
- The thermo acoustical parameters using the measured parameter calculated.
- The role of the different parameters on solute-solvent interaction had been discussed
- The effect of temperature on thermo acoustical parameters had been studied

From the above studies, the nature of forces between molecules such as hydrogen bonds, charge transfer complexes, breaking of hydrogen bonds and complexes had been interpreted. Intermolecular forces (electrostatic forces between charged particles of a permanent dipole and an induced dipole molecules) are weak.Structural characteristics of the components arising from geometrical fitting of one molecules in to another due to the difference in shape and size of the molecules and free volume.

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Table-1Values of density (ϱ) and viscosity (η) at different temperatures

Kelvien (T)	Density			
	Pure milk	PRAGATI	Milk moo	Omfed
303 K	1020.375	1022.513	1023.893	1023.783
308 K	1018.724	1019.503	1020.116	1021.417
313 K	1017.514	1017.142	1016.945	1018.543
318 K	1015.904	1014.344	1016.428	1015.044

Table-2 Ultrasonic velocity (U) at different temperatures

Temp(K)	Velocity			
	Pure milk	PRAGATI	milk moo	Omfed
303 K	1527.750	1511.700	1529.700	1500.000
308 K	1541.850	1522.800	1535.000	1520.000
313 K	1566.000	1537.350	1540.000	1541.550
318 K	1620.150	1608.300	1545.000	1548.150

Table-3 Acoustic impedance (Z)at different temperatures.

Temp(K)	Acoustic impedance (Z):- $Z = U.\varrho (\times 10^6\ kg{\cdot}m^{2}{\cdot}s^{-1})$			
	Pure milk	Pragati milk	Milk Moo milk	Omfed milk
303 K	1.559	1.546	1.566	1.536
308K	1.571	1.552	1.566	1.553
313 K	1.593	1.564	1.566	1.570
318 K	1.646	1.631	1.570	1.571

Table-4Adiabatic compressibility (β)at temperature a

Temp(K)	Adiabatic Compressibility $(\beta)(10^{-10}N^{-1}.m^2)$			
	Pure milk	Pragati milk	Milk Moo milk	Omfed milk
303 K	4.199	4.280	4.174	4.341
308K	4.129	4.230	4.160	4.238
313 K	4.008	4.160	4.146	4.131
318 K	3.750	3.811	4.122	4.110

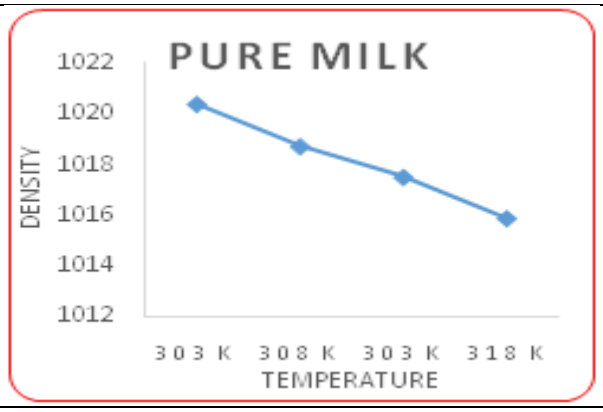

Fig.1 Variation of density of pure milk with temperature

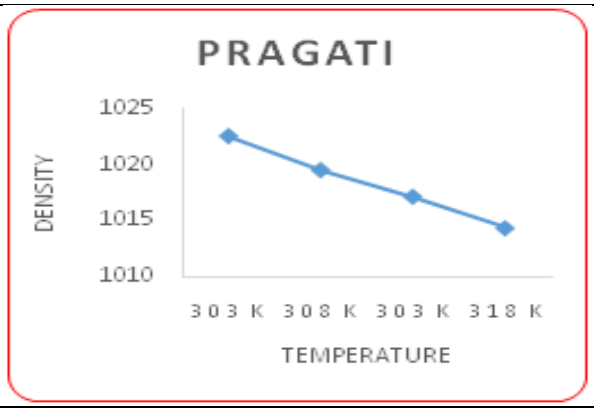

Fig.2 Variation of density of pragati milk with temperature

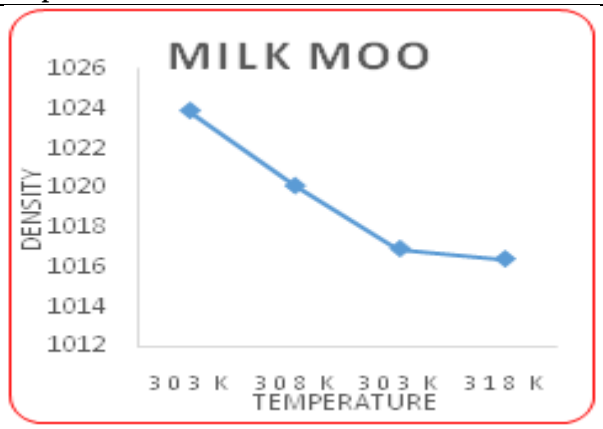

Fig.3Variation of density of milk moo milk with temperature

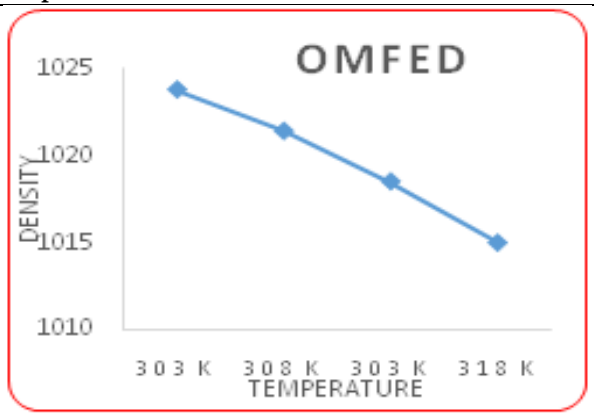

Fig.4Variation of density of omfed milk temperature

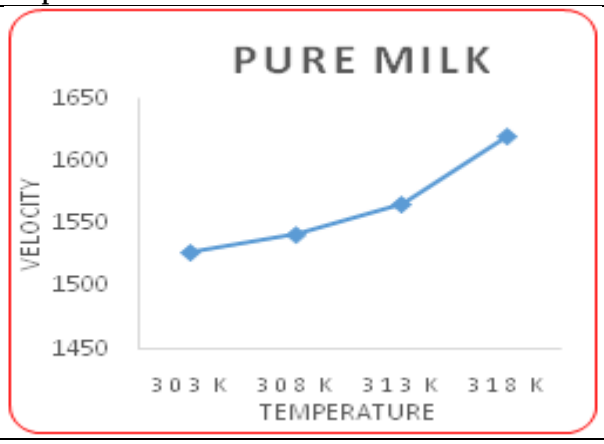

Fig:5 variation of velocity of pure milk with temperature

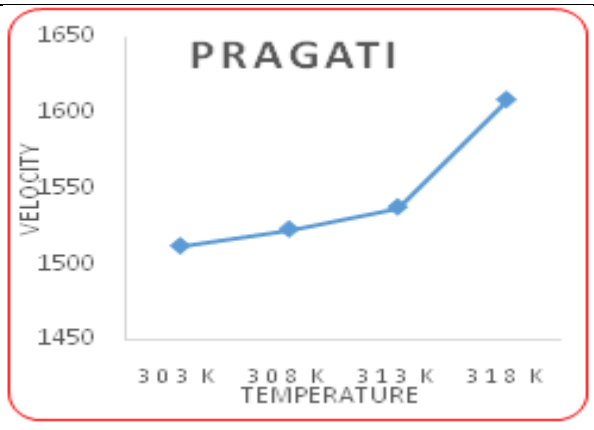

Fig: 6Variation of velocity of pragati milk with temperature

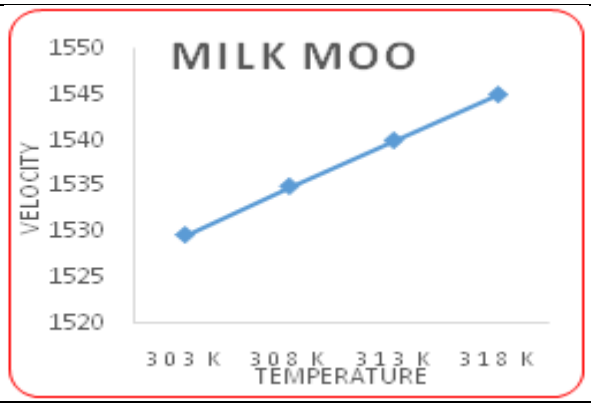

Fig: 7Variation of velocity of milk moo milk with temperature

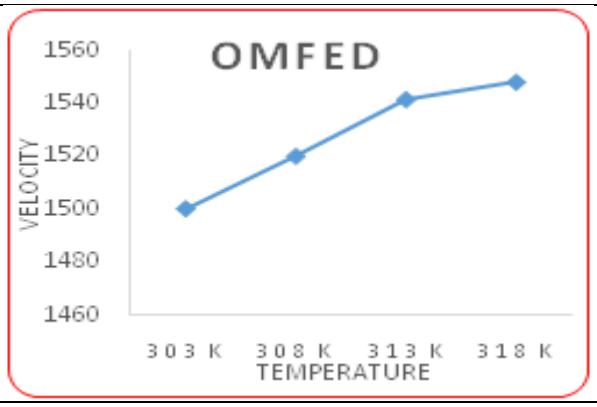

Fig: 8Variation of velocity of omfed milk with temperature

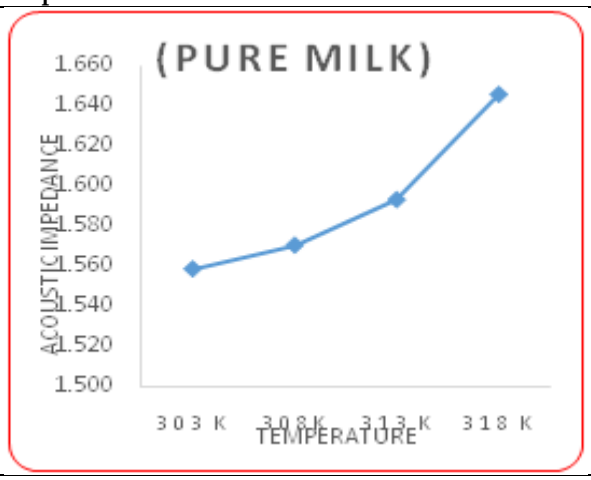

Fig: 9Variation of acoustic impedance of pure milk with temperature

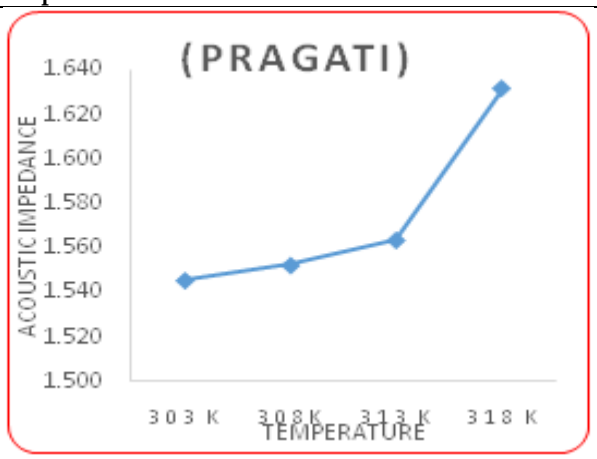

Fig: 10Variation of acoustic impedance of pragati milk with temperature

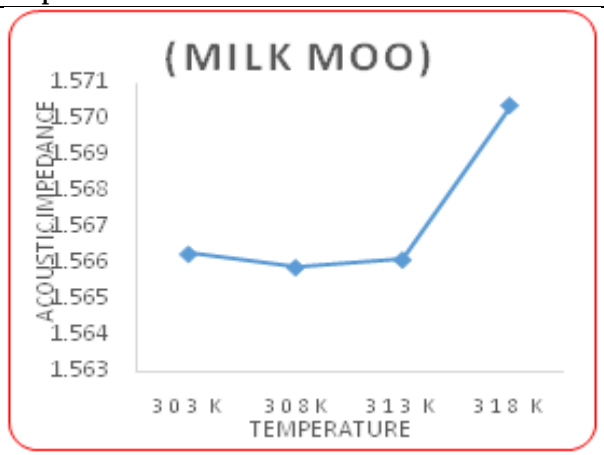

Fig: 11Variation of acoustic impedance of milk moo milk with temperature

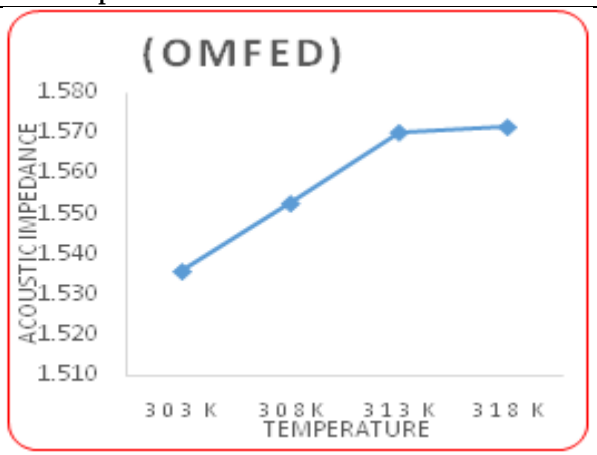

Fig:12Variation of acoustic impedance of omfed milk with temperature

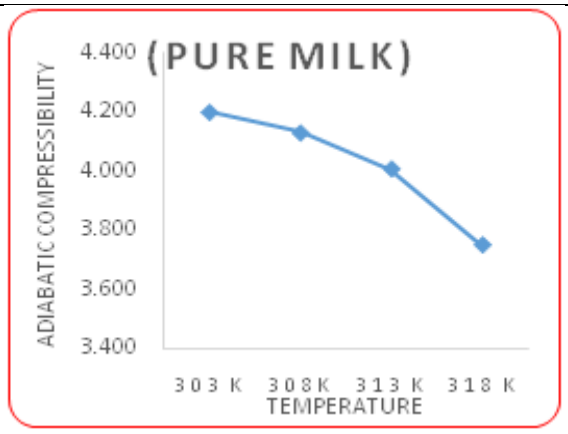

Fig: 13Variation of adiabatic compressibility with concentration

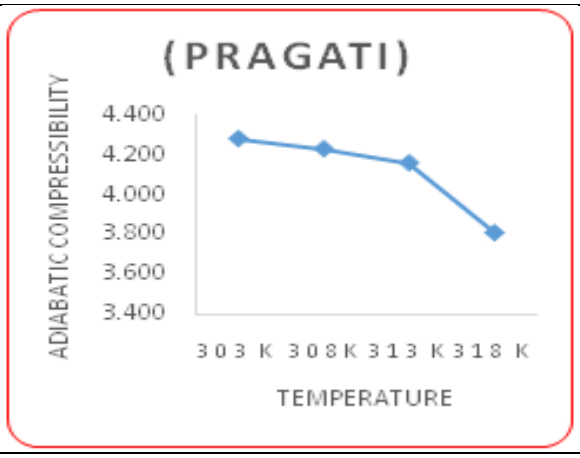

Fig: 14Variation of adiabatic compressibility with temperature

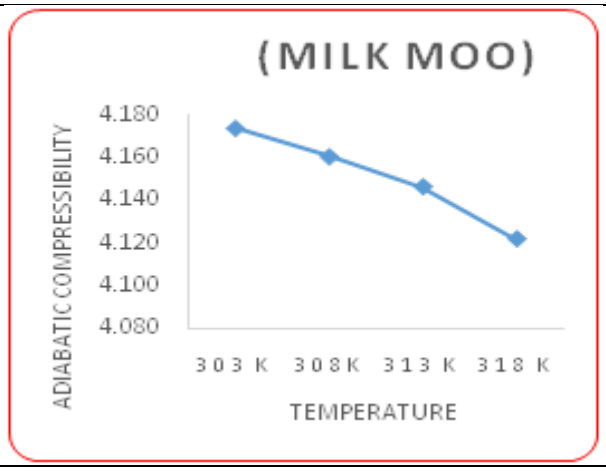

Fig: 15Variation of adiabatic compressibility with temperature

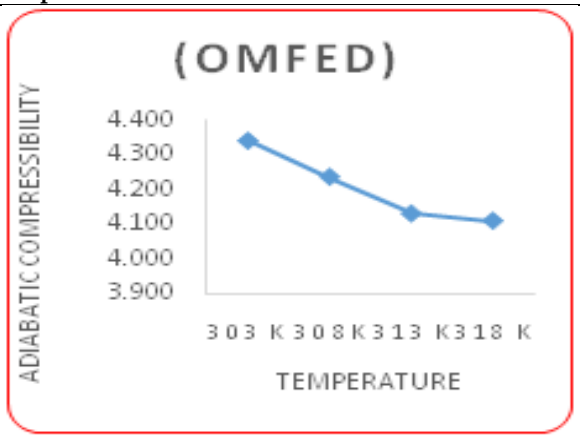

Fig: 16Variation of adiabatic compressibility with temperature

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REVIEW ARTICLE

Suitable Options for Agricultural Waste Management in India

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ABSTRACT

India is predominantly an agriculture-based country where there is a huge load of agricultural wastes and by-products. The wastes and byproducts generated from agriculture are basically organic in nature containing almost all essential plant nutrients. There is enough scope for recycling of the wastes and incorporation of the agricultural byproducts into the crop filed for maintaining the biological cycle. The agricultural wastes can also be used as feed for animals and some other purposes as organic manures and raw materials for ethanol and bioenergy production. The article keeps in account into the quantity of the agricultural wastes produced in India and their value addition and scientific use that could be applicable for other agrarian countries.

Keywords: Agricultural waste, problems, scientific management, value addition

INTRODUCTION

The world population is increasing and expected to reach in 9.8 billion by 2050 (UN, 2022). The population growth resulted in an enhanced food demand (Brahmachari *et al*., 2018; Laik *et al*., 2021). These created a tremendous pressure on agriculture (Sial*et al*., 2021). In the present consequence of climate change and global warming (Bhadra *et al*., 2021), shrinkage and degradation of natural resources (Zaman *et al*., 2017) and inefficient inputs management (Maitra *et al*., 1997) made increased crop productivity more difficult. In this regard, technological developments contributed a lot by standardizing various suitable technologies for nutrient management (Pramanick *et al*., 2020; Midya *et al*., 2021; Mohanta *et al*., 2021), water management (Santosh *et al*., 2021; Singh *et al*., 2021) and other aspects of agronomic management (Maitra *et al*., 2020; Praharaj and Maitra, 2020; Hossain et al., 2021; Kar *et al*., 2021). Also, some underutilized, unutilized and neglected food crops also got importance for achieving the food demand (Palai *et al*., 2019). Agriculture is the most important source of food, feed, fuel and industrial raw materials (Maitra *et al*., 2001; Kumar *et al*., 2019; Das *et al*., 2021; Lakshmi *et al*., 2021).

Industrialization and urbanization caused a change in lifestyle that created a different food habit where value added foods and foods with animal protein gained popularity and customer's choice. This phenomenon increased the volume of agricultural byproducts and wastes. India, the agrarian country, produces a huge quantity of wastes, by-products and crop residues (approximately 1566 million tonnes) and these come from different agriculture and allied activities (Figure 1). Moreover, there are 48.50million pieces of hide and skins that can be used for some other purposes (NAAS, 2010).

A portion of the wastes is used for composting or incorporation to the crop field and livestock feed; however, a sizable quantity is poorly managed causing harm to agroecosystem. During recent time, crop residue burning has become an issue in several parts of the country. A policy paper published by NAAS (2010) mentioned that the estimated value of these by-products/wastes is approximately, Rs. 2,35,000 crores annually calculated on an average rate of Rs 1500/- per tonne. A major portion of these residues/byproducts/wastes are presently being used either as cattle feed, incorporated in the soil as such, converted into farm yard manure and applied in the fields. Only small portion is used for energy purposes either through bio- methanation or bio-gasification routes. The energy generated is used either for thermal application or for decentralized power generation or for both. Small quantities of crop residues are also being used for thatching purposes in rural areas, packaging and in paper industry. However, about 15 million tonnes of rice straw is being burnt in Punjab, Haryana and Western UP, and about 5 million tonnes of cotton stalks are being burnt in Gujarat and Maharashtra. Similarly other crop residues such as wheat straw, hardy portion of soybean straw etc. are also being burnt in small quantities. If such byproducts/wastes are managed properly and proper value addition is done, they will give better economic returns, will pose much less environmental and health hazards and will also generate more income and employment opportunities (Table 1).

Agricultural and livestock diversification, comprising of rice, maize, poultry, cattle, etc. and value addition of the above into ready to consume products to fulfil the food demand of the global population generated huge quantity of agriculture wastes from agriculture and livestock. Sometime the agricultural by products create polluting greenhouse gases, namely, carbon dioxide, ammonia, methane and nitrous oxide (USDA, 2013). Agricultural waste water is also another threat to agro-ecosystem if not reused scientifically by proper treatments. Efficient sewage and sludge management can also be considered (Sagar *et al*., 2022; Praharaj *et al*., 2022). To overcome the burden of agricultural wastes, there is urgent need for management of agricultural wastes in scientific manner inclusive of value addition of the so-called wastes wherever possible. Moreover, the article focuses on some of the SDGs such as "SDG 1 (no poverty), SDG 2 (end hunger, achieve food security and improved nutrition and promote sustainable agriculture), SDG 13 (take urgent action to combat climate change and its impacts) and SDG 15 (protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss)" (UN, 2021).

as "SDG 2 (end hunger, achieve food security and improved nutrition and promote sustainable agriculture), SDG 13 (take urgent action to combat climate change and its impacts) and SDG 15 (protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation and halt biodiversity loss)". Among different suitable options of agriculture waste management, the following promising operations have been discussed below.

Soil incorporation and composting of crop residues

The bulk residues/wastes generate from crop field and it is advisable to incorporate these materials either directly into the soil or after proper composting. In conservation agriculture, crop residue incorporation and organic manures application are important. Composting is a highly complex biodegradable process carried out by a diverse group of microorganisms capable of degrading simple and complex organic substances. During recent times, development has been made through incorporation of chemical ingredients and biological inoculants for composting. The factors affecting the composting process are carbon: nitrogen ratio, moisture, temperature, oxygen supply in the compost pile and microbes that perform the decomposition process. For efficient value addition of the bio-degradable organic wastes, various composting technologies have been developed such as vermicomposting, phosph-

sulfo-nitro composting, microbes enriched composting and P-enriched composting. The farmyard manure (FYM) and compost management should aim at reducing the negative effects and maximizing the positive effects of manure. Scientific methods of composting and its mechanized handling and application should be popularized. Standards for good quality compost need to be formulated and adopted.

Animal feed

Major part of the animal feed in India consists of crop residues with small amount of green fodder and concentrates. Poor ration results into poor health of the animals and low productivity. The country had a demand of feed and fodder for the livestock sector in India is about1800 million tones(1134 Mt of green and 630 Mt of dry fodder). Further increase of feed demand for deed was also estimated due to progress in livestock development sector. In view of the above situations, the first priority should be given for utilization of agricultural by-products for utilization as feed and onlysurplusesbeyondtherequirementofanimalfeedshouldbeutilizedforotherpurposes.

For this purpose, proper management practices should be adopted for collection, compaction, ramparts, scientific handling of feed and fodder for animals. Animal feed plants should be installed at important places in the production catchments to prepare Technically Modified Ration (TMR)for animals in the form of feed blocks which should be transported to fodder deficit areas and stored to be used at times of need. For increasing the nutritive value of straw, the crop residue bales can be treated with anhydrous ammonia. Feed block making machines have also been developed in which the crop residues are fortified with dried green grasses, berseem, salt etc. and compacted into feed blocks. In addition to feed blocks, crop residues can be converted into low density briquettes(0.5-0.6 gm/cc), with or without fortification and can easily be handles, transported to long distances and stored properly for developing concept of Fodder banks in fodder deficit areas.

Briquetting for energy

By the briquetting process, the crop residues are densified and used to enhance the bulk density, reduced moisture, desired size and shape for easy handling and burning as needed as fuel. High density briquettes are used in boilers, gasifiers, furnaces and domestic cook stoves. The calorific value of crop/agro-processing residues vary between 3100-4500 kcal/kg. If used for power generation 1-1.25 kg of such residues can give about 1 kWh of electrical energy. This technology should be popularized and briquetting plants should be established in production catchments. An analysis of briquetting for converting surplus agri-byproducts into briquettes shows the cost-effectiveness of the technology.

Energy production

Depending upon the characteristics of the biomass it could be used as energy for various applications. There are quite a few new developments in bio-chemical conversion processes of agro-residues. More R&D work is required to be done to refine the technology and put-up pilot plants to demonstrate their techno-economic potential for future use and commercialization. Some of these developments are:

- Solid state anaerobic conversion of residues into methane and compost has been demonstrated on bench scale. Based on this development, design of a system and selection of matching machinery for its operation and handling has been done to produce 450 to 2700 m^3 biogas per hour which would be sufficient to generate 1 to 6 MW power or 250 to 1500 m* of natural gas like fuel/hour which could be compressed and used as domestic fuel or running of tractors.

- Low cost and efficient sources of enzymes for saccharification of cellulose and pentosan contents of residues to produce fuel alcohol have been identified and further work on identifying new enzymes is going on.

- Technology for bacterial conversion of lingo-cellulosic materials to ethyl alcohol has also been developed and is being refined.

- Fermentation of producer gas to produce alcohol is being attempted at some places with encouraging results.

More concerted efforts are required to pursue these research and development works to develop appropriatetechnologiesandpilotplantsforproductionofbiogasandalcohol.

Bioethanol production

First clean the sand, dirt metals, etc from the sugarcane trash. Then extract the sugarcane sugar which is known as the sugarcane Bagasse. Treat the sugarcane juice and remove the impurities. After getting of the certified juice sterilize it and then do it the yeast treatment where fermented gases are exist, i.e., carbon dioxide. Then centrifugation process needs for the distillation and rectification. From the distillation and rectification second grade ethanol, vinasse, fusel fuel exists. After the dehydration of the second-grade ethanol the Anhydrous bioethanol produced.

CONCLUSION

Stopping or decreasing waste is one of the cornerstones for running a sustainable agriculture and agriculture production system, and the same warrants investing some time and efforts into figuring out how to do so efficiently and scientifically in respect to a setting. There is ample scope for proper and scientific utilization of crop wastes as well as agricultural wastes through value addition by making wastes into wealth. The article has narrated the suitability and scope for the same. An agrarian country should look into the prospects and opportunities of proper utilization of agricultural wastes and converting the same into valuable products for agricultural sustainability.

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Table 1. Some economic uses of surplus agricultural by-products and wastes from important crops

Item	Future uses
Rice and wheat by-products	Paper industry, mushroom growing, biogas production, low- and high-density briquettes for energy purposes, alcohol production through enzymatic activities of cellulosic material, vermin-compost.
Cotton, jute, pigeon pea, rape seed and mustard stalks	Briquetting for use as domestic and industrial fuel, particleboard
Spent maizecobs	Briquetting for fuel purposes
Sugarcane Bagasse	Animal feed, briquettes to be used as domestic and industrial fuel
Banana stem	Fibre form a king clothes, baskets and other products; some quantity mixed with cow dung for biogas production
Banana Pseudostems	Fiber, chemical extraction ,juice has high potassium
Peal of citrus and oranges	Cosmetic products
Cashew nutshell	Oil
Cashew nut apple	Fenny-alcohol
Saf flower petal	Medicinal use
Mango stone	Vitamins, protein
Lichipeal	Animal feed
Areca nut leaves	For making plates
Lac by product	Lac dye

Figure 1. Agricultural wastes generated from different sources

RESEARCH ARTICLE

Modelling and Prediction of Rainfall by ANN Technique in Krishnanagar, Nadia, West Bengal, India

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ABSTRACT

Uncertainty of rainfall in future can have a negative impact on many sectors of our economy, especially agriculture. Artificial neural network (ANN) was shown to be useful in prediction of weather variables. The goal of this study was to develop a rainfall prediction model based on ANN technique for Krishnanagar weather station, Nadia, West Bengal. The daily rainfall data for the period of 1971-2000 (30 years) were used to develop the ANN structures. Twelve distinctive alternative models were designed and investigated in order to determine the optimal ANN architecture. The ANN models were developed in MATLAB environment with different number of neurons in the input and hidden layers. Both multilayer perceptron (MLP) and radial basis function (RBF) networks with back propagation algorithm were proposed for the development of a suitable model for four rainy months selected for the study. The result of the study inferred that for RBF based ANN, structures with the input layer of five neurons for the past five daily rainfall values i.e., from (t-1) to (t-5) provided best model for predicting rainfall values for all the four months. Whereas, for MLP based ANN, structures with the input layer of five neurons for the past five daily rainfall values i.e., from (t-1) to (t-5) provided best model for predicting rainfall values for July and August. Overall, the study revealed that RBF trained network provided better accuracy for

predicting rainfall values for all the four months compared to MLP trained ANN structures for all the twelve models.

Keywords: Artificial Neural Network, Climate change, Daily rainfall forecasting, Multilayer perceptron, Radial basis function, Water resources management.

INTRODUCTION

All of the natural conditions, rainfall should be regarded as the fundamental so for as progress of the society is concerned (Box and Jenkins, 1976). The changing rainfall pattern, and its impact on surface water resources, is an important climatic problem facing society today. Accurate information on rainfall is essential for the planning and management of water resources (Mohanty and Mohapatra, 2007). Additionally, in the urban areas, rainfall has a strong influence on traffic, sewer systems, and other human activities. Nevertheless, rainfall is one of the most complex and difficult elements of the hydrology cycle to understand and to model due to the complexity of the atmospheric processes that generate rainfall and the tremendous range of variation over a wide range of scales both in space and time (Obeysekera et al., 1987). The monsoon season being the principal rain bearing season of the country, small variations in the timing and the quantity of monsoon rainfall had the potential to impact on agricultural output (Mohanty and Mohapatra, 2007). Also rainfall is a major factor for planning and management of irrigation projects and agricultural production such as reservoir operation, irrigation area, and irrigation water requirement. Therefore, prior knowledge of monsoon behaviour helped Indian farmers and also policy makers, to take advantage of good monsoons and also to minimize crop damage and human hardship during adverse monsoons. Thus, accurate rainfall forecasting is one of the greatest challenges in operational hydrology, despite many advances in weather forecasting in recent decades (Toath et al., 2000).

To design water consuming of irrigation, detailed information about the rainfall with respect to time is required. To provide long sequence record of rainfall data was very difficult, so sometime, to extend the rainfall record, generating the synthetic rainfall record is necessary. Therefore, accurate and timely weather forecasting is a major challenge for the scientific community (Manusthiparom et al., 2003). Rainfalls are periodic and stochastic in nature, because they are affected by climatologically parameter, i.e., periodic and stochastic climate variations is transferred to become periodic and stochastic components of rainfall (Delleur et al., 1978). Hence the rainfall should be computed considering both the periodic and the stochastic parts of the process. Hence periodic and stochastic analysis of rainfall series will provide a mathematical model that will account for the periodic and stochastic parts and will also reflect the daily variation of rainfall.

Rainfall prediction modelling involved a combination of computer models, observation and knowledge of trends and patterns (Sharma, 1997; Tokar and Johnson, 1999). Many methods and approaches for formulating forecasting models were available, among which Artificial neural networks (ANN) is one of the recent one, had been applied in meteorological and agro-ecological modelling (Jain et al., 1996; Su et al., 1997; Rajurkar et al., 2002). Neural network applications have diffused rapidly due to their functional characteristics, which provide many advantages over traditional analytical approaches. Research revealed that the application of the ANN in time series for forecasting hydrological parameters is having great accuracy (Hsu et al., 1995; Zhang et al., 2000). It is primarily based on the ability of neural networks to approximate nonlinear functions. This technique corresponds to human neurological system, which consists of a series of basic computing elements, called as neurons interconnected together to form a network. A neural network contained large amounts of parallel distributed processors made up of simple processing units (Rummelhart and McClelland, 1996; Haykin, 1999). These units have a natural propensity for storing experiential knowledge and making it available for use. Neural networks acquire knowledge from its environment through a learning process, and use its interneuron connection strengths, i.e. synaptic weights, to store the acquired knowledge (Haykin, 1999). The parallel-distributed processing architecture of ANN has proved to be a very powerful computational tool which is now being used in several fields to model the dynamic processes successfully

including the rainfall (Rummelhart and McClelland, 1996). With this background, the present study aims at developing a rainfall prediction and forecasting model using ANN techniques using 30 (1971-2000) years' daily rainfall data for Krishnanagar rain gauge station, Nadia, West Bengal, India.

MATERIALS AND METHODS

Study area and data collection

Daily rainfall data of 30 years (1971-2000) was collected for Krishnanagar weather station. The rainfall data were obtained from the records of the Indian Meteorological Department (IMD), Alipore, Kolkata. The weather station is located at Krishnanagar sub-division, Nadia District, West Bengal (latitude 23^0 24′ N and longitude 88^0 33′ E). This sub-division is situated on the southern banks of the Jalangiriver. Krishnanagar lies between the tropic of cancer and the tropic of Capricorn. The climate of the sub-division is characterized by oppressively hot summer, high humidity and high rainfall during the monsoon. Winter starts from the middle of November which continues up to the end of February. During the monsoon from June to September about 71% of annual rainfall occurs. The rainiest month is August. The mean annual rainfall is about 1400 mm. Average elevation of the area is 14 m from mean sea level. The daily rainfall data for the 30 year (1971-2000) period of June, July, August and September as the rainiest months were used in the present study. The data from 1971 to 1995 were used for training the MLP and RBF-based ANN structures while the data from 1996 to 2000 has been used for testing the performance of the models.

Development of Artificial Neural Network (ANN) Model

Neural networks essentially involved a nonlinear modelling approach that provided a fairly accurate universal approximation to any function. Its power came from the parallel processing of the information from data. No prior assumption of the model form was required in the model building process. Instead, the network model was largely determined by the characteristics of the data. Single hidden layer feed-forward network was the most widely used model form for time series modelling and forecasting. The most commonly used family of feed-forward networks was a layered network in which neurons were organized into layers with connections strictly in one direction from one layer to another (Jain et al. 1996). The back-propagation network (BPN) was one of the neural network algorithm which is formalized by Lippmann (1987) and Rummelhart& McClelland (1986) etc. It was extensively used for inversion, prediction that consisted of two passes: a forward pass and a backward pass. In the forward pass the input was applied to input layer and its effect was propagated through network, layer by layer. The net effect was computed as the weighted sum of the output of the neurons of the previous layer. The sum of squared deviation of the output from the target value at the nodes of the output layer defined the error signal that was to be propagated back to previous layers such that the parameters were adjusted to minimize the error in further computations. The process of developing an ANN model is to find a) suitable input dataset, b) pre-processing the data, c) building the network, i.e., determine the number of hidden layers and neurons, d) training of the network, and e) testing the performance of model as shown in Fig 1.

Selection of Suitable Input Dataset

The daily data for 30 years from 1971 to 2000 were arranged as a time series with length of the 900 (months with 30 days) / 930(months with 31 days) daily data. Then, a matrix was constructed with m rows and n columns in which, each row corresponded to one of data to be given to the ANN model. Each row was an augmented data in which the columns 1 to n-1 were the information that were required to be used to predict the target data in the last column. In other words, columns 1 to n-1 were the inputs of the ANN and the last column was the data to be estimated (target data). Among these collected data samples, 750/775 data samples were used for the training phase and the rest were used for the validation phase. The training data could be selected in order; however, more comprehensive approach of training was random selection of augmented data in the constructed matrix. In this case, the ANN model had more chance to capture the dynamics of the system and later on, the trained model was able to respond to the given data in any order. Twelve distinctive alternative models were designed with different number of neurons in the

input and hidden layers. Each structure was introduced in the form of *Mijk*, in which the indices *i*, *j*, and *k* stand for number of neurons in the input layer, the hidden layer, and the output layer, respectively.

Data Pre-Processing

After collection of data, three data pre-processing procedures were conducted to train the ANNs more efficiently. These procedures were: (1) solve the problem of missing data, (2) normalize the data, and (3) randomize the data.

Building the Network

This stage of ANN model development included specification of the number of hidden layers, neurons in each layer, transfer function in each layer, training function, weight/bias learning function, and performance function. In the present study, both multilayer perceptron (MLP) (Fig 2) and radial basis function (RBF) (Fig 3) networks were used for the development of a suitable model for four rainy months selected for the study. Various network architectures were investigated in order to determine the optimal MLP architecture (i.e., the highest coefficient of determination and the lowest root mean square error) for each combination of input variables. Different training algorithms were used with changes in the number of neurons in the input and hidden layers. The use of one hidden layer was generally recommended at least in preliminary studies. The use of more than one hidden layer substantially increased the number of parameters to be estimated. Such an increase in the number of the parameters might slow down the training process without substantially improving the efficiency of the network. A single hidden layer was adopted in the present study. The determination of the appropriate number of neurons in the hidden layer was important for the successful application, since it greatly enhanced the performance of the neural network.

If the hidden layer had too few neurons then the performance of the neural network might deteriorate. On the other hand, if the hidden layer had too many neurons, then there were too many parameters and there was a danger of over-fitting the training data set. The best strategy for selecting the appropriate number of neurons in the hidden layer was to experiment, i.e. adopting a trial and error procedure. The root mean square error (RMSE) was considered as criteria for selecting the number of hidden neurons in the present study. In the above mentioned procedure, after trying different structures of MLP models, the number of hidden layer neurons was chosen to achieve the best possible output. In addition different transfer functions including the tangent sigmoid, log-sigmoid, and linear functions in the hidden layer were also investigated. In the present study the standard back-propagation algorithm was used to train the ANN models.

For the better performance of the RBF network, the radius value (known as spread) of the function and the number of neurons were varied. Basically, the larger the value of spread, the smother the function approximation would be. However, if the spread value was too large, many neurons might be required to fit the rapidly-changing function. On the other hand, very small spread values would require many neurons in order to fit he smooth function and networks could not be generalized well (Beale et al., 2010). In the present study, the spread was varied from 1 to 60 whereas; the number of neurons was changed from 5 to 600 in order to come up with the most suitable ANN prediction models.

Software Used for Development of Models

The ANN model was developed in MATLAB environment. MATLAB was an interactive software tool for engineering analysis and mathematical computations entirely written in C language. Furthermore, ANN models involved many repetitive matrix operations that could be easily implemented by the MATLAB.

Algorithms Used for Development of ANN Models

It was very difficult to know initially which training algorithm would fit best to a given problem. It depended on many factors, like (1) complexity of the problem (2) the number of data points in the training set (3) the number of weights and biases in the network (4) the error goal. Therefore, comparison of different algorithms was needed and the two different algorithms used in the present study were described here.

Normalization of Data

Prior to exporting the data to the ANN, the data were normalized (Eqn. 1). This was done to restrict their range within the interval of 0–1, because the inputs of the middle layer were assigned a sigmoid activation function. The shape of this function played an important role in ANN learning. The weight changes corresponding to a value near 0 or 1 were minimal where as closer to 0.5 they responded more. Keeping these facts in view, the normalization was carried out so that the mean of the data series would be equal to 0.5. The four month data of two consecutive years was divided into two groups. Four month data of earlier year was used to train the networks and the rest four months data was used to validate the model. The input data was normalized by following equation.

$$X_{norm} = 0.2 + [0.6*(X_i - X_{min})] / (X_{max} - X_{min}) \quad (1)$$

Where, X_{norm} is the normalized variable, $X_i$is the variable, X_{min} is the minimum value of the related variable and X_{max} is the maximum value of the related variable.

Training the Network

During the training process, the weights were adjusted in order to make the actual outputs (predicated) close to the target (measured) outputs of the network. In this study, 25 years data period from 1971-1995 were used for training. In the present study, the standard back-propagation algorithm was used to train the ANN models.

Testing the Network

The next step was to test the performance of the developed model. At this stage unseen data were exposed to the model. For the present case, the data between 1996 and 2000were used for testing the ANN models.

Performance Evaluation of the Models Performance Indices

Various performance evaluation statistics employed for evaluation of the models developed in predicting the groundwater table with respect to observed values are as follows:

(1) Correlation Coefficient (r)

Mathematically, Correlation Coefficient is defined as:

$$r = \frac{\sum_{i=1}^{n}(O_i - \overline{O_i})(P_i - \overline{P_i})}{\sqrt{\sum_{i=1}^{n}(O_i - \overline{O_i})^2 \sum_{i=1}^{n}(P_i - \overline{P_i})^2}} \quad (2)$$

Where, n = total number of data sets; O_i= Observed groundwater level for i^{th} data set; P_i = Predicted groundwater level for i^{th} data set and $\overline{O_i}$ = mean of observed groundwater level for i^{th} data set. Correlation coefficient is a measure of how well the variation in the output is explained by the targets. 'r' value equal to one implies a perfect fit between the outputs and the targets.

(2) Root Mean Square (RMSE)

Mathematically, root mean square error is defined as:

$$RMSE = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(O_i - P_i)^2} \quad (3)$$

RMSE indicates the discrepancy between the observed and predicted values. A RMSE value close to zero indicates better performance of the model. The best fit between observed and predicted values, which is unlikely to occur, would have RMSE = 0.

After developing both models, a comparative assessment of the models was done to check which model gave better result.

RESULTS AND DISCUSSION

Comparison of Models for Forecasting Rainfall

In the present study, three different structures of MLP and RBF were designed with three day lag, four day lag and five day lag rainfall values to forecast the next day rainfall for each of the four rainiest months namely, June, July, August and September. Each structure was introduced in the form of $M_{ijk,}$ in which M stands for the abbreviation of corresponding month's name and the indices i, j, k stand for number of neurons in the input layer, hidden layer and the output layer, respectively. The prediction accuracy of the twelve models was evaluated using Root Mean Square Error and Coefficient of Determination.

ANN Structures for the Month of June using MLP (multi layer perceptron) Network

The input to the models was daily rainfall data. Three MLP network structures were considered with three, four and five neurons in the input layers, respectively. For the first structure the input layer consists of three neurons for the past three daily rainfall values i.e., from (t-1) to (t-3), while the output of the structure was the rainfall for the day 't', i.e., the current day. Similarly for the second structure the input layer consisted of four neurons for the past four daily rainfall values i.e., from (t-1) to (t-4) and for the third structure the input layer consisted of five neurons for the past five daily rainfall values i.e., from (t-1) to (t-5). The output for both the structures was the rainfall for the day 't', i.e., the current day. The numbers of the neurons in the hidden layer for the above structures were taken as 1, 2 and 50, respectively. The network structures and the prediction performance of the corresponding structures were presented in the Table 1. It could be inferred from the table that the structure JN_{421} yielded the best

ANN Structures for the Month of June using RBF (radial basis function) Network

The input to these models was also the daily rainfall data. Three RBF structures were developed with three, four and five neurons in the input layers, respectively. The data used for the three structures were taken as discussed in the section 3.1.1. The output for the structures was the rainfall for the current day. The numbers of the neurons in the input layer and hidden layer for the above structures were 5 and 374 respectively that yielded the best prediction performance for the month of June using RBF network. The network structures and the prediction performance of the corresponding structures were presented in the Table 2. The scatter plot of rainfall prediction against the observed record of the best structure was presented in Fig 5.

ANN Structures for the Month of July, August and September using MLP (multi layer perceptron) Network

The input to these models was also daily rainfall data. For July, August and September three MLP network structures were considered with three, four and five neurons in the input layers, respectively as for the month of June. For the three structures the input layer consisted of three, four and five neurons, respectively as discussed in the section 3.1.1. The output for the structures was the rainfall for the current day. The numbers of the neurons in the hidden layer for the three MLP structures for each of the month of July, August September was taken as 1, 2 and 50 respectively. The network structures and the prediction performance of the corresponding structures for the month of July, August and September were presented in the Table 3, 4 and 5, respectively. It could be inferred from the Tables 3, 4 and 5 that the structure JL_{511}, AU_{511} and SEP_{311} yielded the best prediction performance for the month of July, August and September, respectively using MLP network. The scatter plots of rainfall prediction against the observed record of the best structures were presented in Fig 6, Fig 7 and Fig 8 for the month of July, August and September respectively.

The ANN Structures for the Month of July, August and September using RBF (radial basis function) Network

The input to the models was also the daily rainfall data. Three RBF structures for each month were developed with three, four and five neurons in the input layers, respectively. The data used for the three structures were taken as discussed in the section 3.1.1. The output for the structures was the rainfall for the current day. The numbers of the neurons in the input and hidden layers were 5 and 375 respectively, which yielded the best prediction performance for the month of July using RBF network. Similarly the numbers of the neurons in the input and hidden layers were 5 and 361 for the month of August and 5 and 369 for the month of September which yielded the best prediction performance for the month of August and September respectively using RBF network. The network structures and the prediction performance of the corresponding structures were presented in the Table 6. The scatter plots of rainfall prediction against the observed record of the best structures for the month of July, August and September were presented in Fig 9, Fig 10 and Fig 11, respectively.

Comparative study between predicted & actual data

The predicted value of daily rainfall (mm) and the actual estimated daily mean rainfall of 30 years were compared and represented graphically (Fig 12). The blue line and red line representedthe predicted and actual value respectively.

CONCLUSIONS

The result of the study inferred that for RBF ANN network, structures with the input layer consists of five neurons for the past five daily rainfall values i.e., from (t-1) to (t-5) provided best model for predicting rainfall values for all the four months. Whereas, for MLP ANN network, structures with the input layer consisted of five neurons for the past five daily rainfall values i.e., from (t-1) to (t-5) provide best model for predicting rainfall values for July and August. The input layer consisted of four neurons for the past four daily rainfall values i.e., from (t-1) to (t-4) provided best model for predicting rainfall values for June and it was past three rainfall values that predicted best result for the month September. The study also revealed that RBF trained network provided better accuracy for predicting rainfall values for all the four months compared to MLP trained ANN structures. Not only that, the prediction accuracy for RBF trained structures was very high for all the twelve distinctive models considered in the present study and the best fit model could be used for practical applications such as rainfall forecasting (forecasting of climate change) and other water resources management program. The results of the study were from one station only, thus the result required to be explored further through similar studies in other stations.

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Table 1 Statistical error parameters of developed MLP models for different network structures for the month of June

MODEL	R-VALUE	MSE
JN_{311}	0.37924	0.00655311
JN_{321}	-0.20494	0.00655311
JN_{3501}	0.38746	0.00655311
JN_{411}	0.46119	0.00139329
JN_{421}	**0.54005**	**0.00139329**
JN_{4501}	0.08014	0.00139329
JN_{511}	0.34935	0.00165455
JN_{521}	0.39551	0.00165455
JN_{5501}	0.04891	0.00165455

Table 2 Statistical error parameters of developed MLP models for different network structures for the month of June

MODEL	R-VALUE	MSE
$JN_{5\text{-}374\text{-}1}$	0.92052	0.15232
$JN_{4\text{-}360\text{-}1}$	0.88705	0.22091
$JN_{3\text{-}259\text{-}1}$	0.84203	0.290962

Table 3 Statistical error parameters of developed MLP models for different network structures for the month of July

MODEL	R-VALUE	MSE
JL_{311}	0.1594	0.000539509
JL_{321}	0.063559	0.000539509
JL_{3501}	0.06367	0.000539509
JL_{411}	0.09351	0.00183051
JL_{421}	-0.12494	0.00183051

JL_{4501}	0.19563	0.00183051
JL_{511}	**0.405**	**0.000401433**
JL_{521}	0.39157	0.000401433
JL_{5501}	0.23123	0.000401433

Table 4 Statistical error parameters of developed MLP models for different network structures for the month of August

MODEL	R-VALUE	MSE
AU_{311}	-0.081478	0.00175496
AU_{321}	0.070597	0.00175496
AU_{3501}	-0.046661	0.00175496
AU_{411}	0.092205	0.000816629
AU_{421}	-0.11655	0.000816629
AU_{4501}	0.12137	0.000816629
AU_{511}	**0.32711**	**0.00134672**
AU_{521}	0.081828	0.00134672
AU_{5501}	0.063312	0.00134672

Table 5 Statistical error parameters of developed MLP models for different network structures for the month of September

MODEL	R-VALUE	MSE
SEP_{311}	**0.4433**	**0.00203476**
SEP_{321}	0.19903	0.00203476
SEP_{3501}	-0.47707	0.00203476
SEP_{411}	0.39601	0.000175696
SEP_{421}	0.076726	0.000175696
SEP_{4501}	0.068821	0.000175696
SEP_{511}	0.28125	0.000468702
SEP_{521}	0.19927	0.000468702
SEP_{5501}	-0.036978	0.000468702

Table 6 Statistical error parameters of developed RBF models for different network structures for the month of July, August and September

MODEL	R-VALUE	MSE
$JL_{5\text{-}375\text{-}1}$	**0.99083**	**0.0213811**
$JL_{4\text{-}366\text{-}1}$	0.97682	0.047476
$JL_{3\text{-}355\text{-}1}$	0.90169	0.186487
$AU_{5\text{-}361\text{-}1}$	**0.97294**	**0.545422**
$AU_{4\text{-}362\text{-}1}$	0.9068	0.17909
$AU_{3\text{-}317\text{-}1}$	0.87117	0.240629
$SEP_{5\text{-}369\text{-}1}$	**0.91712**	**0.158468**
$SEP_{4\text{-}292\text{-}1}$	0.84221	0.0.288965
$SEP_{3\text{-}286\text{-}1}$	0.81189	0.339971

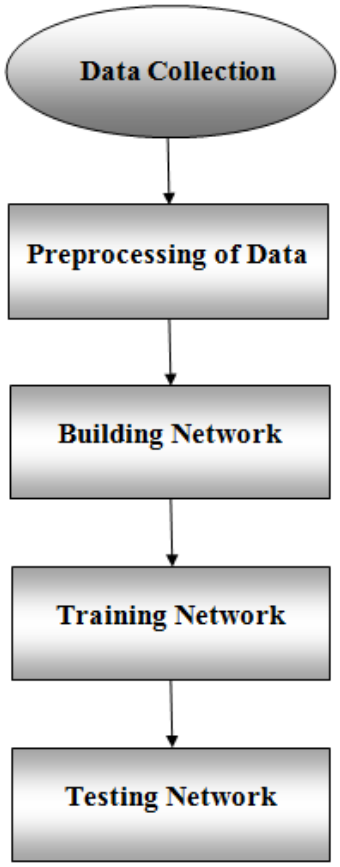

Fig 1 General procedural steps in developing ANN models

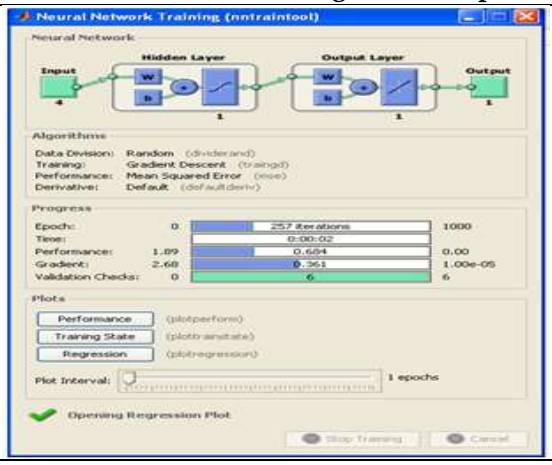

Fig 2 MLP network training window

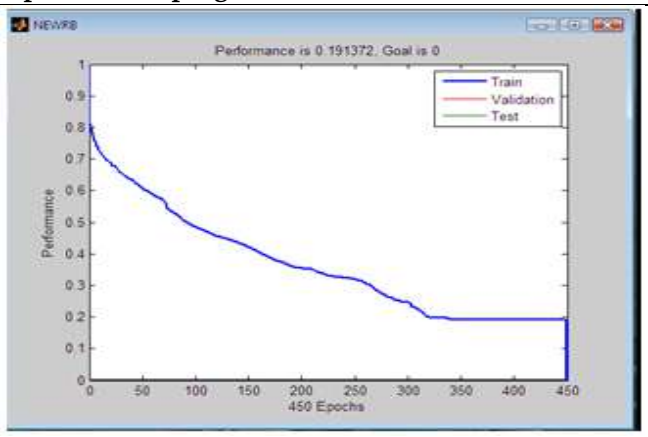

Fig 3 RBF network training window

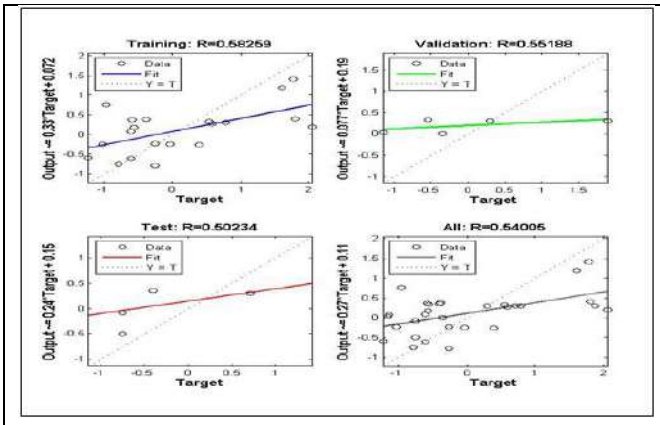

Fig 4 Scatter plot of observed and forecasted rainfall for Model JN421

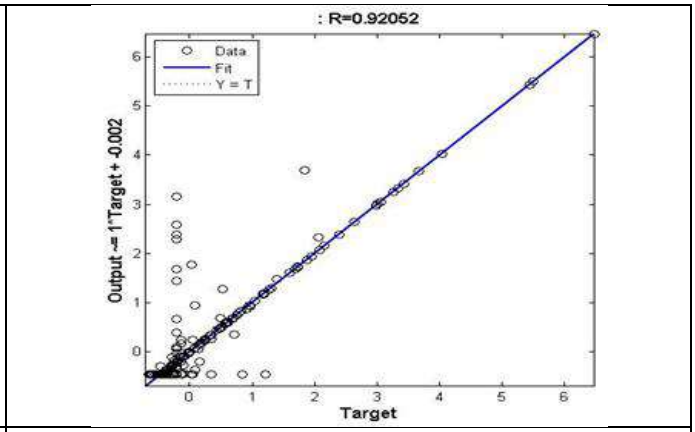

Fig 5 Scatter plot of observed and forecasted rainfall for Model JN5-374-1

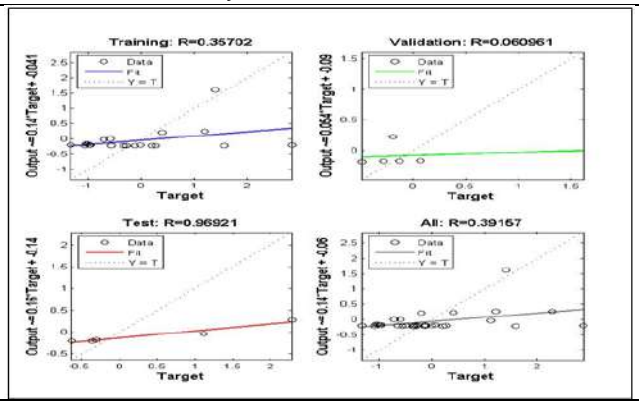

Fig 6 Scatter plot of observed and forecasted rainfall for Model JL511

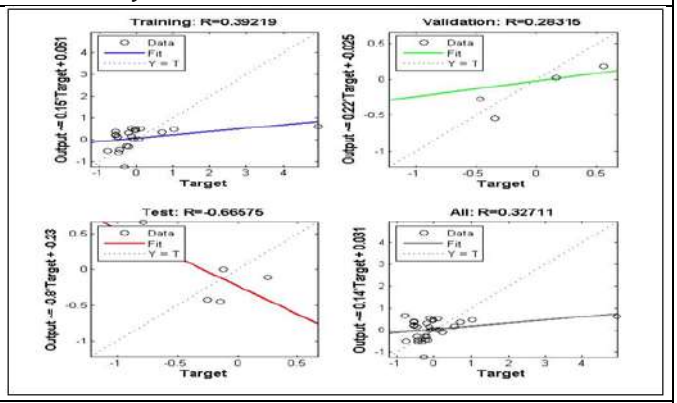

Fig 7 Scatter plot of observed and forecasted rainfall for Model AU511

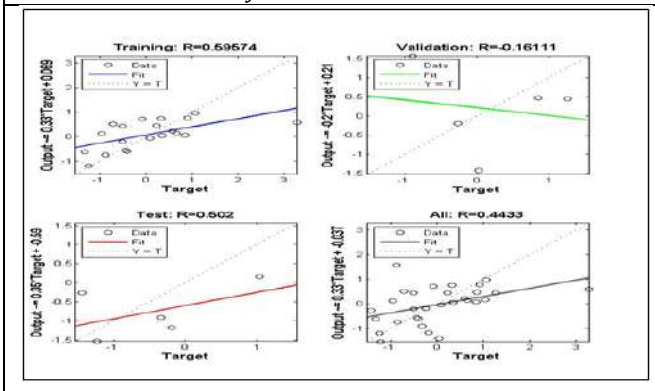

Fig 8 Scatter plot of observed and forecasted rainfall for Model SEP311

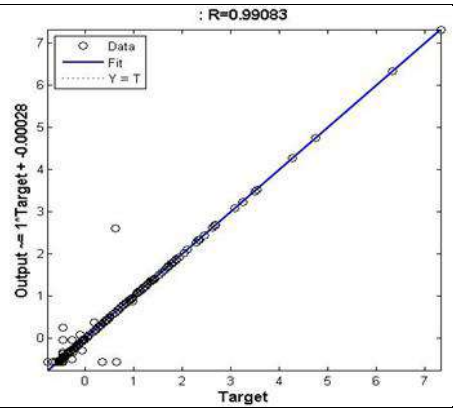

Fig 9 Scatter plot of observed and forecasted rainfall for Model JL5-375-1

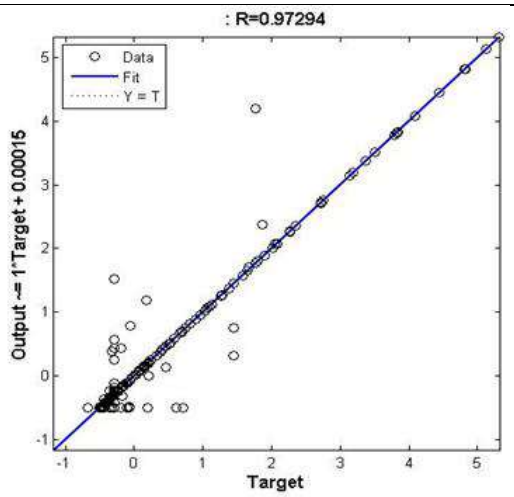

Fig 10 Scatter plot of observed and forecasted rainfall for Model AU5-361-1

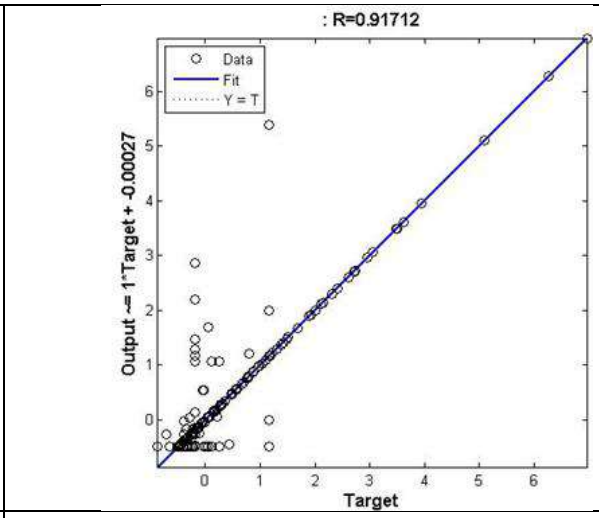

Fig 11 Scatter plot of observed and forecasted rainfall for Model SEP5-369-1

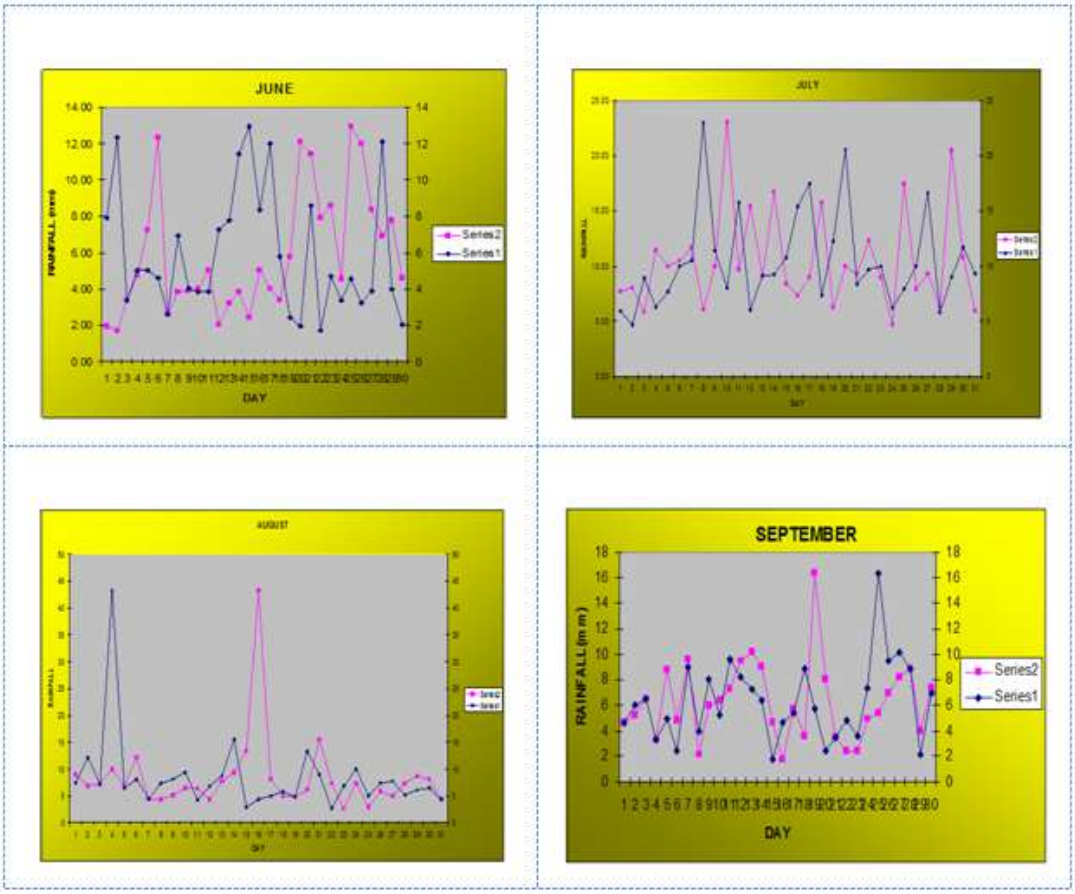

Fig 12 Comparative study between predicted & actual data for June, July, August and September

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RESEARCH ARTICLE

Issues and Challenges Faced by Service Industry in India

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ABSTRACT

The intent of the paper is to address the importance of service industry and key issues faced in this industry. Articles from peered reviewed journals are studied to gain knowledge related to the issues in current scenario. The findings of the study shows that job dissatisfaction, low productivity and performance, turnover, lack of growth, low engagement, and mismanagement are some of the major negative challenges faced by service industry, in India. The study shows the importance of human resources for the success and failure of an organization and provide tips for better management of these resources. Besides this, the study helps to gain better understanding related to the challenges in service sector.

Keywords: Service industry, Banking industry, Insurance industry, Hospitality industry, Telecom industry.

INTRODUCTION

The service sector in India is one of the crucial sector attracts significant level of foreign investment flows. Services sector covers a wide varied range of activities such as financing, insurance, trade, hotel and restaurants, transport, storage and communication, real estate, business services, community, social and personal services etc. In India, service sector is contributing 55.3% GVA in 2019-2020 (retrieved from economic survey on 20th January, 22). It has been witnessed that this sector is facing challenges (Gupta, 2016). It is essential to make necessary changes for the advance this sector, which can bring growth to a developing nation like India. Human resources are considered as the most precious assets for the success any business (Armstrong & Taylor, 2014). Therefore, scholars have viewed that organization should have employee-friendly approach, which is necessary for the prosperity of an entity (Guchait, and Cho, 2010). It has been found that very less attention is given to service sector, particularly in India (Idris et al. 2018). Thus, the paper attempts to gather knowledge related to challenges faced by service industry,

especially in India. As, HR department serves a crucial role for developing an enterprise (Vivares-Vergara *et al.,* 2016), knowing the key challenges can help the HR manager to modify the policies related to work system that can address the problems.

Scholars have witnessed the importance of maintaining staff well-being as a necessary policy that is essential for smooth organizational functioning, and performance (Deloitte, 2014; Reitman and Benatti, 2014; Hamori, *et al.,* 2012, Hansen and Leuty, 2012; Chuang, 2019; Teng, *et al.,* 2018; Weyland, 2011; Solnet and Hood, 2008). This also can acts as a motivational tool and thus provides mutual benefit that makes employee to work devotedly to fulfil organizational goals (Craig *et al.,* 2013; McDonald and Hite, 2005). So, organization should act as a platform for creating chances that fosters growth of employee. The paper is focused on sustainable development goal number 8 that deals with promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all. It attempts to understand the barriers faced by employees basically in service sector that can help the managers to undertake innovative measures to tackle with it. Besides this, the study can be useful for providing a better workplace to employees that can bring well-being to all and build up long-term relation between employee-organization, thus enhancing the productivity of the organization.

Issues in Service Industry

Banking Industry

Banks are the main source of financial system, have been going through heterogeneous challenges like demographical, economic and technological that demands change in skills, new business models, customer services etc. (Bhatta, 2012). The study conducted in Indian banks shows the absence of proper employee attention given by the department of HRD (Chhabra and Thangaraj, 2018). Evidences have shown the lack of proper individual growth and development in public sector banks (Henry et al, 2014), therefore scholars have suggested for implementing employee welfare practices internally (Moschetto, 2014). As per the report of RBI, the industry is facing various financial losses every year and uneven problems associated with employee (Kawad and Patinder, 2014; Singh, 2013). Other surveys highlights the need for tackling internal issues like promotion, career wellbeing, compensation, job dissatisfaction, individual growth etc. (Parveen and Khan 2014; Bora, 2014; Pragya and Sandeep, 2015).

Insurance Sector

Insurance industry is one of the fastest growing industry, as this industry provides shield by minimizing damage caused to life and property (Naval, and Kumar, 2017; Kamalanathan, 2016). This industry is facing employee related challenges. There is a need to designing plan of action that could help to sort out the current problems that employees are facing in insurance sector (Adeoye *et al.,* 2014). Training is a valuable program that can upgrade the skills to match with the job requirements, helps in personal growth, and hence can generate higher productivity for any firm (Yean and Yahya, 2013). Hence, promotion and developmental opportunities, if made avail within the organization can be a main source of employee attraction and they become dedicated towards their organizational goal (Chowdhury, 2016). The attrition of insurance agents gives around 12 percentage of the total loss to the sector as per the annual report of IRDA (2015). Therefore, it is urgent to work for the betterment of staff by changing the organizational practices. This can be done by creating the provision of training the staffs who directly deal with the customers Ahmed et al. (2019). Some researchers have noted that high work stress has led to job dissatisfaction (Gupta, 2014), and work life imbalance in this industry (Dolai, 2015).

Hospitality Industry

Hotel and tourism are studied under hospitality industry. Nowadays, traveling has been the need of general mass because of maintaining their health, business, and other social matters. And when there is traveling, there occurs a need of hotels to stay. Hospitality industry is facing issues related to talented staff (MdSadique, 2014). The issues faced by these industries are discussed below.

Hotel Industry

The hotel industry comprises a broad category of services that includes lodging, food and drink services, etc. where researchers have felt the need of skilled staff and thus suggested the requirement of providing training to the staffs as they directly deal with the customers (Seal, 2020). A well trained staff builds the image of the organization and brings customer satisfaction. Investigators have opined that providing growth opportunities for employee can generate positive attitudes among them, which ultimately can give benefit to both individual and organization (Joseph, 2013). Such benefits can lead to job satisfaction and employee can work with their full potential for fulfilling customer requirements (Kiruthiga and Magesh, 2015; Petrovic and Markovic, 2012). The attitude of employee develops goodwill and builds up organizational image. Hotels functions in an uncertain environment due to fluctuations for seasonal demands, trends, and lack of labour and skilled employees (Poescu and Avram, 2012; Sonia and Neetu, 2012), where occupation is transitory and employees gets frustrated due to lack of opportunities of skill generation and growth (Ladkin, 2013). This can be a strong reason behind the turnover of employee, which can be minimised through relational contracts, and organizational support (Guchait *et al.,* 2015).

Tourism Industry

In the tourism sector, it has been figured out the unavailability of required skills and high turnover (People 1st, 2015). Employees are vital for the success an organization and therefore it is an essential job of an organization to work for the development of employee that could help in the realization of individual goals (Cappelli and Keller, 2014). Scholars have viewed that individuals join organisations to develop and fulfil their own professional ambitions (Panda and Sahoo, 2015) and therefore it should not be neglected by organization.Aynalem et al (2016) observed that very minimal attention are given to the employee working in this industry.So, evidences have shown the employees' demand for the provision of safety and security through appropriate policy formulation (Hole, 2019). This can bring stability and financial growth by generating willingness among the employee to perform better.

Telecom Industry

In the world of competition, telecom industry is struggling hard to maintaining its position and is suffering a lot of employee related challenges (Gupta, *et al.,* 2019). A study investigated on the employee turnover intention in a leading telecom organization has found lack of job satisfaction, career opportunities, and pays and other financial benefits leads to turnover of employees (Krishnan, 2011). This sector has lost over 100,000 employees in the last two years due to financial turmoil, where it is quite difficult to maintain its policies (retrieved from economic times on 14th January, 2022). Employees are facing challenges related to job satisfaction, and work life balance that is creating an adverse impact on the industry's growth (S.kaskar and Patel 2021). Evidences shows talent shortage and employee engagement are the issues faced in the industry. So, proper attention by HR department is necessary to tackle with employee related problems, and mismanagement are suggested by scholars (Buddhapriya, 2018; Yadav, 2015).

CONCLUSION, SUGGESTIONS, AND FURTHER RESEARCH

The study the literatures shows that service industries like banking, telecom, hospitality and insurance are facing lack of employee related challenges like absence of required skills, talents, turnover, organizational support, customer satisfaction, engagement, job dissatisfaction, financial problems etc. By encapsulating the previous literatures it can be found that very less attention is given employee welfare aspect in the organization. The reason may be unawareness in the part of organization about the benefits that it can achieve through the employees development. The study can help the HR mangers to become proactive by handling the risk associated with employees. This can further build up organizational image and help in the continuity of business by overcoming the problems mentioned above and can stabilize the current situation by providing a good work practice and supportive organizational environment can generate health relationship between employer and employees (Eversole *et al.,* 2012; Guan et. al., 2014, 2015). There are some limitation associated in the study. The study is based on secondary information that are available through research papers. The future investigators can study any particular service

industry to know in-depth challenges. It has shown the importance of this sector for the development of employees, organization, and Nation as a whole.

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RESEARCH ARTICLE

Solubility Parameter Investigation of Bistriflimide Based Ionic Liquids through Molecular Dynamics Simulation

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ABSTRACT

Ionic liquids (ILs) is one of the most investigated solvent in recent times. ILs are liquids at room temperature and composed of salts. ILs have several interesting properties such ashigh thermal and electrical stability, good dissolving capability, low toxicity and so on. The most sophisticated property of any solvent is its dissolution/solubilizing capability. ILs considered as green solvent having good solubility and can solubilize a range of substances. In this regard we have investigated the solubility capability of bis (trifluoromethane) sulfonimide based ILs via theoretical means and compared the results with experimental data points available in literature. For theoretical calculation we have used Materials Studio software from Biovia. The results obtained are quite intersing and matching with the literature data points. We believe that these results would be useful for the application of ILs in several field of applications.

Keywords: Ionic liquid, Solubility Parameter, Hildebrand, Hansen, Density.

INTRODUCTION

Ionic liquids (ILs) are considered as sustainable solvents due to their low toxicity and biodegradility nature. ILs also proved itself for many industrial applications since its inception. Their applications ranges from biomass dissolution, drug delivery, electrochemical applications and so on. The advange with ILs is their unmatching characteristic properties such as higher thermal and electrochemical stability, higher liquious range, higher dissolution properties and so on. Among the several other properties, solubility is one of the key property and is the most important one from a solvent point of view. Therefore, in this work solubility parameters are exploited for imidazolium based ILs from a theoretical point of view. Also, the calculated results were compared with literature values for verification of our hypothesis and logic that has been utilized during theoretical calculations. There are different ways how solubility of a solvent can be defined. Solbility is very much necessary for any kind of work. Without solubility no

solvent can be used for any kind of applications [7,8]. Mathematically Hildebrand solubility parameter is expressed as;

$$\delta = \sqrt{c} = \sqrt{\frac{\Delta H_V - RT}{V_m}} \quad (1)$$

Where, c is the cohesive energy density, ΔH_V is enthalpy of vaporization, V_m is molar volume, R is gas constant, and T is temperature.

Hansen and Hildebrand solubility parameters are best considered as solubility parameters due to their advantgaes [7,9]. Mathematically, Hansen solubility parameter is given as;

$$\delta_t^2 = \delta_d^2 + \delta_p^2 + \delta_h^2 \quad (2)$$

Where, δ_t is the total Hildebrand parameter, δ_d is the dispersion component, δ_p is the polar component, and δ_h is the hydrogen bonding component.

ILs can be used for several applications such as biomedical applications, CO2 absorption, super capacitor, and many more. For all these applications solubility parameter is a very important factor and decides whether an ILs can have potential to work on. Therefore, it was utmost necessary to calculate the most important property of ILs by Biovia [10,11,12]. Solubility parameter can be determined both experimentally and theoretically [13]. ILs can also be used for drug delivery where solubility play an important role to solubilize the drug. Therefore, solubility parameters for those ILs are necessary to understand from a theoretical and molecular level point of view [7,8]. Theoretically many ILs can be prepared. Therefore, it is difficult to synthesize each individual ILs and measure their solubility. Therefore, theoretical calculation of solubility is very much necessary. In literature, there are many different techniques that have been used such as PC-SAFT and Non-random Hydrogen bonding (NRHB) model, Regular Solution Theory, and Lattice Energy Model [14–17] for solubility parameter measurement. However, the methodology we have used in this manuscript is the simple way of calculating solubility parameter. .

Computational Details

To calculate the solubility parameters of ILs using materials studio software, first of all the ILs were drawn and then geometrically optimized for their stable structure. After that suitable force field such as compass has been used for several other calculations. A three dimentional data structure was prepared by combining different cations and anions of ILs for solubility parameter calculations are depicted in Figure 1. The density data of ILs as mentioned in Table 1, were used from literature to construct the Amorphous cell [18,19]. Different ensembles were used for MD simulation calculation [9,20]. The NPT and NVT ensembles were the two important ensembles and are used for all the cation and anion combinations. All the calculations were conducted at room temperature because it is easy for comparison as well. All thedifferent interactions were calculated from variety of calculations that are helpful for the ILs. The cohesive energy density also have been calculated for all the studied ILs followed by solubility parameter determination.A representative example of Amorphous Cell containing 1-Hexyl-3-methylimidazolium bis(trifluoromethane) sulfonimide (HMIM NTf2) IL is depicted in Figure 2.

RESULTS AND DISCUSSION

To prove that we have used correct methodologies, we have calculated solubility parameters for the considered ILs. As can be seen from Table 2, the solubility parameters values deviate from that of experimental values that are reported in literature The deviations could be due to some inconsistent parameters choosen during our calculations.
The total solubility parameter which is the combination of two parameters such as van der Waals (dispersive) and electrostatic component are showing good results. The second part is the mixture of H-bond interaction and ionic interaction. As illustrated in Table 2, the total solubility parameter for bis(trifluoromethane) sulfonimide based ILs decreases when the chain length elongates on main components. The trend we get from our calculation is similarly matching with the literature experimental data points. Moreover, the increment for carbon chain length of solubility parameter is 0.25 The possible arguments for this development could be strong electrostatic interactions between the

cation and anion of imidazolium ILs. Furthermore, the solubility parameters also depends upon the geometry of cations and anions. There are many different types of interactions that guide the solubility parameters value such as hydrogen bonding, electrostatic interactions and so on [22].

CONCLUSION

Bis(trifluoromethane) sulfonimide based imidazolium based ILs are choosen for the solublity parameter calculation by Materials Studio software. The results are quite interesting and is matching with the experimental results form literature. Therefore, we may conclude that the assumptions we made and the methodologies we have used during the calculation of solubility parameters are perfectly correct. This results will encourage many researchers to find out the theoretical solubility data for ILs without even synthesizing them. In this way we can save the time, resources and energy. Furthermore, the solubility data can be useful for many applications such as biomass dissolution, catalysis, electrochemistry, and so on.

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Table 1: The cations, anions, ionic liquids, abbreviations and density of ILs at 298.15 K.

Cation	**Anion**	**Ionic Liquid**	**Abbre-viation**	**Density[18,19]/g.cm^{-3}**
1-Ethyl-3-methylimidazolium	bis(trifluoromethane) sulfonimide	1-Ethyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	EMIM NTf2	1.352
1-Butyl-3-methylimidazolium	bis(trifluoromethane) sulfonimide	1-Butyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	BMIM NTf2	1.239
1-Hexyl-3-methylimidazolium	bis(trifluoromethane) sulfonimide	1-Hexyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	HMIM NTf2	1.147
1-Octyl-3-methylimidazolium	bis(trifluoromethane) sulfonimide	1-Octyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	OMIM NTf2	0.984

Table 2: Solubility parameters of ImidazoliumILs.

Sl. No.	Ionic Liquid	δ (this work)	δ (Literature)
1	1-Ethyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	22.43	22.58[17]
2	1-Butyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	21.57	21.21[21, 14]
3	1-Hexyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	20.81	20.98[16,7]
4	1-Octyl-3-methylimidazolium bis(trifluoromethane) sulfonimide	20.24	20.25[22]

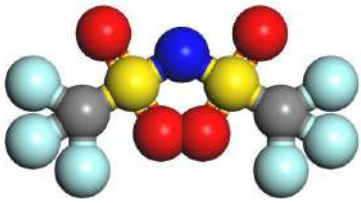
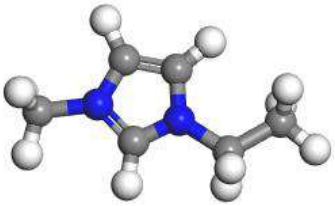
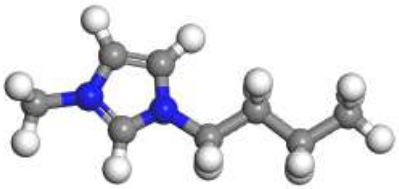
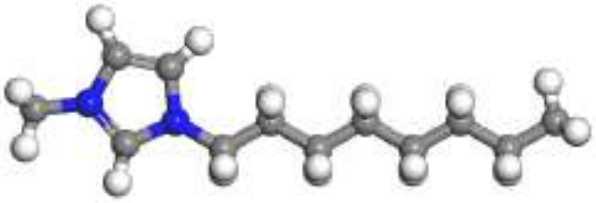
		
bis(trifluoromethane) sulfonimide	**1-Ethyl-3-methylimidazolium**	**1-Butyl-3-methylimidazolium**
		
1-Hexyl-3-methylimidazolium	**1-Octyl-3-methylimidazolium**	

Figure 1: Geometry optimized structures of cations and anions of ILs used for calculation.

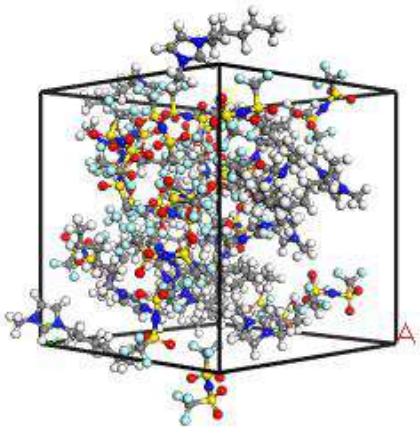


Figure 2: Bulk IL 1-Hexyl-3-methylimidazolium bis(trifluoromethane) sulfonimide (HMIM NTf2) prepared in Amorphous cell module of Materials Studio software.

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REVIEW ARTICLE

Role of Immunomodulatory agents in Treatment of COVID-19: A Review

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ABSTRACT

The severe acute respiratory syndrome corona virus 2 causes corona virus disease-19 (COVID-19) (SARS-CoV-2). The new virus's long incubation time, this is generally asymptomatic yet contagious, is one of the main reasons for its rapid spread over the world. There is currently no treatment for COVID-19 that has been approved internationally. As a result, the clinical and scientific communities are working together to mitigate the outbreak's severity. Previous research on emerging infectious illnesses has yielded significant information that is being used to repurpose drugs and speed up vaccine development. Nonetheless, it is critical to gain knowledge about SARS-CoV-2 infection processes and their impact on host immunity in order to lead the development of COVID-19 specific treatments and vaccines for mass vaccination. The success of these preventative and therapeutic techniques is predicted to rely heavily on nano-scale delivery devices. This review analyses immune-mediated techniques currently being investigated for COVID-19 therapies, with a focus on nanotechnological tools, and provides a description of SARS-CoV-2 pathogenesis.

Keywords: SARS-CoV-2, preventative, disease, virus, COVID-19

INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) worldwide pandemic, which began in China in late 2019, has quickly spread over the world to become a global pandemic [1]. The development of this highly infectious virus has wreaked havoc on communities all across the world, infecting millions and killing thousands of people. Corona virus has no known cure at this time. Although a diagnostic test for PCR testing of the virus by

nasopharyngeal swab is available, there are cases where clinical symptoms such as cough, shortness of breath and temperature are present but a swab test is negative. These symptoms are frequently accompanied by laboratory changes such as lymphopenia, elevated serum C - reactive protein (CRP), ferritin levels, and pulmonary infiltrates on chest radiographs. High temperatures, cough, headache, sore throat, shortness of breath, arthralgia, myalgia, chest pain, altered taste, and confusion are all symptoms of the Corona virus, which affects the lungs. The illness can trigger a fast inflammatory response in the body, resulting in cytokine release and rapid deterioration. The corona virus outbreak has opened up new avenues for research into the immune response to corona virus and the development sustainable growth for good health and well being. Due to the lack of a treatment, a massive multinational effort is underway to discover viable vaccines and pharmacotherapies for SARS-CoV-2. Immunomodulatory drugs have been recommended as a candidate treatment to target the inflammatory reaction that occurs in the lungs of affected patients, as well as the cytokine storm that occurs in severe cases. TNF factors, corticosteroids, hydroxychloroquine, biologic inhibitors of IL-6 and IL-1, such as tocilizumab and anakinra, and janus kinase inhibitors have all been suggested as potential SARS-CoV-2 treatments[2,3] with some of them now in clinical trials, such as the Recovery trial [4]

WHAT IS IMMUNOMODULATION?

Immunomodulation is the process of adjusting the immune system's regulation. It comes in both natural and man-made forms, and the term can be used to describe the following:

- The immune system's self-regulation to modify immune responses to adaptive rather than maladaptive levels is known as homeostasis (using regulatory T cells, cell signalling molecules, and so forth)
- Immunomodulation is a type of immunotherapy that involves inducing, amplifying, attenuating, or preventing immune responses to achieve therapeutic aims**.**

There are two types of immunomodulators. These are-

1. Natural immunomodulator
2. Synthetic immunomodulator

Natural immunomodulators

Natural compounds have made a significant contribution to immunomodulatory therapies. Natural medicines have been used as treatments with few side effects since ancient times. Thousands of natural compounds have been found to influence the immune system by affecting immune cell functions or antibody secretion in order to control infection and maintain immune homeostasis. Some natural immunomodulators are described below.

Allium sativum (Lasun – Liliaceae) –

Garlic organosulfur compounds have been demonstrated to suppress tumour formation in animals and regulate the activity of a variety of chemical carcinogens [5-6]. This effect could be linked to natural killer (NK) cell activation, T-lymphocyte stimulation, and increased IL-2 production .

Azadirachta indica (Neem- Meliaceae)-

In India, A. indica is one of the most common wild-growing trees. It has considerable non-specific immunomodulatory capabilities, according to recent investigations [6]. Plant components of the neem tree (Azadirachta indica) have an antibacterial effect by inhibiting microbial development and the potential for cell wall collapse. Azadirachtin, a complex tetranortriterpenoid limonoid found in seeds, is the main component responsible for insect antifeedant and poisonous actions.

Ocium sanctum(Tulsi- Labiatae)-

Anticancer properties of O.sanctum extract was investigated. Despite the fact that this plant extract did not fully prevent the development of solid tumours, it did cause a significant delay in tumour growth [6].

Phyllanthus emblica (also known as *Emblica officinallis*) (amla - Euphorbiaceae)-
Many Ayurvedic tonics for rejuvenation, recuperation, and validity contain P. emblica as one of the main ingredients. It also has a high amount of vitamin C [7]. Suresh and Vasudevan discovered that *P.emblica* had an immunomodulatory influence on the immunological profile of tumour-bearing mice. In syngeneic Bal b/c mice with Dalton's lymphoma ascites tumour, *P. emblica* fruit powder was observed to increase NK cell activity and antibody dependent cellular cytotoxicity (ADCC) when given orally.

Piperine*(Piper longum Linn)*-
IL-1, IL-6, and TNF- are pro-inflammatory cytokines that should be reduced. COX-2, NOS-2 and NF-B expression are all down regulated. Inhibit the production of eicosanoids by inhibiting the activity of phospholipase A2 and TXA2 syntheses.[8]

Tetramethylpyra-zine(TMP)*(Ligusticum Chuanxiong Hort)*-
Inhibit the synthesis of pro-inflammatory cytokines and reactive oxygen species. Chemotaxis, neutrophil infiltration, and nitric oxide synthase activity in macrophages are all inhibited. Phosphorylation of the p38 mitogen-activated protein kinase is inhibited.[6]

Wogonin *(Scutellana baicalensis Georgi)*-
Inhibit leukocyte adherence and migration by inhibiting the expression of cell adhesion molecules. Reduces allergic airway inflammation by activating caspase-3 and causing eosinophil death.[7]

Rutin *(Ruta graveolens)*-
Inhibit the movement of leukocytes.TNF- and IL-6 production are reduced.
Inhibit NF-B and extracellular regulated kinase activation.[8]

Puerarin *(Pueraria lobata (wild)* –
Reduce the amount of cytokines in the body. NF-B inhibition and signal transducers and transcription activators are activated 3 (STAT3). [9]

Licochalcone E *(Glycyrrhiza inflata)* –
By reducing the action of NF-B and activator protein, you can prevent the secretion of pro-inflammatory cytokines including IL-1, IL-6, and TNF- (AP-1). [10]

Ginger *(Zingiber officinale)* - The medicinal properties of ginger are due to the presence of gingerol and paradol, shogaols. This is employed as anti-diabetic, antioxidant, anti-inflammatory, hepatoprotective, antimicrobial and many sort of disease. Ginger scientifically known as *Zingiber officinale* Roscoe, belonging to family Zingiberaceae is one of the most important plant with several\medicinal, nutritional and ethnomedical values therefore, used extensively worldwide as a spice\flavouring agent and herbal remedy [11]. Traditionally, *Z. officinale* has been used to treat nausea, vomiting, asthma, cough, breathlessness, inflammation, dyspepsia, loss of appetite, constipation, indigestion, and pain in Ayurveda, Siddha, Chinese, Arabian, African, Caribbean, and other medicinal systems [12].

Rudanti *(Capparis moonii wight)* - *Capparies mooni* wight is a huge woody climber or shrub popularly called as Rudanti that has revitalising properties and is used by ayurvedic physicians to treat respiratory diseases such as cough, bronchial asthma, and pulmonary tuberculosis. Rudanti is a medicinal shrub that grows primarily in saline and sandy oil. The herb rudanti is used to treat dyspepsia, flatulence, asthma, and bronchitis [13].

Pistachio *(Pistacia integerrima)* - The medicinal plant *Pistacia integerrima* is very valuable. The herb is also used to cure a wide range of human problems in various folkloric cultures around the world, including diarrhoea, dysentery, fever, vomiting, skin disease, respiratory ailments, and psoriatic appetiser, hepatitis, and liver-related disorders. The essential oil content of the plant, which contains several key phytochemical elements such as alpha-pinene,

camphene, di-limonene, caprylic acid, alpha-terpineol, and aromadendrene, is a distinguishing feature. The plants, on the other hand, have antibacterial, anti-oxidant, anti-inflammatory, anti-cancer, cardio-protective, anticonvulsant, and muscle relaxant properties [14-17].

Guduchi *(Tinospora cordifolia)*

Cordifolia has been demonstrated to boost osteoblast growth by enhancing cell differentiation into the osteoblastic lineage and increasing bone-like matrix mineralization [17-21]. In mammals, ecdysteroids extracted from the plant have been shown to have protein anabolic and anti-osteoporotic properties. Ayurvedic medicine uses its root, stems, and leaves. *Tinospora cordifolia* is claimed to treat hay fever, sports performance, diabetes, high cholesterol, upset stomach, gout, an itchy skin illness caused by mites (scabies), and a variety of other ailments, however there is little scientific evidence to back up these claims.

Holy Basil *(Ocimum sanctum)*

Various parts of *Ocimum sanctum* Linn (known as Tulsi in Hindi) have been recommended for the treatment of bronchitis, bronchial asthma, malaria, diarrhoea, dysentery, and skin diseases in traditional systems of medicine. In order to establish the scientific basis of therapeutic use of O. sanctum in modern medicine, several Indian scientists and researchers have studied the pharmacological effects of various parts of Tulsi [22-28]. Tulsi's therapeutic usage in the management of many disorders was characterised in terms of reproductive, cardiovascular, gastrointestinal, urinary system, blood biochemistry, and blood biochemistry. OS is classified as a stimulant, aromatic, and antipyretic in Ayurvedic scriptures. It balances kapha and vata while aggravating pitta. It has a wide range of effects on the human body, primarily as a cough reliever, a sweat inducer, and a dyspepsia and anorexia reliever.

Indian barberry *(Berberry aristata)*

Berberis aristata, popularly known as Indian barberry, "daru haldi," or tree turmeric, is a Berberidaceae (Berberis family) and Berberis genus shrub [29]. This herb is most effective when it comes to eye problems. It is also used to speed wound healing, and the paste of this herb can be used to treat syphilis, ulcers, and anal fistula. Daruharidra relieves spasmodic pain and is very good to menorrhagia and leucorrhoea sufferers.

Indian Sandalwood *(Santalum album)*

Sandalwood oil has long been used in folk medicine to treat common colds, bronchitis, skin disorders, heart problems, general weakness, fever, urinary tract infection, mouth and pharyngeal irritation, liver and gallbladder problems, and other ailments [30]. Its capacity to cause cell-cycle arrest and killing in cancer cells is the most well-known anticancer method. The current review examines studies that support the anticancer activity of sandalwood oil and -santalol in carcinogenesis, as well as the efficacy.

Ashwagandha *(Withania somnifera)*

Withania somnifera, often known as ashwagandha, is a tropical winter cherry that belongs to the Solanaceae family and is used to treat a number of ailments such as asthma, diabetes, hypertension, stress, arthritic disorders, and cancer. In the Ayurvedic tradition of India, Ashwagandha (*Withania somnifera* or WS) is referenced in the Rasayana group of drugs and has been widely explored as an immunomodulatory agent. The immunomodulatory action of the components in WS, primarily withanolide glycosides, is mediated via the mobilisation and activation of macrophages, as well as the induction of proliferation in murine splenocytes [31].

Candayleaf (*Stevia rebaudiana)*

It is a kind of Bertoni is a perennial herbaceous plant belonging to the Asteraceae family. S. *rebaudiana* leaf extracts have been utilised in the treatment of diabetes for centuries [32]. Stevioside is the major sweet component in the leaves of S. rebaudiana [33]. Stevia sweetener extracts have been shown to have antihypertensive, antihyperglycaemic, noncariogenic, and anti-human rota virus properties [34-36].

Spanish Chamomile (*Anacyclus pyrethrum*)

The roots of *Anacyclus pyrethrum* DC (Compositae), also known as akarkara (pellitory root) in Ayurvedic medicine, have been widely praised for their rasayana characteristics (Ministry of Health and Family Welfare, 2004). It's commonly used in traditional medicine to stimulate the salivary glands. It can also be used to treat toothaches, paralysis of the tongue and throat muscles, and neuralgic dental issues [37].

Clove *(Syzygium aromaticum)*

The Myrtaceae family includes the *Syzygium aromaticum* (clove) plant. It grows wild in Indonesia and is cultivated in many other countries, including Iran. It is a well-known food taste as well as a common cure used in traditional medicine in Australia and numerous Asian nations for tooth problems, respiratory problems, headaches, and sore throats. Clove has anti-inflammatory, cytotoxic, and aesthetic qualities in addition to anti-microbial, anti-fungal, and anti-viral characteristics. Clove components have been shown to have anti-oxidant properties and reduce lipid per oxidation [38].

True cinnamon tree (*Cinnamomum verum***)**

The bark of the cinnamon verum tree is widely used as a spice. *Cinnamon* has also been used for millennia in the treatment of diabetes and other ailments. It has been demonstrated that it can be used to treat salmonella infections. H., anti-nematodal agent and type 2 diabetes. A wide range of experiences have been shared. *Cinnamomum* sp. investigation as well as their possible roles in diabetes, and melanoma. Vascular dementia is a kind of dementia, end-stage glomerular disease, and kidney disease in general. Rheumatoid arthritis, for example, is a disease caused by oxidative stress [39].

SYNTHETIC IMMUNOMODULATORS

Synthetic immunomodulators can effectively increase host immunocompetence, but they are not a cure-all for all microbial infections. Because no medicine is successful in all phases or effectors cells of the immune response, Chemical agents can alkylate biological material, and it was later discovered that aliphatic nitrogen mustards had a specific effect on lymphoid tissue such as the spleen, bone marrow, thymus, and lymph nodes [32]. Alkylating agents were one of the first chemical substances to be studied for their immunosuppressive effects [33]. Another option in clinical immunosuppression, particularly for kidney transplantation, is azathioprine [34,35]. Other chemical compounds utilised for immunosuppression include b,b-diethylcysteine, penicillamine, procarbazine, and others [35]. Cinanserin is a powerful serotonin antagonist that inhibits the generation of circulating antibodies, prolongs mouse skin homograft, and shows effectiveness in both the EAE and adjuvant-induced arthritis tests [36]. Several unrelated compounds with immunopotentiating properties have come into focus throughout the decades, and the usage of adjuvants, their nature, and the notion underpinning immunostimulation have received increased attention [37,38]. Adjuvants are chemicals that aid the immune system's growth and manifestation[39]. Another synthetic drug that has shown great potential in mice for restoring a weakened immune response is SRBC. Levamisole, an immunomodulator, has been used successfully as a powerful antihelminthic in humans and animals to treat a variety of nematodal diseases [40]. Isoprinosine is also utilised to control immunological responses and boost the activity of thymic hormones [41]. It also acts on T cell precursors through a receptor for an inosine-like molecule. It has been shown to help with a variety of viral illnesses, including acute and recurrent herpes simplex virus, rhinovirus, and the progression of measles-related subacute sclerosing panencephalitis [41,42].

MECHANISIM OF DIFFERENT IMMUNOMODULATORY AGENTS

Immunomodulators affect the immune system at many levels. As a result, medications that selectively inhibit or intensify specific populations and subpopulations of immune response cells, such as lymphocytes, macrophages, neutrophils, natural killer (NK) cells, and cytotoxic T lymphocytes, have been produced (CTL). Immunomodulators have an effect on cells that produce soluble mediators like cytokines [43]. As a result, immunotherapy targets the immune system in order to aid in the healing of a disease. Figure1 depicts the inflammatory processes involved in rheumatoid arthritis as an example.

Immunosuppressants suppress the immune response in organ transplantation and autoimmune illnesses, whereas immunostimulants boost it in infections, immunodeficiency (such as AIDS), and cancer. A drug that induces observable changes in immune function is referred to as immunomodulation rather than immunostimulator. They can behave in a variety of ways, both particular and vague. Immunomodulators with selective specificity for immune response impact the immune system of cells in response to the presence of a specific antigen or immunogen. When the stimulation results in an immune response to one or more antigens, such as with adjuvants or therapeutic vaccinations, immunomodulation is selective. Vaccines using synthetic antigens, especially new-generation antigens, benefit from immunological adjuvants. These

compounds are also employed in vaccine research to obtain polyclonal antiserums and monoclonal antibodies for use in vaccines [44]. Immunomodulators having a non-specific action are used to stimulate or decrease the immune response without directing activated cells' activity to a specific antigen. They are classified as type I, which affects the normal immune system, type II, which affects the immunosuppressed immune system, and type III, which affects both the functionally normal and immunosuppressed immune systems [45]. Symptoms and indicators of autoimmune illnesses vary based on the type of disease and the individual affected. Skin and joints, for example, can be affected by lupus, whereas skin, kidneys, and lungs can be affected by other autoimmune illnesses. Immunosuppressant's are also among the most effective medications for inflammatory bowel disease treatment. Corticosteroids, for example, are used to prevent reactivation and post-surgical relapse in Crohn's disease [46].

THERAPEUTIC ACTION OF DIFFERENT IMMUNOMODULATORS

The immunostimulating and immunosuppressant medicines, as well as their pharmacological effects, are included in Tables 1 and 2. Immunomodulators are employed when the immune system isn't up to the task of fighting an infection or cancer, for example [47]. However, as the tables show, there are a range of immunomodulatory drugs that are employed for a variety of therapeutic purposes. Tumour necrosis factor (TNF) antagonists are specifically included among the new generation immunomodulators. TNF- stimulates inflammatory responses that are critical in the pathophysiology of rheumatoid arthritis and is released by activated monocytes, macrophages, and T lymphocytes. TNF- is found in significant amounts in the synovial fluid of patients with rheumatoid arthritis [48]. As a result, TNF antagonists are commonly employed in the treatment of rheumatic illnesses

INFORMATION ABOUT CORONA VIRUS

Corona virus disease 2019 (COVID-19), a highly contagious viral illness caused by the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), has wreaked havoc on the world's demographics, killing more than 3.8 million people worldwide and establishing itself as the most serious global health crisis since the 1918 influenza pandemic. After the first instances of this primarily respiratory viral illness were discovered in late December 2019 in Wuhan, Hubei Province, China, SARS-CoV-2 quickly spread around the world, prompting the World Health Organization (WHO) to designate it a worldwide pandemic on March 11 2020. COVID-19 has decimated numerous countries and overloaded many healthcare systems since it was proclaimed a global pandemic. Long-term shutdowns caused by the pandemic have led in the loss of livelihoods, which has had a ripple effect on the worldwide economy. Even though significant progress in clinical research has led to a better understanding of SARS-CoV-2 and the management of COVID-19, limiting the virus's and its variants' spread has become a growing concern as SARS-CoV-2 continues to wreak havoc around the world, with many countries experiencing a second or third wave of outbreaks attributed primarily to the emergence of mutant virus variants.

While adapting to their new human hosts, SARS-CoV-2, like other RNA viruses, is susceptible to genetic evolution with the formation of mutations over time, resulting in mutant variations with different features than their ancestral strains. Several SARS-CoV-2 variations have been identified during the pandemic, however only a few are classified variants of concern (VOCs) by the WHO due to their worldwide public health impact. According to the WHO's most current epidemiological update, four SARS-CoV-2 VOCs have been discovered since the beginning of the pandemic as of June 22, 2021: Coronaviruses (CoVs) are members of the Orthocoronavirinae subfamily of the Coronaviridae

family of the Order Nidovirales. According to the WHO's most recent epidemiological update, there are four genera in the Orthocoronavirinae subfamily as of June 22, 2021, namely[49,50]:

- **Alpha corona virus(α-Cov):**In late December 2020, the United Kingdom (UK) reported the first variation of concern.
- **Beta corona virus(β-Cov):** In December 2020, it was first reported in South Africa.
- **Gamma Corona virus(γ-Cov):**In early January 2021, it was first reported in Brazil.
- **Delta Corona virus(δ-Cov):** In India, it was first reported in December 2020.

The CoV genome is a single-stranded, enclosed, positive-sense RNA with a size ranging from 26 to 32 kb, making it the biggest genome of any known RNA virus. Both the - and -CoV genera have been shown to infect mammals, while the - and -CoVs have been found to infect birds. The introduction of these novel SARS-CoV-2 variations threatens to undo the tremendous success made so far in restricting the spread of this viral infection, despite the exceptional speed with which vaccines against COVID-19 have been developed and robust global mass immunisation efforts. Despite the amazing speed with which COVID-19 vaccines have been created and vigorous global mass vaccination efforts, the arrival of these novel SARS-CoV-2 variants threatens to undermine the tremendous success accomplished so far in controlling the spread of this viral infection.

VARIENTS OF CORONA VIRUS:

What Is a COVID-19 Variant and What Does It Mean ?

Viruses are rapidly developing, and this might result in the emergence of a new variant, or strain, of the virus. In most cases, a variation has little effect on how the virus functions. However, they can make it act in a variety of ways at times. Changes in the virus that causes COVID-19 are being researched by scientists all over the world. Their findings are assisting researchers in determining if some COVID-19 variants spread more quickly than others, how they influence your health, and how effective different vaccines are against them.

HOW DO VARIANTS HAPPEN ?

Corona viruses have all of their genetic information in RNA (ribonucleic acid). Although RNA and DNA have some similarities, they are not the same. When viruses infect you, they connect to your cells, enter them, and replicate their RNA, allowing them to spread. If a copying error occurs, the RNA is altered. Mutations are the term used by scientists to describe these alterations. These modifications occur at random and by chance. It's a natural component of the process of viruses multiplying and spreading.

Because the changes are unpredictably occurring, they may have little or no impact on a person's health. They may also cause disease in some cases. One reason you need a flu vaccination every year, for example, is that influenza viruses evolve year to year. This year's flu virus isn't likely to be the same as the one that swept the country last year. When a virus undergoes a random mutation that makes it simpler to infect humans and spreads, that variety becomes more frequent. In the end, all viruses, including corona viruses, can evolve over time.

CONCERNS ABOUT SARS-CoV-2 VARIANTS (VOCs)

The CDC and WHO have created their own classification method for categorising SARS-CoV-2 variations into variants of concern (VOCs) and variants of interest (VOIs) as a result of the increasing number of variants (VOIs).

Alpha (B.1.1.7 lineage): B.1.1.7 lineage, commonly known as Alpha variant or GRY(formerly GR/501Y.V1), a novel SARS-CoV-2 variant of concern was discovered in the UK in late December 2020, based on whole-genome sequencing of samples from patients who tested positive for SARS-CoV-2. [51] [52] This type of worry began to circulate in the United Kingdom as early as September 2020, and was based on numerous model estimates. It was believed to be 43 percent to 82 percent more transmissible than previous SARS-CoV-2 variants, and it has since emerged as the prevalent SARS-CoV-2 variety in the United Kingdom. [53] At the end of December 2020, the B.1.1.7 variant was recorded in the United States (US). When compared to other existing variants, a matched case-control study found no significant difference in the risk of hospitalisation or associated death with the B.1.1.7 lineage

mutation. However, further studies have found that persons infected with the B.1.1.7 lineage variant had a more severe illness than those infected with other circulating virus variants. [54][52] In a large matched cohort research conducted in the United Kingdom, patients infected with the B.1.1.7 lineage variant had a mortality hazard ratio of 1.64 (95 percent confidence interval 1.32 to 2.04, P0.0001) compared to those infected with previously circulating strains.

Beta (B.1.351 lineage): Tegally et all. Discovered a novel SARS-CoV-2 strain lineage B.1.351, also known as Beta variation or GH501Y.V2, with numerous spike mutations in October 2020, resulting in the second wave of COVID-19 infections in Nelson Mandela Bay, South Africa. [53]The B.1.351 variant contains nine mutations in the spike protein (L18F, D80A, D215G, R246I, K417N, E484K, N501Y, D614G, and A701V), three of which are located in the RBD and increase the binding affinity for the ACE receptors. [54-56] At the end of January 2021, SARS-CoV-2 501Y. V2(B.1.351 lineage) was reported in the United States. This variation has a higher risk of transmission and is less resistant to monoclonal antibody treatment, convalescent sera, and post-vaccination sera [55].

Gamma (p.1 lineage) : The P.1 variation, also known as Gamma variant or GR/501Y.V3, was discovered in Brazil in December 2020 and was first detected in the United States in January 2021. [52-54]The spike protein in the B.1.1.28 variant has ten mutations (L18F, T20N, P26S, D138Y, R190S, H655Y, T1027I V1176, K417T, E484K, and N501Y). The RBD contains three alterations (L18F, K417N, and E484K), which are similar to the B.1.351 variation. [52] This variety has spread to 45 countries, according to a WHO epidemiological bulletin from March 30, 2021. Importantly, monoclonal antibody treatments, convalescent sera, and post-vaccination sera may be less neutralised by this type. [55]

Delta (B.1.617.2 lineage) : The fourth variety of concern, B.1.617.2 (also known as the Delta variant), was first found in India in December 2020 and was responsible for the deadly second wave of COVID-19 infections in India in April 2021. This variation was first spotted in the United States in March 2021, and experts expect it to become the most prominent SARS-CoV-2 strain in the US in the next weeks. Initially, the Delta variant was thought to be a variant of interest. However, due to its rapid spread over the world, the WHO classified this strain as a VOC in May 2021. The spike protein of the B.1.617.2 variation has 10 mutations (T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, D950N).

What is the Omicron Variant (B.1.1.529) ?

The new variation (B.1.1.529) was discovered for the first time in Botswana on November 11, 2021. On Nov. 24, 2021, experts in South Africa reported the Omicron variant to the World Health Organization (WHO). They detected the variation after an increase in COVID-19 infections. Omicron is classified as a "Variant of Concern" by the World Health Organization. This classification indicates that the variant may be more transmissible, cause more severe disease, and be less likely to react to immunizations or therapies. However, more data is needed to substantiate these factors [46-47].

Early evidence suggests that the Omicron variant, when compared to other variants, increases the likelihood of reinfection. Current COVID-19 PCR tests are capable of detecting Omicron instances. Experts discovered that one of the three target genes (dubbed the S gene dropout) in persons infected with Omicron is missed by a specialised PCR test. As a result, these tests can distinguish between positive Omicron instances and, as a result, can discover this variety faster than prior surges. Even if you're fully vaccinated, breakthrough infections with the Omicron strain are conceivable, according to studies. COVID-19 vaccines and boosters, on the other hand, remain effective in reducing serious disease, hospitalisation, and death. In the United States, the Omicron variety has become the widely recognized strain.

SARS-CoV-2 VARIANTS OF INTREST (VOIs) :

Variants with specific genetic markers have been linked to changes that may result in increased transmissibility or virulence, decreased neutralisation by antibodies obtained through natural infection or vaccination, the ability to evade detection, or a decrease in therapeutic or vaccination effectiveness. Epsilon (B.1.427 and B.1.429); Zeta (P.2); Eta (B.1.525); Theta (P.3); Iota (B.1.526); Kappa (B.1.617.1) and Lambda (B.1.617.1) were described in the WHO Weekly Epidemiological Update on June 22, 2021. (C.37). These were once classified as variations of interest, but the WHO degraded them. They're still being kept an eye on.

EPIDERMIOLOGY OF CORONA VIRUS

The World Health Organization (WHO) considers the rise of viral infections to be a severe public health threat. Several viral epidemics occurred between 2002 and2003, including the severe acute respiratory syndrome corona virus (SARS-CoV), H1N1 influenza in2009, and the Acute Respiratory distress syndrome corona virus (MERS-CoV) in 2012, have had a substantial influence on world health in the last two decades.

THE EPIDEMIC'S PROGRESS AND PRESENTSTATE

Multiple cases of pneumonia with an unknown aetiology have been recorded in the Chinese city of Wuhan since December 2019. The sickness was determined after they shared a history of exposure to the Huanan seafood market in Wuhan, it was determined to be an acute respiratory illness caused by a novelCoV. To date, a number of patients who have never been exposed to the seafood market in Huanan has risen dramatically. Furthermore, some instances have surfaced that have no prior history of travel to Wuhan[32]. These early signs show that human-to-human transmission is possible.

ORIGIN OF SARS-COV-2

Although the first cases were connected to the Huanan seafood market in Wuhan city, the initial source of SARS-CoV-2 is still unknown. Aside from seafood, the Huanan seafood market is said to have sold wild animals such as birds, snakes, marmots, and bats, according to social media reports. Samples from the environment acquired have come from the marketplace found to be positive for the newly discovered CoV, although the exact species has yet to be identifying [55]. Bats may be an intermediate host for SARS-CoV-2, according to several recent research [51-53]. SARS- all CoV-2's nucleotide sequence of a bat CoV genome is 96 percent equivalent. [50]. Pangolins have been used to isolate SARS-CoV-2 and the isolated pangolin CoV genomes have a similarity to SARS-CoV-2 of 85.5–92.4 percent, suggesting that pangolins Severe acute respiratory could use it as an intermediary host. [51].

SEVERE ACUTE RESPIRATORY TRANSMISSION PATH

The new CoV is allowed to passed from one person to that other by respiratory tiny droplets. It's worth emphasising that the respiratory tract isn't likely to be the sole way for the virus to spread. Severe acute respiratory is a virus that can cause SARS which is potentially transmission by close contact. Severe acute respiratory, for example, could be spread by mucous membranes in the eyes, mouth, or nose, either wholly or partly. [48-50]. Aerosol transmission is also a viable option in a reasonably contained setting with long-term exposure to high aerosol amounts. Furthermore, COVID-19 patients have been observed to experience gastrointestinal problems such as vomiting, nausea, and diarrhoea [48]. Furthermore, it is unknown unless Severe acute respiratory may be transmitted vertically from mother to newborn or through breast milk.

POPULATION AT RISK

SARS-CoV-2 affects people from many walks of life. The elderly, persons with underlying disorders, and people with a weakened immune system are more susceptible to develop incidents of extreme severity [47]. SARS-CoV-2 infected pregnant women and neonates are also at risk of developing severe pneumonia [41]. As a result, these at-risk patients should be prioritised in the prevention and treatment of SARS-CoV-2 infection.

INCUBATION PERIOD

The incubation time of SARS-CoV-2 is estimated to be 3–7 days (range, 2–14 days) [52], showing that SARS-CoV-2 has an extended Severe acute respiratory transmission time latency was thought to be comparable to that of other human CoVs, such as non-SARS human CoVs (mean 3 days, range 2–5 days) [50], SARS-CoV (mean 5 days, range 2–14 days) [46], and MERS-CoV (mean 5.7 days, range 2–14 days) [48]. Furthermore, it has been reported that asymptomatic COVID-19 patients can effectively transmit SARS-CoV-2 [45]during their incubation periods [47], which differs from of the Acute respiratory syndrome in that The majority of Severe acute respiratory cases are caused by 'superspreders' During the time of incubation, Severe acute respiratory infections cannot infect vulnerable people. Findings clearly justify moreover WHO's introduce active monitoring time period 14 days.

SARS-BASICCOV-2'S REPRODUCTIONNUMBER (R0)

The basic reproduction number, which is commonly represented as R nought, is a highly significant threshold connected to the virus's transmissibility (R0). An infection's average percentage of subsequent infections infected individual can be implicitly defined as the R0. If R0 is more than one, it is thought that the number of infected patients will grow exponentially, resulting in an epidemic or even a pandemic. Liu et al. looked at the R0 of SARS-CoV-2 and discovered that it ranged from 1.4 to 6.49, with a mean of 3.28 [48], which is greater than the R0 of SARS-COV (R0 of 2~5).

CLINICAL PRESENTATION

Fever, dry cough, myalgia, and dyspnoea are the most prevalent symptoms of COVID-19 during the start of the disease, with Headache, runny nose, sore throat, vomiting, and diarrhoea are all symptoms of nasal congestion being less common. Dyspnoea and/or hypoxia are common in severe patients 1 week following the onset, followed by ARDS, septic shock, and a tough situation -to-correct metabolic acidosis, and coagulation failure. Severe and critical patients may only have a low fever or no visible fever, while mild patients may only have a low fever, mild fatigue, and no pneumonia [48]. SARS-CoV-2 can spread between humans in asymptomatic or mild cases.

MECHANISM OF ACTION OF CORONA VIRUS

Corona virus, one of the viruses that cause the common cold, has infected humans for a long time. Coughing, sneezing, and touching an infected surface are the primary sources of infection since it is a contagious viral infection that can be disseminated through inhalation or ingestion of virus droplets. The corona virus genome is about 30000 nucleotides long Nucleocapsid (N) protein, Membrane (M) protein, Spike (S) protein, and Envelop (E) protein are four structural proteins, and additional non-structural proteins (nsp) are also encoded (Figure 1). The capsid is a protein shell that contains nuclear capsid (N-protein), which is attached to the virus's single positive strand RNA and allows it to hijack human cells and turn them into virus factories. The N protein covers the viral RNA genome and is necessary for replication and transcription [53]. In MHV and IBV virions, the N-terminal of the N protein binds to genomic and sub-genomic RNAs and processes viral replication and transcription

EFFECT OF IMMUNOMODULATION TOWARDS TREATMENT OF COVID-19

ANTIMALARIALS

Anti-infectious drugs like chloroquine (CQ) and hydroxychloroquine (HCQ), which were first used as anti-malarial drugs before being used as immunomodulatory treatment for autoimmune and rheumatic diseases like SLE and rheumatoid arthritis, have shown a potential antiviral effect against SARS and avian influenza H5N1. Their activities are linked to the change in cell membrane pH that is essential for viral fusion, as well as interference with viral protein glycosylation.

INTERLEKIN-6 BLOCKADE [ANTI-IL-6]

Tocilizumab (TCZ) is an anti-human IL-6 receptor monoclonal antibody that binds to both sIL-6R and mIL-6R and blocks signal transmission. The plasmatic levels of IL-6 were found to be significantly elevated on COVID-19 individuals with severe cases. In a biopsy sample from a severe COVID-19 patient, histological evaluation of lung tissue revealed extensive alveolar destruction interstitial mononuclear inflammatory infiltrates and cellular

fibromyxoid exudates, indicating significant immunological injuries [54]. For Severe acute respiratory patients in bad way pulmonary consequences, TCZ has been now accepted.

INTERLEUKIN-1 BLOCKADE (ANTI-IL-1)

Anakinra, an anti-IL-1 drug, is another treatment option for people with severe acute respiratory COVID-19. It's a recombinant protein that blocks the human interleukin 1 receptor that's been significantly tweaked (IL-1Ra). It's a protein produced spontaneously Binds to IL-R and controls its activity in monocytes and tissue macrophages. Inflammatory responses are inhibited when IL-1 is inhibited [51]. In a phase 3 randomised controlled studies in sepsis, IL-1 blocking (anakinra) was shown to improve survival without increasing adverse effects [53]. Because severe infection as well as systemic infection COVID-19 have a similar "cytokine storm," anakinra may be useful in the treatment of some severe or refractory cases.

INTERLEUKIN-2 INHIBITION:

The cyclosporine-cyclophilin A complex inhibits calcineurin, a calcium/calmodulin-dependent phosphatise that is considered to prevent rejection of organs by inhibiting it synthesis of TNF- and interleukin 2 are pro-inflammatory cytokines (IL-2). Cyclosporine A (CyA) has been shown to be particularly effective in the treatment of autoimmune illnesses as a result of these effects. Experimental studies have shown that cyclophilin inhibitors, such as CyA, have an SARS-CoV inhibitory impact via inhibiting the calcineurin signalling pathway, which is also critical in SARS-CoV viral replication.

JANUS KINASE PATHWAY [JAK] INHIBITION:

In COVID-19, JAK inhibition may alter both inflammation and cellular viral entry. As a result [51], Richardson et al. suggested that baricitinib could be used to treat SARS-CoV-2 infection-related acute respiratory illness. The Janus kinase 1/2 inhibitor ruxolitinib, which is currently licenced by the FDA in the United States for the treatment of primary myelofibrosis, polycythemia vera, and rheumatoid arthritis [55], has been tested in a mouse model of HPS. Ruxolitinib was given to mice with HPS symptoms, which resulted in improved symptoms and a quick drop in blood TNF- and IL-6 values. This favourable rewards Clinical trials in individuals to treat autoimmune or inflammatory-based disorders could be undertaken swiftly using an off-the-shelf, commercially accessible medication [53]. As a result, a ruxolitinib clinical trial in patients with SARS-CoV-2/COVID-19 has begun, with promising preliminary results.

CONCLUSION

COVID-19 is becoming more widely recognised as a viral replication and host inflammatory response syndrome. Effective pharmaco-immunomodulating therapies may be able to slow the evolution of COVID-19, especially in the latter stages. Several immunomodulators are being developed or repurposed in light of COVID-19's immunological dysfunction and lymphopenia [51-55]. Prostaglandin D2 (PGD2) is one possible target, as it is naturally elevated in the airways of the elderly, and is further augmented by SARS-CoV RNA, which stimulates the promoter of the cyclooxygenase (COX) genes. By activating through the DP2 (CRTH2) receptor, PGD2 is thought to play a key role in dampening the host immunological response to the virus.

With so many novel targeted medicines in the works, more choices for COVID-19 treatment may become accessible. Recent research suggests that hydroxychloroquine and chloroquine may not be useful in the treatment of COVID-19, and that the medications' known and prospective benefits do not balance their known and possible hazards. Low-dose dexamethasone (6 mg orally or intravenously once daily for 10 days) has been proven to reduce fatalities by one-third in patients on mechanical ventilation and one-fifth in patients receiving only oxygen. Future research should concentrate not only on the most effective immunomodulatory techniques, but also on the best times to use them in order to maximise therapeutic efficacy.

FUTURE PERSPECTIVE OF IMMUNOMODULATORS

Immunomodulators' future relevance in medical practise has yet to be determined. The big question is whether these new compounds will make a big difference in transplantation or in the treatment of diseases like cancer, AIDS, and autoimmune diseases, or if they'll just be a nice bonus. The immune system is explained as a background to the discussion of immunomodulating agents, with a focus on the roles of T and B cells, macrophages, phagocytes, human leukocyte antigen, and the complement system. The cytokines, notably the lymphokines, are given special attention. Immunosuppressive medications, such as FK 506 and rapamycin, are classified as immunomodulators; immunostimulating agents, of which BCG vaccination is the most important; and remaining immunomodulators, which include biological response modifiers, are classified as immunomodulators.

It is apparent that immunomodulation has advanced significantly, both in terms of the sophistication of immunomodulating substances and in terms of our grasp of the basic principles that underpin the discipline. Indeed, immunomodulators have progressed from their early status as vaccine adjuvant to being recognised as stand-alone therapies. Beyond CpGs, the next logical step in the field's evolution would be to design orally available small compounds that avoid the less desirable proinflammatory cytokine responses. Small molecules are preferred by the pharmaceutical industry in medication development because they are inexpensive to produce and frequently available orally, however they haven't appeared as swiftly as expected in immunomodulation. However, the scale of recent acquisitions in the industry suggests that the financial drivers for such innovations are growing, and there is little doubt that tiny molecule technologies provide limited options for growth and exploitation.

As a result, immunomodulation is moving from the relative obscurity of vaccine adjuvants to mainstream therapy, as evidenced by these immunomodulator agreements from the first half of 2005. The interest of big pharma is growing, and investments are being made. This is unsurprising given that this class of compounds has the potential to treat a wide range of diseases, including cancer and viral infections, with minimal interaction or interference with other drugs. The idea of 'powering up' the immune system is appealing, and it will become more so when new classes of small molecule drugs enter the market and demonstrate their efficacy in the clinic.

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TABLE 1 IMMUNOSTIMULATORS:

FAMILY	DRUG	PHARMACOLOGILCAL EFFECT
Bacterial and fungal products	Bacillus Calmette-Guerin(BCG)	Activation of macrophages(APC), NK cells and B lymphocytes
	Lipopolysaccharides(LPS)	Activation of macrophages and B lymphocytes
	Propionibacterium	APC, Phagocytes, Activation of Tc and B Lymphocytes
	Muramyl dipeptide(MDP) L-MTP-PE	Activation of macrophages (APC and phagocytosis) Activation of macrophases(APC and phagocytosis)
	Glucan	Phagocytosis
Thymic factor	Thymosins	Maturation of thymocytes into T lymphocytes
Synthetic drugs	Levamisole Isoprinosine	Maturation and activation of T lymphocytes, phagocytosis, and chemotaxis Proliferation of T lymphocytes; activation of Th, Tc,NK, phagocytosis and chemotaxis
Polyclonal antibodies	Specific antibodies	Triggering effector phase of specific immunity agents various antigents
Vaccines	Antigens	Triggering of specific immunity(phase of recognition ,activation and effector

TABLE 2: IMMUNOSUPPRESSANTS

FAMILY	DRUG	PHARMAACOLOGICAL EFFECT
Drugs that bind to immunophilins	Cyclosporine A, Tacrolimus and Sirolimus	Inhibition gene transcription of cytokines(e.g.,II-2) in T lymphocytes(blocking their proliferation), inhibition of cytokines of T lymphocytes.
Glucocorticoids	Prednisone and dexamethasone	Inhibition of transcription of cytokines into T lymphocytes and macrophages
Antilymphocyte antibodies	Polyclonal antibodies Anti-thymocytes	Triggering effector phase of specific immunity against lymphocytes
Monoclonal antibodies	Muromonab(OKT3) Anti-cytokines and anti-receptors	Destruction of CD3+cells(T lymphocytes), Neutralization or destruction of molecules of the immune system
Cytostatics	Azathioprine, Cyclophosphamide, Mophetil mycophenolate and Leflunomide	Inhibition of cell proliferation, Inhibition of proliferation of T & B lymphocytes, Inhibition of cell proliferation

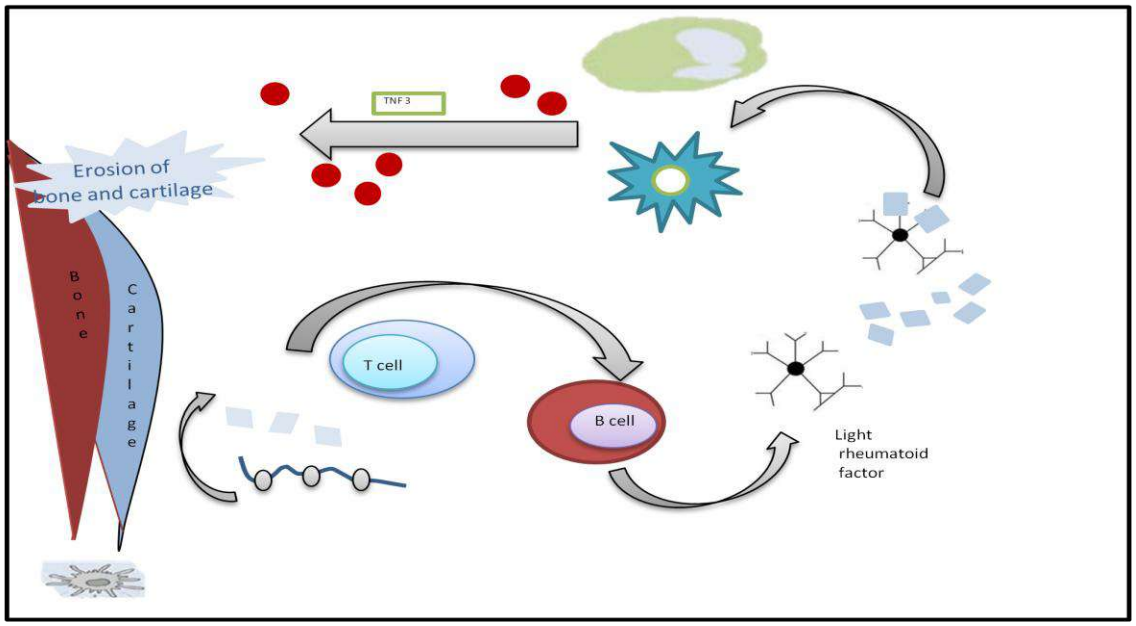

FIG.1. Inflammation in the Rheumatoid Joint. Antigen-presenting cells absorb exogenous antigens. Phagocyte cells such as dendritic cells and macrophages, as well as B lymphocytes, are among them (B cells). Polymorph nuclear leukocytes and macrophages are stimulated to produce cytokines.

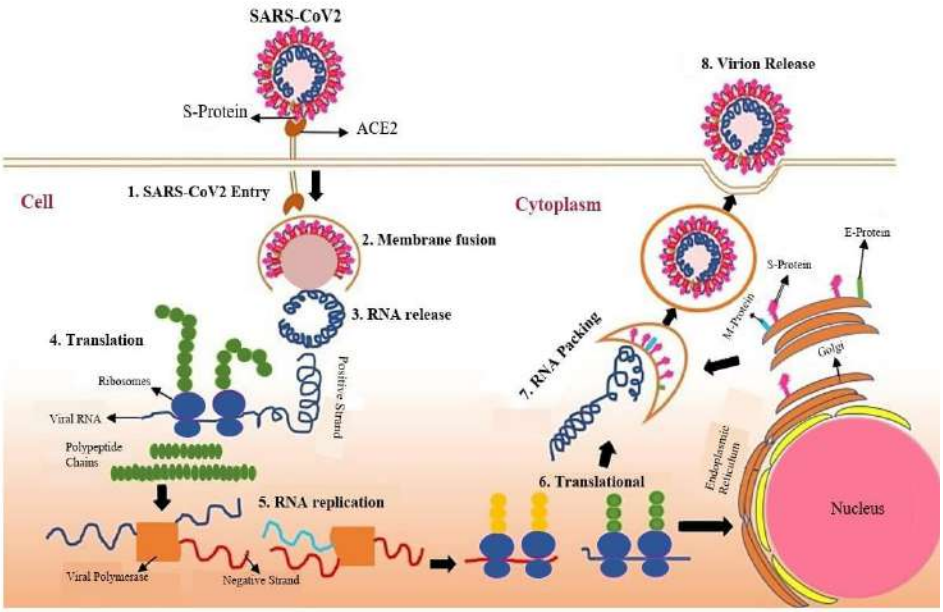

FIG.2- In a human cell, the pathway of covid19 entrance, viral replication, and viral RNA packaging is depicted schematically.

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RESEARCH ARTICLE

A Comparative Study of Soil Bacteria in Compost and Vermicompost Manure: Review

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ABSTRACT

Vermicompost is an essential nutrients which improvised soil quality and plant growth. Vermicompost is generated from organic waste. In vermicompost many microorganisms like bacteria, fungi, rotifer and macro-organisms like earthworms are playing major role. By the combining action of earthworm and microorganisms vermicompost is generated. Compost is a nutrient rich soil in which oxygen, water, organic materials and microbes are present. It is made up of by mixture of some ingredient like green manure, food products, lawn clippings twigs and dry leaves. Compost keep the soil moisture and its natural health at a high level. Both compost and vermicompost helps in improvement of the soil. Both provide sufficient nutritional elements to the soil. They helps the soil to fight against disease and control weeds. But vermicompost is better than compost as both earthworm and microorganisms are involved to form it. Vermicompost have many nutrients which along with potassium, calcium, magnesium etc. Vermicompost can be used to aid sustainable farming as well as the safe management of agricultural, industrial, household and medical waste.

Keywords: vermicompost, microorganisms, macro-organisms, earthworms, compost

INTRODUCTION

Composting is currently one of the most recommended techniques for recycling nutrients from organic matter (Aguelmous et al., 2019), as opposed to landfills and incinerators, because it may substantially minimise the processing cycle and recover nutrients from organic waste more efficiently (Kulkarni et al., 2019, Fernandez et al., 2018). In China, around seventy six percent of agriculture and livestock manure received by livestock production was composted in 2015 (Liu et al., 2020), which can contribute to promoting the organic fertiliser sector and development platform nutrient circulation. Even though promising results have been obtained in composing research. When microbes transform complex materials into finally beneficial products in the fermentation process,

by-products such as ammonia (NH3), carbon dioxide (CO2), methane (CH4), nitrogen oxide (N2O), and others contaminate the atmosphere, there is still a substantial difficulty. (Li et al., 2020, Faverial et al., 2016). Compost is a nutrient rich soil in which oxygen, water, organic materials and microbes are present. It is made up of by mixture of some ingredient like green manure, food products, lawn clippings twigs and dry leaves. Compost keep the soil moisture and its natural health at a high level.

Vermicomposting has been described as a cost-effective, practical, and quick method for efficiently utilising organic wastes and crop residues. Vermicomposting is the non-thermophilic biodegradation of organic matter by earthworms and microorganisms working together (Suthar et al., 2009). Earthworms have been said to act as mechanical blenders. Earthworms break down organic matter, changing its physical, chemical, and biological properties while gradually lowering the C: N ratio. It provides a large surface area of organic compounds, making it more accessible to microbes and thus more favourable to further deterioration (Yadav et al., 2011, Dominguez et al., 2017). Vermicomposting is quicker than traditional composting because the debris goes through the guts of earthworms, which speeds up the process. The products of earthworm castings (worm manure) are high in plant growth regulators, microbiological activity, and pest repellent properties (Gandhi et al., 1997).

Role of earthworm

Garbage can be transformed into "gold" by earthworms. Because they can absorb a wide variety of biological substances, Charles Darwin referred to earthworms as the "unheralded warriors of mankind". Aristotle referred to them as the "intestine of the earth" (Martin 1976). Earthworms are important players in carbon cycling, soil formation, cellulose degradation, and humus accumulation. All properties of soil are influenced by earthworm behavior. In contrast to traditional composting, earthworms' guts contain a variety of microorganisms, enzymatic, and hormones that aid in the rapid decomposition of partially digested materials, transforming them into vermicompost in a short period of time (almost 8 weeks), as opposed to traditional composting, which relies solely on microbes and thus needs a lengthy time period for compost development.

Characteristics of *Eisenia fetida*

1. Red wiggler (according to the warms dark colours), brand-ling warm (according to the movement of shaking or thrashing), dung warm (related to one of the heats typical habitats) or tiger warm are some of the names given toit (due to strip).
2. *Eisenia fetida* is the scientific or binomical name for this species. When these worms are handled harshly, they release a foul, pungent liquid, hence the epithet fetida, which meaning unpleasant or foul odorous.
3. It is the tiniest of all the earthworm species on the planet.
4. It has a long, tubelike body with a slick exterior.
5. Inside the body, there is a simple closed circulatory system and two main blood vessels.
6. The tube contains the digestive system.
7. The body is made up of parts that narrow as they approach the front.
8. Its changing red and shine stripes differentiate it from other worms.
9. This species, like all earthworms, is a hermaphrodite, which means it has both male and female reproductiveorgans.
10. Their numbers are rapidly increasing.

Role of bacteria in compost

Composting is an aerobic process involving a crucial microbiota that rapidly decomposes compostable and putrescent waste products in wet, self-heating, and aerobic conditions. Microbial community structure refers to the composition of a microbial community as well as the abundance of its members (Friedrich et al., 2011). During the composting process, bacteria and fungi from the composting area's microbial variety are actively

involved. Various bacteria and fungus can have a positive or negative impact on the composting process. Their diversity also indicates at the workings of the composting systems. Microbial populations and composting output can be affected by

changing the kind and quantity of beginning organic waste (Franke-Whittle et al., 2014). Physical elements including oxygen, heat, relative humidity, and food availability influence the microbial community diversity and development during composting (Leow et al., 2018).

Physical metrics are critical for understanding the activity of various microbe groups, which will reflect the quality of the composting process' end result (Bohacz et al., 2019). Many collected garbage in Scandinavian nations during the initial phases of the composting process have a low pH, which correlates to a large concentration of lactic acid bacteria. Anaerobic digestion (Sturmer et al., 2020) which uses biogas production from food waste, as well as waste management and nutrient recycling, is another excellent method for composting. The microbial population is involved with breaking down large organic materials into carbohydrates, lipids, and proteins, which are subsequently hydrolyzed into permanent, simple elements of carbohydrates, long-chain fatty acids, and amino acids by enzymes including protease, lipases, cellulase, and amylase (Lauwers et al., 2013). By showing the decomposition of organic matter and nitrogen changes that occur during composting, quantifying enzyme reactions can provide knowledge on the maturation of composted materials. The rise and fall in temperature during composting is triggered by this entire decomposition process, which defines the types of bacteria. This is something that can happen at any point during the composting process.

Role of bacteria in vermicompost

In their gut, earthworms have 'nitrogen-fixing' and 'decomposer bacteria,' which they excrete as well as minerals in their faeces (Singleton et al. 2003). Earthworms stimulate and accelerate microbial activities through increasing the population of microbes, microbial populations and organic matter (Edwards and Bohlen 1996), and increasing aeration through digging operations. Vermicomposting has a variety of effects on the waste's original microbial ecology. Vermicompost had a lot of Actinobacteria and Gammaproteo bacteria, but conventional compost had a lot of Alphaproteo bacteria, the taxonomic groups of bacteria found in non-cured compost (Vivas et al. 2009). Nitrobacter, azotobacter, phosphate solubilizers were among the bacteria found in greater than 10- 10/ g of vermicompost (Suhane 2007). In the worm-treated compost, there was a significant rise in total viable number of actinomycetes and bacteria, according to several observations. The boost in microbes population could be because of the earthworm's digestive tract's favourable conditions for microbe growth, as well as the consumption of nutrient- dense organic wastes that give energy while also serving as a microorganism growth substrate (Tiwari et al. 1989). The fact that the earthworm alimentary canal or burrow has different microbial community structures than the soil is supported by differences in microbial species, numbers, and activity. In earthworm guts, casts, and burrows, specific phylogenetic groups of bacteria have been found in higher numbers.

Vermicompost enhance soil fertility due to the action of microbiology

Because of its micro and macro components, vitamins, enzymes, and hormones, vermicomposts can have a considerable impact on plant development and productivity (Sinha et al. 2009). Vermicomposts have a high specific surface area, which gives many platforms for microbial growth and strong nutrient retention, and contain nutrients in plant-available forms such as nitrates, replaceable phosphorus, soluble potassium, calcium, and magnesium (Edwards 1998). By introducing beneficial bacteria to the soil, vermicomposts boost biological fertility. Earthworm mucus promotes competition and antagonism among distinct microbial populations, As a result, antibiotics and hormone-like biochemicals that help plant development are produced (Edwards and Bohlen 1996).

Vermicompost enhanced plant growth

Because of their high nutritional content and increased microbial and antagonistic activity, vermicomposts are becoming more popular as biofertilizers. When utilised as a media supplement, vermicompost derived from a variety of parent materials such as food waste, bovine manure, pig manure, and so on boosted seedling growth and increased crop productivity in a variety of crops (Atiyeh et al. 2000c). Vermicompost increased the germination, development, flowering, and fruiting of a range of green house vegetables and ornamentals, including marigolds, pepper, strawberries, and petunias, when applied to soilless bedding plant media (Chamani et al. 2008).

NPK value in vermicompost

N2, which makes up 78% of the atmosphere, is inert and unavailable to plants, but it can be fixed in this form by bacteria that live as symbionts with leguminous plants. Soil organic matter contains around 5% organic nitrogen andis therefore the most biologically active terrestrial stock.

C/N ratio- Because carbon and nitrogen are two of the most crucial ingredients for cell growth, a suitable carbon-to-nitrogen ratio is critical to the vermicomposting process' effectiveness. There is no predetermined C/N ratio for vermicomposting. That feed substrate, earthworm species, intended end result all influence the ideal C/N ratio. According to Ndegwa and Thomson, lower Vermicompost increased the germination, development, flowering, andfruiting of a range of green house vegetables and ornamentals, including marigolds, pepper, strawberries, and petunias, when applied to soilless bedding plant media, lowering the C/N ratio increased earthworm biomass production, while raising the C/N ratio produced a more stable end-product (Ndegwa et al., 2000).

Physical parameter related with microbial activity during vermicompost

Moisture content-The amount of moisture in the soil affects the growth of earthworms. Low moisture levels can have a big impact on earthworm survival and reproduction (Wever et al., 2001). The amount of moisture preferred by earthworms depends on the feed material. When employing cow dung for vermicomposting, Reinecke and Venter (1987) propose a moisture level of 65 to 70%. For vermicompost biosolids, Ndegwa and Thomson (2000) used a moisture content of 75%.

Temperature - Temperature has an impact on earthworm reproduction and growth (Wever et al., 2001). Temperatures between 15 and 20 degrees Celsius are thought to be ideal for vermicomposting (Wever et al., 2001). Edwards found that vermicomposting at 15 ^{0}C and 20 ^{0}C grew *Eiseniafetida* substantially better than vermicomposting at 10 ^{0}C.

Light -Worms that compost want a gloomy atmosphere. They are moving away from the light and toward the darkness. One of the characteristics that distinguishes earthworms from vermicastings is their aversion to light.

CONCLUSION

From the review it is studied that the vermicompost is more organic and consist of beneficial microbes as compare to natural compost. But in this review work, it was observed the role of *Eisenia fetida* during vermicomposting that enhance the soil quality by allowing mass of bacteria as compare to compost. The region of the vermicompost is enhanced with soil bacteria due to the activity of earthworm that maintain the physico-chemical parameters of soil. Based on this, the present work focus on the soil bacterial analysis that enhance during vermicomposting of industrial wastes by using *Eisenia fetida.* This present work is relevant to the SDG no. 11- Sustainable cities and communities and SDG no.-15-Life on land.

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RESEARCH ARTICLE

Impact of Plastic Mulching on Production of Cereals

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ABSTRACT

Plastic film mulching has a significant impact on agriculture leading to enhancement of soil temperature and maintenance of soil water along with management of weeds population**.** In certain areas, this has eased soil salinity by restricting the evaporation and capillary movement of ground water and thus, accumulation of salts on the top soil is checked. Plastic mulch not only influences on soil temperature as well as soil water, but also effects on bulk density and aggregate stability. The flourish of plants and productivity are additionally influenced by the mulching because it alters the soil microclimate. Research carried out on plastic mulching on performance of cereals also showed beneficial effects by maintaining soil moisture and weeds reduction that eventually reflected into greater water use efficiency (WUE)as well as higher water productivity. Productivity enhancement of major cereals, namely, maize and rice were noted under plastic mulching. Despite the fact of numerous benefits, high preliminary expenditure, evacuation and removal of plastic, and presence of leftover plastic in soil are major constraints recorded by the users. To conquer the constraints, biodegradable mulch films can be considered which are ecologically friendly also.

Keywords: Plastic mulch; types, advantages, limitations, rice, maize

INTRODUCTION

In the present context of growing human population, the need of resources for food production is increasing day to day(Maitra *et al*., 2019a, 2021; Mohanta *et al*., 2021).Water is an essential resource for agriculture and inappropriate use of water caused pollution and shortage. The arid and semi-arid regions of the world are having water scarcity which is a severe problem for enhancing the farm output (Zaman *et al*., 2017; Brahmachari *et al*., 2018).Further, these regions represent two-fifths of the farm land of the world supporting one-third of the human population of the globe (Farooq and Siddique, 2016).Therefore, farm productivity these regions are important to ensure food as well as

nutritional security for majority of the human population (Maitra, 2020; Das *et al*., 2021). Resource optimization is a vital factor in for crop production indryl and and resource-poor areas (Samadder *et al*., 1997; Sarkar *et al*., 1997; Yin *et al*., 2016) that is important in agricultural sustainability (Gan *et al*., 2013; Pramanick *et al*., 2018). In these regions, mulching can play a key role in resource optimization and improving agricultural productivity (Ghouse Peera *et al*., 2020; Singh *et al*., 2021).Mulching with plastic film restricts water loss from the soil in the form of evaporation (Mondal *et al*., 1997; Zhao *et al*.,2014; Maitra and Zaman, 2017).

The fresh water availability in the world is about 45 thousand cubic km of which about 70% is used in agriculture. The growing population of the world requires 60 percent more food by 2050 (UN, 2022) and obviously for increasing farm output, there will be more water needs than the current level. Most of the Indian agriculture is of cereal-based cropping system. If we look into the rice (*Oryza sativa* L.) cultivation scenario, it is observed that92% of paddy is produced and consumed in Asia (IRRI, 2021). Major cereals such as rice, wheat (*Triticum aestivum* L.) and maize (*Zea mays* L.) are considered as important staple food crops across the globe. In Asia, rice is main source of dietary calorie for about 700 million population who are living in the rice producing tracts and rice plays a prime role as source of calories. Rice requires a fairly good quantity of freshwater because the crop is widely cultivated under flooded and water stagnated situations(Bouman *et al*., 2003). In the Asian countries, flood irrigation is a common practice in rice cultivation and the crop shares more than 45% of freshwater resource(Barker *et al*., 1999). Further, industrialization and urbanization are also in increasing pace which created an enhanced requirement of freshwater (Ghatak *et al*., 1997; Wang *et al*.,2010; Midya *et al*., 2021). Hence, water saving methodologies for crop cultivation has to be adopted (Maitra and Pine, 2020) in order to prevent the rapid water degradation and to ensure the demand of cereals to meet the food needs. Under these consequences, cultivation of cereals under plastic mulch can emphasize the water productivity and enhance the yields of cereals. Further, under plastic film mulching conditions incereal production, limited or micro irrigation system is followed (Santosh and Maitra, 2021; 2022). Broad-bed and furrow, and drip irrigation are common practices under plastic mulching. The present article focused to review the earlier research carried out on plastic mulching in cereals and the article, further, addresses the issues related to SDG 1 (no poverty), SDG 2 (zero hunger), SDG 6 (clean water and sanitation) and SDG 15 (life on land) as mentioned by the United Nations (UN, 2022).

Advantages of plastic mulch

Mulching with plastic or polyethylene was first distinguished to enhance soil temperature in 1950 (Emmert *et al*., 1957). It has the capability to alter the microclimate of the crop field by changing the soil energy balance(Tarara, 2000). Modification of the microclimate causes changes in soil temperature there by affecting plant growth and yield (Ibarra-Jimenez *et al*., 2006). Several types of plastic mulches are available in which they are having unique usage in various agriculture practices. Various types of mulches are available which alter soil radiation resulting in an adequate amount of light penetration into the soil, weed control, pest control and soil solarization (Figure 1). Black and colored mulches also have the properties of increasing soil temperature (Ham *et al*., 1993).Plastic mulches modify the solar radiation falling on the ground and thus impact on the microclimate in the crop environment, help in retention of soil water and check soil erosion caused by water and wind (Liakatas *et al*., 1986).

Plastic mulching develops a microclimate around the plant zone which is rich in carbon dioxide content (Figure 2). Moreover, plastic mulch prevents weed germination, helps in retaining the soil moisture content by reducing evaporation loses, channelizes the plant's fertilizer intake and also prevents nutrient leaching. Under plastic mulching, soil structure remains porous with proper aeration facilities as roots can get sufficient oxygen (Liakatas *et al*., 1986).The root mass and other crop residue when decomposed under polyethylene mulch sheets, these improves organic acid content that may result in lowering soil pH leading to bioavailability of some micro-nutrients, namely, manganese, zinc, copper and iron. Plastic mulching can induce faster crop emergence, seedling vigour and faster biomass production. Mulching with polyethylene sheet facilitates early reproductive phase, producing more spikelets and number of grains per panicle in rice (Liang *et al*., 1999). The black polyethylene mulch maintained high soil water concentration than compared to non-mulching treatments. Crop yield enhancement was noted under plastic mulching in soil moisture stressed conditions and it was mainly due to enhanced WUE.

Suppression of weed growth is an important benefit of polyethylene mulching. Growth of weeds is restricted by mulch cover and germination of weed seeds is checked; and thus, plastic mulching act as a physical barrier against weeds menace (Rajablarijani *et al*., 2014). Weed control can be achieved in crop production by black coloured polyethylene sheets, solarization plastic covers and long-use plastic mulch sheets (Franquera, 2015; Ullah *et al*., 2021). Some reports showed that plastic mulch has the capability to reduce weed biomass by 63.8% in comparison to non-mulched conditions and black plastic mulch was superior to other mulches (Rajablarijani *et al*., 2014). Plastic mulching has impacts on insect-pest population dynamics. However, a study revealed that black polyethylene sheet (lower PAR reflection) and silver plastic mulch (high PAR reflection) did not show any significant variation in thrips population (Díaz-Pérez, 2010). On contrary to this, research results reported that plastic mulch attracted green pea aphids, striped beetles and spotted beetles of cucumber (Braul*et al*., 2002). Moreover, among colour of the mulching materials, white mulch sheets are efficient in reduction of the occurrence of viral disease, and presence of whiteflies, and aphids (Brown *et al*., 1992).

Plastic mulching in maize

Maize is one of the important food grain crops among cereals (Liu *et al*. 2005; Maitra *et al*., 2019b). Maize contributes 30% of human caloric intake and also performs as vital part in silage, and animal feed. Further, it is used as industrial raw material which in turn increased the area under maize cultivation (Figure 3).Keeping in view the global climate change and water availability crisis, plastic mulching can be effective as compared to open field maize production. Plastic film mulching has been generally used for further advancement in maize yields and water productivity. Research evidence proved that plastic mulching could increase the grain yield of maize by 22% over non-mulched crop (Bu et *al*., 2013).

Some studies revealed that plastic mulching significantly increased the yield attributes like number of grains per cob, cob length, cob weight and 100-grain weight than non-mulched cultivation practices (Liu *et al*., 2015).According to Xu *et al*. (2015), plastic mulching significantly affected the soil temperature and soil moisture content, there by enhanced vegetative growth, accumulation of dry matter, grain yield, and WUE. Mulching with polyethylene sheets also significantly affected grain filling and increased grain weight. Plastic mulching also significantly increased the leaf water potential of maize even with less water application (Liu *et al*., 2015). Growth, productivity and water use efficiency of maize was significantly influenced under plastic mulching in comparison to straw mulching as mentioned by Javed *et al*., (2019).

Plastic mulching in Rice

Rice is synonymous to life in India and is cultivated on 43.79 mha with a production of 168.5 million tonnes of un-milled rice (FAOSTAT, 2019; Sarathkumar *et al*., 2020; Ghosh *et al*., 2020). Plastic mulching in rice can be adopted during both rainy and non-rainy season, out of which it is easy to manage during the non-rainy months of the year (Figure 4). Mulching assumes to be a prominent technique for weed management in rice. Field studies were conducted in rice during *rabi* season to see the effectiveness of plastic mulching in various parameters of the crop which resulted as the number of weeds and weeds dry matter of rice varying greatly between mulched and non-mulched plots (Gangaiah *et al*., 2019).Mulching with plastic materials excluded the weeds growth in rice crop irrespective of its color (black/transparent). Weeds that germinated below the mulch died because of non-presence of solar radiation for photosynthesis. However, very few weeds came out from the holes of plastic along with rice-hills. Thus, a weeds population was reduced drastically in rice where mulching was done with polyethylene sheet (Gangaiah *et al*., 2019)The applied water from rice field was also saved where mulching was done and it was because of minimized evaporation and transpiration loss from soil and weeds, respectively. Also, the application of mulching in rice is affective in WUE in rice. According to He *et al*. (2013), WUE was maximum where plastic mulching was done with drip irrigation facility than conventional flooding method.

Limitations of Plastic Mulching in Cereals Production

Incorporation of plastic mulchin agriculture could be one of the major contributors of micro plastic contamination in soil (Astner *et al*., 2019). The use of polyethylene mulching is increasing daya by day and the annual growth for the enhancement on the same is about 5.6%. However, there is a chance for contamination of farmlands with the increased use of mulch sheets (Von moos *et al*., 2012). Micro plastics retained in the mulching sheets can have a negative effect on soil microorganisms (Huang *et al*., 2019), soil structure, and other physico-chemical properties(Boots *et al*., 2019).In general, the production of polyethylene mulch sheet is cost and energy intensive. Laying of mulch sheet and its removal and disposal after crop period are also labour intensive(Sideman, 2015). Plastic mulching is known to increase the soil temperature and temperate zone it is useful. However, in the tropical climatic conditions, high temperature in the root zone may be fatal during summer season (Onwuka, 2018).Moreover, the coloured mulching sheet impacts on the soil microbiota and thus, soil biological health (Helaly *et al*., 2017).Hence even if the use of plastic mulches has positive impact in increasing crop productivity and quality, care should be taken in amount, type, and rate of use of plastic mulches. The limitations are to be taken care while using the polyethylene mulch sheets.

CONCLUSION

Plasticulture is vital to Indian agriculture and as it enhances the plant microclimate. Mulching with plastic increases plant growth, quality, and yield of crops. Black and silver-coloured sheets are proved to perform better than other coloured mulching sheets. Also, the use of plastic is a fast-growing concern to the environment, hence use of biodegradable or linear low-density polyethylene (LLDPE) plastic mulching can be encouraged. Plastic mulching is a boon to farmers of arid areas as the water saving recorded from 20 to 75 %.Water saving is very crucial for arid and semi-arid regions. Similarly, yields are also considerably increased by the use of plastic mulching for which government can take initiative to enhance the more use of mulching in farm fields by subsidizing on purchase of mulch sheets and also aware the farmers about its uses and advantages.

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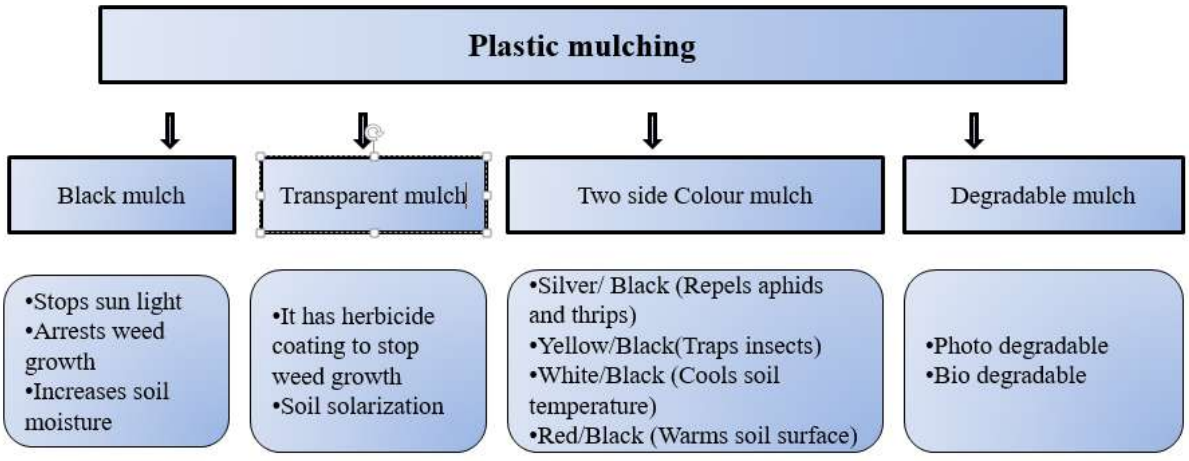

Figure 1. Types of plastic mulching with specific uses

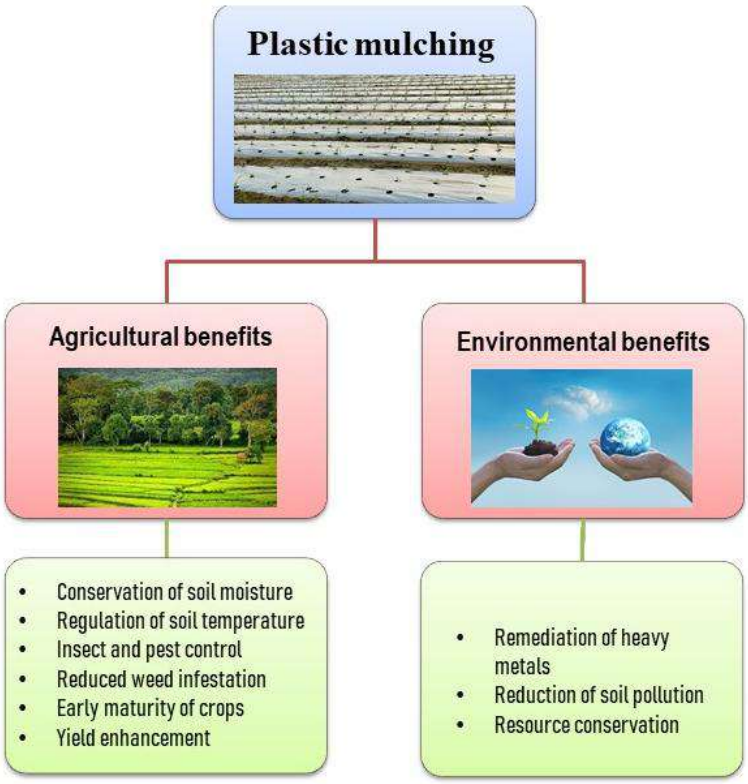

Figure 2. Advantages of plastic mulching

Figure 3. Plastic mulching in maize

Figure 3. Plastic mulching in *boro* rice

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RESEARCH ARTICLE

Effect of Manures and Biofertilizers on the Growth and Yield of the Black Gram (*Vigna mungo*)

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ABSTRACT

Biofertilizer are living microorganisms that is used for enrich the soil quality. As they are eco-friendly so these biofertilizers play a great role on enhancing the production of crop. Manures and biofertilizers are a renewable source of energy and also cost effective as compared to other chemical or inorganic fertilizers. It helps to maintain long term fertility in soil also. To increase the productivity of soil, biofertilizers and manures are used. The application of biofertilizer and manures are easy to used. It helped in eliminating pollution related problem. They also help in increasing the growth of the plant and the yield by increasing the activity of desired microorganisms in the root environment. Present study was carried out in Centurion University of Technology and Management, Bhubaneswar campus to analyse the effect of different biofertilizers (*Rhizobium* and *Azotobacter*) and different manures (Goat manures and vermicompost) on black gram (*Vigna mungo)* duringthemonthofJanuary2022. The growth and yield parameters, such as root and shoot length, fresh and dry weight of plant, no of pods per plant, no of seed per plant were analysed. The effect of *Rhizobium* bacteria with the combination of Vermicompost and Goat manure was found more on the *Vigna radiata.*

Keywords: Biofertilizer**,** inorganic fertilizers, *Rhizobium, Azotobacter,* Vermicompost

INTRODUCTION

Currently, a major issue for agricultural researchers is to eliminate the usage of costly agrochemicals and chemical fertilisers. Which has a harmful impact on both the environment and human health. Chemical fertilisers are used to replenish soil nitrogen in large quantities, but they are extremely expensive and pollute the environment (Dai et al, 2004). Biofertilizers fix atmospheric nitrogen in a form that plants can use (Chen 2006). Biofertilizers are low-cost,

renewable plant nutrients that are used in conjunction with chemical fertilisers. Biofertilizer is one of the most advanced and sophisticated agricultural technologies available. Biofertilizers are crucial since they are part of integrated nutrient management, as well as a cost-effective and sustainable source of energy for plants and a way to help reduce pollution. Due to growing demand of safe and healthy food the priority of organic farming has developed globally as well as in our country (Kalyansundaram et al. 2008) . To improving soil fertility bio fertilizers, play an important role by fixing atmospheric nitrogen. The importance and role of bio fertilizers in sustainable crop production has between studied by several authors. But their progress in the field of technology production always remained below satisfaction in Asia and Europe due to various constraints, either economically or politically and in some cases even ecologically (Kumudha et al. 2007). Rhizobia encompassed a range of bacteria genera including *Rhizobia, Prady Rhizobia Sino Rhizobia, Mesorhizobia , Allorhizobia , Azorhizobia* which are used to symbiosis of leguminous plants , to increase the productivity. Also *Azotobacter* is a genus of motil, oval or spherical bacteria with thick walled cysts used for nitrogen fixation which is important to increase the productivity. To stop the use of expensive agrochemical / chemical fertilizers currently the use of organic fertilizers or bio fertilizers was increased. It is a real challenge for the farmers to stop the use of expensive agrochemicals / chemical fertilizers. It have a negative effect on environment as well as human health.

Need of Bio-Fertilizers

Synthetic fertilisers are being used indiscriminately, resulting in pollution of the air, water, and soil. Contaminated soil and water basins kill microorganisms and beneficial insects, rendering crops more susceptible to disease and lowering soil fertility. Biofertilizers are more cost-effective and environmentally friendly over time, and they are more productive and cost-effective for smaller and average farms than chemical fertilisers (Mishra et al., 2013). Biofertilizers are microorganism like bacteria, fungi, algal strains which differ from chemical fertilizer in their mode of action. Biofertilizers has an important role to play in improving soil fertility by fixing atmospheric nitrogen and improving the quality of nutrient available in the soil thus, enhancing crop yield by natural method. Chemical fertilisers provide a similar purpose, but they do it at the expense of the ecosystem by causing severe soil d isturbance. Agriculture is India's most important economic industry.

Biofertilizers boost soilfertility naturally and do not have the same negative impact on the so as chemical fertilisers,as a result, using a biofertilizer to boost soil productivity is a necessary. (Dixit, 2013). Microorganisms play an important role in soil processes that determine the plant productivity. There are many soil microorganisms like *Rhizobium, Azotobacter, Azospirillum ,Phosphates olubilizers* (Phosphobacteria), Blue green algae, *Azolla* and *Mycorrhiza* which can be used to increase the productivity of the plants. It includes mainly nitrogen fixing and, phosphate solubilizing microorganisms (Goel et al., 1999). In the present study effect of different bio fertilizers (*Rhizobium* and *Azotobacter*) and different manures (Goat manures and vermicompost) were treated on black gram (*Vigna mungo)* Thus, the aim of the experiment was to increase the productive of the crop with the help of Biofertilizers, which is eco-friendly. Use of organic biofertilizer will reduce the risk of chemical fertilizer and the organic fertilizer also enhances the soil fertility and ensures good health of human beings and also a sustainable approach of good health.

MATERIALS AND METHODS

The seed of black gram (*Vigna mungo),* bio fertilizers (*Azotobacter* and Rhizobium) and manures (goat manure, vermicompost) are used for the experiment . The experiment was conducted during end of winter season (December 2021 to January 2022) at Centurion University of Technology and Management, Bhubaneswar, Odisha. The field is situated in a subtropical climate on North latitude 20.17 and 85.70 East longitude. The soil is red soil and it was free from pebbles and stones were filled in the pot separately. The soil was mixed with only goat manures, only vermicompost and mixed 2:1 and 1:2 ratio of vermicompost and goat manures for the experiment. The goat manures was mixed with soil in different ratio as well as vermicompost also. Untreated soil also used for this experiment as control.

After the soil prepared for sowing the seed was treatment with bio fertilizers. The black gram seed was treated with the *Rhizobium*, *Azotobacter* with the minimum amount of water to coat the seed. After that the undamaged healthy seeds were dried under shade over a clean paper and gunny bag nearly about 5 to 6 hours and showed immediately in the plastic pots with loose soil. Irrigation was done in regular time interval according the condition and the growth parameters were studied at a regular time. The plant samples were randomly observed with morphological parameters like root length, shoot length, fresh weight and dry weight of seedlings. Plants were randomly selected from each pot for recording of the root length with centimetre scale and recorded. Also plants were randomly selected for recording of shoot length with centimetre scale and recorded.

For fresh weight of seedling samples were randomly selected at regular intervals (seedling,flowering and yielding) from each pot . They were thoroughly washed with tap water and then distilled water. After that they were air dried to removed the moisture content. By using a electrical single pan balance their fresh weights were recorded (Jali et al. 2021).For dry weight the sample were kept in a hot air oven at 80°C for 24 hours . After that their dry weights were taken by using an electrical single pan balance.Hand weeding was done randomly from each pot and the number of pod per plant were counted and recorded. Pods were randomly selected from each pot and number of seeds per pod were counted and recorded. The pods were weighed by using a electrical single pan balance. The seed were weighed after removed from the seeds by using an electrical single pan balance.

RESULT AND DISCUSSION

The experiment was conducted to analyze the effect of the bio fertilizers and manures on growth and yield of black gram. The growth and yield of black gram is presented in the table 1. Better growth performance are observed in plants treated with biofertilizer as compared to the control. In general, it was observed that plants treated with biofertilizer showed significantly better growth performance in root length, shoot length and fresh weight yield parameter.

Root length

The result on the application of biofertilizer and manures on the root length of black gram at various stages of its growth (seedling, flowering, and yielding) are shown in tables 1. Significantly highest root length of 11.5 cm and the lowest root length of 2.2 cm were noted at seedling stage of the plant growth. The highest root length was found on application of *Rhizobium* with combination of vermicompost and goat manure at 2: 1 ratio and the lowest root length was found on application of *Azotobacter* and *Rhizobium* with goat manure in the seedling stage. In the flowering stage the highest root length was found with the application of *Rhizobium* with the combination of Vermicompost and goat manures with 2:1 ratio i.e. 17.5cm and the lowest root length was found with *Azotobacter* with vermicompost 500 gram/pot i.e. 5.9 cm. The highest root length at yielding stage was 18.9 which is found with the application of *Rhizobium* with vermicompost and goat manure at 2:1 ratio and the lowest root length was found on no fertilizer and no manure which is 6.1 cm.

Shoot length

The result on the effect of bio fertilizers and manures on the shoot length of black gram at seedling stage are shown in table 1 and 2. In seedling stage significantly highest shoot length 16 cm was recorded in which *Rhizobium* vermicompost and goat manure was applied. The lowest number of shoot length 9.5 cm was recorded at seedling stage in the plant. In this mixture of *Azotobacter* and *Rhizobium* was applied. In flowering stage the highest shoot length 35.9 cm was recorded in which *Rhizobium* vermicompost and goat manure was applied. The lowest number of shoot length 11.5 cm was recorded at flowering stage in the plant. In this no bio fertilizers and manures are used. In yielding stage the highest shoot length 38 cm was recorded in which *Rhizobium,* vermicpompost and goat manure was applied. The lowest number of shoot length 18,5. cm was recorded at yielding stage in the plant in which no bio fertilizers and manures are used.

Fresh weight (g/ plant)

The results on the effect of bio fertilizers and manures on the weight of black gram at various stages of it growth (seedling, flowering and yielding) are shown in the tables 1 . In seedling stage, the highest fresh weight was recorded 101.59 g/plant in which *Rhizobium* vermicpompost and goat manure was applied. The lowest number of fresh weight 92.39 g/plant was recorded at seedling stage in the plant. In this combination of vermicompost and goat manure was applied. In flowering stage, the highest fresh weight 106 g/plant was recorded in which *Rhizobium,* vermicompost and goat manure was applied. The lowest number of fresh weight 97.19 g/plant was recorded at flowering stage in the plant. In this *azotobacter* and vermicompost 500 gram/pot manures was used. In yielding stage the highest fresh weight 137.77 g/plant was recorded in which *Rhizobium,* vermicompost and goat manure was applied . The lowest number of fresh weight 104.36 g/plant was recorded at yielding stage in the plant in which *Rhizobium* and vermicompost 750g//pot was used.

Dry weight (mg /plant)

The results on the effect of bio fertilizers and manures on the weight of black gram at various stages of it growth (seedling , flowering and yielding) are shown in the tables . In seedling stage significantly highest dry weight was recorded 23.79 g/plant in which *Rhizobium* vermicompost and goat manure was applied . The lowest number of dry weight 12.41 g/plant was recorded at seedling stage in the plant. In this no biofertilizer and manure was applied. In flowering stage the highest dry weight 39.09 g/plant was recorded in which *Rhizobium* , vermicompost and goat manure was applied . The lowest number of dry weight 29 g/plant was recorded at flowering stage in the plan. In this no biofertilizer was used .Only vermicompost 250 gram /pot was used. In yielding stage the highest dry weight 64.67 g/plant was recorded in which *Rhizobium,* vermicompost and goat manure was applied . The lowest number of dry weight 57.32 g/plant was recorded at yielding stage in the plant in which *Rhizobium* and vermicompost 750g / pot was used.

Yield parameters

The yield parameter observation was shown in Table 4.The highest no of pods per plant 35.19 was found with the application of *Rhizobium* and combination of vermicompost and goat manure in 2:1 ratio while the lowest 31.19 was found in the application of *Azotobacter* and vermicompost 250g/pot Highest no of seeds per plant was found in *Rhizobium* and vermicompost and goat manure in 2:1 ratio i.e.76.39 and the lowest is 60.22 in which no organic fertilizer and manures are used.The highest weight of 100 seeds was 4.3857 g found in the application of *Rhizobium* and combination of vermicompost and goat manure in 2:1 ratio while the lowest is 3.7486 found in the combine application of *Rhizobium* and *Azotobacter* with goat manure 750 gram/pot (Table 2).

In India Biofertilizers and manures are cost effective, ecofriendly and renewable sources of plant nutrients. Biofertilizers are microbial inoculants and manures are animal extracts that enhance crop production through improving the nutrients supplier and their availibility. They are boosted not only the food production but also it shows the good effect on the environment as well as physiochemical properties of soil. It is very common that the application of biofertilizers and manures in leguminous crops, oilseeds and other important crop. According to India population India needed to produced large number if food grains. Green revolution and application of modern and smart technology can boost the productivity as per the requirement. Also application of appropriate biofertilizers and manures can reduce the cost for the farmer.

CONCLUSION

The present investigation deals with the effect of biofertilizers and manures on growth and yield of black gram *(Vigna mungo).* This experiment concludes that the application of *Rhizobium* with combination of vermicompost and goat manure in 2:1 ratio gives the best result in the black gram crop. So , in the agricultural system the application of *Rhizobium* bacteria with manures should which was more effective in the productivity. Also, this experiment help to reduce the waste of biofertilizers and manures by apply of appropriate amount of biofertilizers and manures in

the crop. The use of manures and biofertilizers in agricultural system with a particular amount should encourage by Govt. of Odisha & India for improving the productivity and stop the unnecessary use of manures and biofertilizers.

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Table 1: Morphological parameters of black gram

Sl. No.		Seedling stage				Flowering stage				Yielding stage			
	Treatment	Root length	Shoot length	Fresh weight	Dry weight	Root length	Shoot length	Fresh weight	Dry weight	Root length (cm/plant)	Shoot length (cm/plant)	Fresh Weight (g/plant)	Dry weight
1	Control	4.8	13.6	91.5	12.41	6.5	11.5	99.41	35.12	6.1	18.5	125.96	57.32
2	*Rhizobium*	6.5	15.5	93.51	13.61	8.5	32.5	101.05	36.09	9	37.6	140.05	59.39

3	*Azotobacter*	4.7	14	96.27	15.01	6.9	35	102.02	36.58	7.3	37	138.46	60.8
4	Goat manure 250 gram/pot	3.4	14	99.18	16.69	6.3	30	102.01	37.12	6.9	34	139.89	61.82
5	Goat manure 500gram/pot	10.5	13.5	100.13	17.21	17.3	33.3	101.09	34.29	18	37.3	125.69	61.9
6	Goat manure 750 gram /pot	7.3	13.5	95.13	18	13.5	38.5	101.07	38.15	14.2	35.3	138.46	58.23
7	Vermicompost250gram/ pot	11.2	13.8	94.76	15.21	11.8	33	101.18	29	12.5	38	137.16	57.33
8	Vermicompost500/pot	4.5	14	92.29	19.23	17	30	101.23	36.19	18.2	36.9	138.96	60.08
9	Vermicompost750/pot	9.5	16	91.17	17.23	6.7	33.5	101.07	35.95	7.5	35	117.98	61
10	*Rhizobium* +Goat manure 250gram/pot	5	15.2	100.59	23.79	17.5	31	106	37.58	18.9	28.27	140.35	62.4
11	*Rhizobium* +Goat manure 500gram/pot	6.3	16	93	17.18	6.3	24	100.15	37.95	6.7	24.9	138.25	61.19
12	*Rhizobium* + Goat manure 750/pot	3.7	12.4	94.15	21.12	7.5	26	101.34	38	7.9	27.2	134.23	59.69
13	*Rhizobium* +vermicpompost 250 gram/pot	4.2	14.6	96.67	16.69	8.4	36	99.78	35.05	9.1	37.2	119.91	58.76
14	*Rhizobium* +vermicpompost 500 gram/pot	4	12.6	89.95	16.23	6.2	33.3	98.92	34.18	6.6	34.7	138.64	59.1
15	Rhizobium +vermicompost 750 gram/pot	3.7	12.5	89.23	17	6.8	34.8	101.57	36.85	7.2	36.2	104.36	59.49
16	*Rhizobium* +Vermicompost 2 :Goat manure 1	11.5	16	101.59	23.79	17.5	35.9	106	39.09	18.9	38	137.77	64.67
17	*Rhizobium* +Vermicompost 1:Goat manure 2	4.7	14.8	91.21	17.55	6.2	31	102	35.61	6.6	31.6	126.11	61.32
18	*Azotobacter* +Goat manure 250 gram/pot	3.4	3.5	92.6	18.65	7.6	33	101.17	34.92	7.7	31.4	125.25	61.17
19	*Azotobacter* +Goat manure 500gram/pot	2.2	10.9	101.02	17.18	6.4	32	102.18	36.19	6.9	36.9	124.68	59.08
20	*Azotobacter* + Goat manure 750/pot	9.4	12.2	101.03	21.18	6.8	34	105.17	35.28	7.3	32.5	127.18	61.29
21	*Azotobacter* +vermicpompost 250 gram/pot	4.3	9.5	100.98	18.69	6.1	33	103.96	36.85	6.5	33.9	127.69	62.2.01
22	*Azotobacter* +vermicpompost 500 gram/pot	9.4	12.2	100.56	19.55	5.9	32	97.19	34.19	18.2	32.8	123.66	61.39
23	*Azotobacter*+vermicompo	4.2	12.5	101.56	19.25	6.7	31.8	101.9	36.51	7.1	32.9	140.5	60.14

	st 750 gram/pot												
24	*Azotobacter* +Vermicompost 2 :Goat manure 1	4	12.7	99.97	17.21	11.2	29.9	102.34	37.12	11.9	31.1	140.1	60.8
25	*Azotobacter* +Vermicompost 1:Goat manure 2	8.4	16.4	95.13	18.25	6.7	30	102.08	35.14	7.2	31.3	118.91	61.18
26	Goat manure 250 gram/pot	2.7	11.3	99.09	17.29	6.3	30.2	101.56	36.19	6.8	33.4	129.35	59.29
27	Goat manure 500gram/pot	4	9	101.91	17.56	9.9	32	102.09	36.58	10.1	32.8	130.18	60.19
28	Goat manure 750/pot	4	10	98.56	17.23	6.0	32.3	105.11	37	6.2	33.1	131.11	60
29	vermicpompost 250 gram/pot	3.2	11	99.56	16.23	6.5	30.5	101.24	36.02	6.9	31.6	130	60.52
30	vermicpompost 500 gram/pot	4.5	10.4	98.27	19.27	6.4	29	100.59	36.52	6.8	30	131.12	60.18
31	vermicompost 750 gram/pot	6.5	9.7	99.37	19.23	6.3	28	102.31	37.12	7	28.6	125.96	61
32	Vermicompost 2: Goat manure 1	4.6	10.5	96.76	19.25	6.8	35	101.11	34.09	7.2	36.2	127.19	62
33	Vermicompost 1: Goat manure 2	4.4	10.2	92.39	17.23	8.5	33.5	99.98	35.08	8.9	37.1	123.63	59.5
34	*Azotobacter +Rhizobium*	2.2	10 9	99.97	17.25	6.9	33	101.22	36.15	7.2	34.3	119	56.28
35	*Azotobacter +Rhizobium* +Vermicompost +Goat manure	9.4	12.2	100	17.22	7.2	34	101	35.8	7.6	37	120	55.86

Table 2: Effect of bio fertilizers on yield parameters of black gram at different growth stages.

Sl.no	Treatment						
	Bio fertilizers	Manure	Number of pods per plant	Number of seeds per plant	Weight of pods per plant(g)	Weight of seeds per plant (g)	Weight of 100 seeds (g)
1	No organic fertilizer	No manures	31.43	60.22	44.57	24 .03	3.7915
2	*Rhizobium*	No manures	33.46	62.14	46.59	25.31	3.8716
3	*Azotobacter*	No manures	32	64.33	49.09	32.12	3.8480
4	*Rhizobium*	Goat manure≅250 g/pot	33.13	63.17	50.96	35.19	3.9038
5	*Rhizobium*	Goat manure≅500 g/pot	33.45	68.15	60.69	34.29	3.9643
6	*Rhizobium*	Goat manure≅750g/pot	34.19	67.19	69.24	31.26	3.9079
7	*Rhizobium*	Vermicompost ≅ 250g/pot	31.69	69.39	68.67	33.16	3.8290

8	*Rhizobium*	Vermicompost ≅ 500g/pot	32.49	68.65	66.29	34.41	3.9857
9	*Rhizobium*	Vermicompost ≅ 750g/pot	33.16	69.29	69.69	33.03	4.01
10	*Rhizobium*	Combination (Vermicompost 2: Goat manure 1)	35.19	76.39	70.99	35.06	4.3857
11	*Rhizobium*	Combination (Vermicompost 1: Goat manure 2)	33.16	76.17	69.79	28.69	3.8174
12	*Azotobacter*	Goat manure≅ 250g/pot	32.50	69.18	69.79	27.62	3.9241
13	*Azotobacter*	Goat manure≅500g/pot	33.15	66.00	70.10	25.92	3.92.3
14	*Azotobacter*	Goat manure≅750g/pot	33.34	68.96	65.39	26.27	3.7270
15	*Azotobacter*	Vermicompost ≅ 250 g/pot	31.19	67.65	67.78	27.19	3.7349
16	*Azotobacter*	Vermicompost ≅ 500g/pot	32.00	67.78	69.96	28.19	3.7814
17	*Azotobacter*	Vermicompost ≅ 750g/pot	33.13	68.29	70.29	28.39	3.7966
18	*Azotobacter*	Combination (Vermicompost 2: Goat manure 1)	35.67	65.29	64.75	24.30	3.8249
19	*Azotobacter*	Combination (Vermicompost 1: Goat manure 2)	34.28	64.69	66.57	25.31	3.7383
20	*Azotobacter* + *Rhizobium*	Goat manure≅250g/pot	33.61	66.29	69.08	32.14	4.1662
21	*Azotobacter* + *Rhizobium*	Goatmanur≅500g/ pot	34.78	63.29	68.19	33.00	4.0391
22	*Azotobacter* + *Rhizobium*	Goat manure≅750g/pot	34.24	68.79	70.16	34.18	4.0749
23	*Azotobacter* + *Rhizobium*	Vermicompost ≅ 250g/pot	33.69	67.29	70.12	33.89	4.0076
24	*Azotobacter* + *Rhizobium*	Goat manure≅ 500g/pot	32.15	68.21	70.13	34.19	3.8436
25	*Azotobacter* + *Rhizobium*	Goat manure≅ 750g/pot	31.69	67.19	69.96	33.25	3.7486
26	*Azotobacter* + *Rhizobium*	Combination (Vermicompost 2: Goat manures 1)	34.28	80.92	70.00	34.80	3.9631
27	*Azotobacter* + *Rhizobium*	Combination (Vermicompost 1: Goat manure 2)	34.42	79.82	69.69	34.26	4.0155
28	No biofertilizer	Goat manure≅ 250g/pot	34.69	70.21	66.59	30.23	4.0867
29	No biofertilizer	Goat	34.79	70.42	67.12	28.18	3.9044

		manure≅500g/pot					
30	No biofertilizer	Goat manure≅750g/pot	33.00	70.19	67.69	28.58	4.1103
31	No biofertilizer	Vermicompost ≅ 250g/pot	32.92	69.79	68.96	29.24	4.0170
32	No biofertilizer	Vermicompost ≅ 500g/pot	33.13	69.21	67.79	30.98	4.2240
33	No biofertilizer	Vermicompost ≅ 750g/pot	35.00	69.22	69.63	32.16	4.0010
34	No biofertilizer	Combination (Vermicompost 2: Goat manure 1)	33.69	70.21	69.58	31.37	4.2866
35	No biofertilizer	Combination (Vermicompost 1: Goat manure 2)	31.39	69.29	70.86	32.18	3.8833

Fig .1 Control

Fig .2 *Rhizobium*

Fig. 3 *Azotobacter*

Fig .4 Goat manures 250 g/pot

Fig. 5 Goat manures 500 g/pot

Fig .6 Goat manures750g/pot

Fig .7 Vermicompost 250g/pot

Fig.8 Vermicompost 500g/pot

Fig.9 Vermicompost 750g /pot

Fig .10 *Rhizobium* + Goat manures 250 g/pot

Fig 11. *Rhizobium* +Goat manures 500g/pot

Fig 12. *Rhizobium* + Goat manures 750g/pot

Fig 13.*Rhizobium* +Vermicompost 250 g/pot

Fig 14. *Rhizobium* + Vermicompost 500g/pot

Fig 15 .*Rhizobium* +Vermicompost 750g/pot

Fig 16. *Rhizobium* +Vermicompost 2: Goat manures 1

Fig 17. *Rhizobium* + Vermicompost 1: Goat manures 2

Fig 18. *Azotobacter* +Goat manures 250 g/pot

Fig 19. *Azotobacter* + Goat manure 500g/ pot

Fig 20. *Azotobacter* +Goat manures 750g/ pot

Fig 21. *Azotobacter* + Vermicompost 250g/ pot

Fig 22. *Azotobacter* +Vermicompost 500g/ pot

Fig 23. *Azotobacter* +Vermicompost 750 g/ pot

Fig 24. *Azotobacter* +Vermicompost 2: Goat manure1

		
Fig 25. *Azotobacter* +Vermicompost 1: Goat manure2	**Fig 26. Goat manure 250 g/pot**	**Fig 27. Goat manure 500g/ pot**
		
Fig 28. Goat manure 750 g/pot	**Fig 29. Vermicompost 250g/pot**	**Fig 30. Vermicompost 500g/ pot**
		
Fig 31. Vermicompost 750 g/pot	**Fig 32. Vermicompost 2: Goat manure 1**	**Fig 33. Vermicompost 1: Goat manure2**

Fig 34. ***Azotobacter +Rhizobium***

Fig 35. ***Azotobacter +Rhizobium***

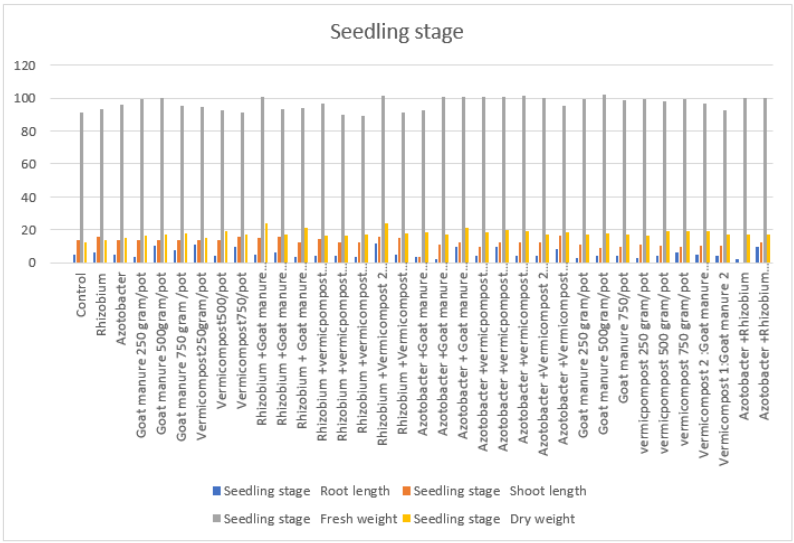


Fig 36. Graph of seedling stage

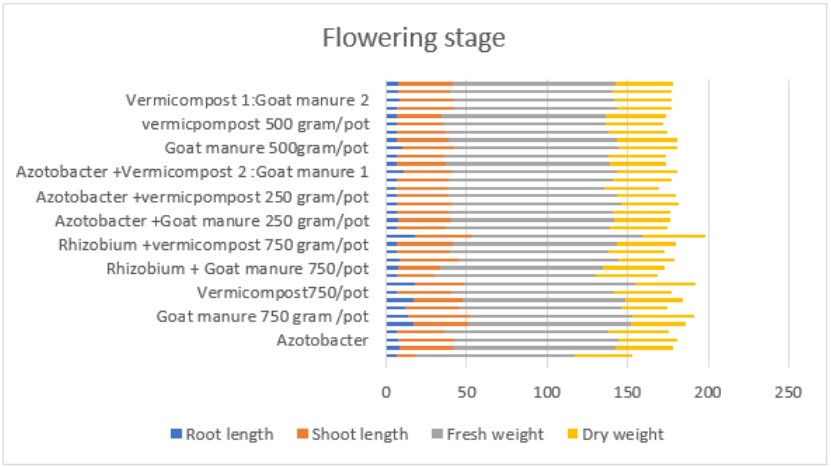


Fig 37. Graph of Flowering stage

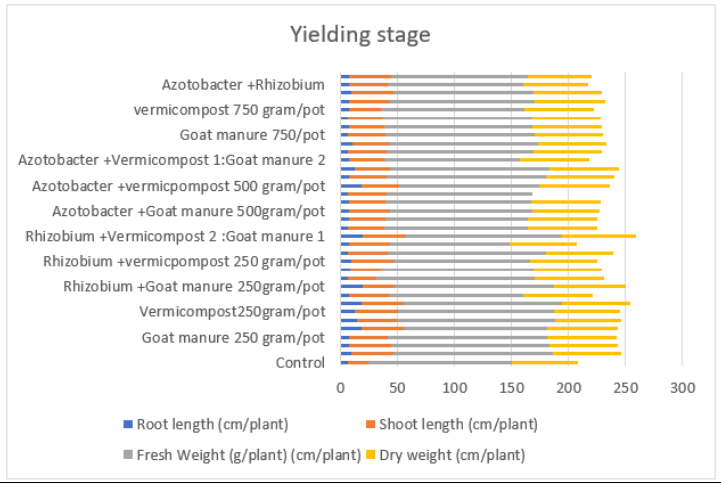
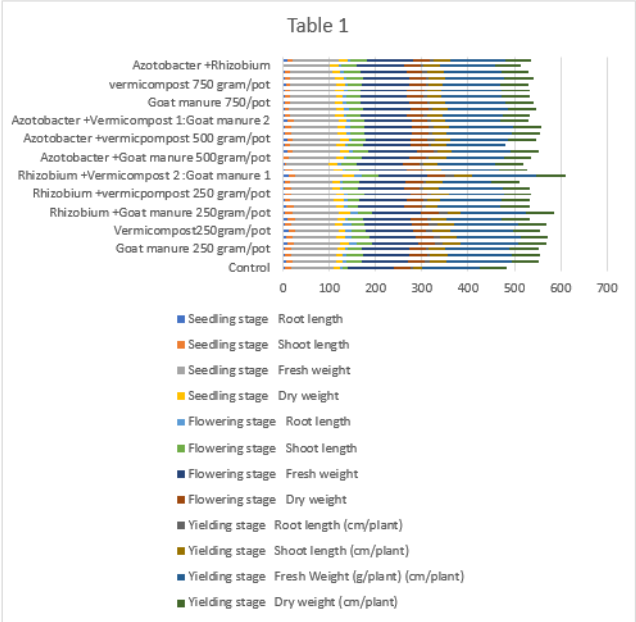
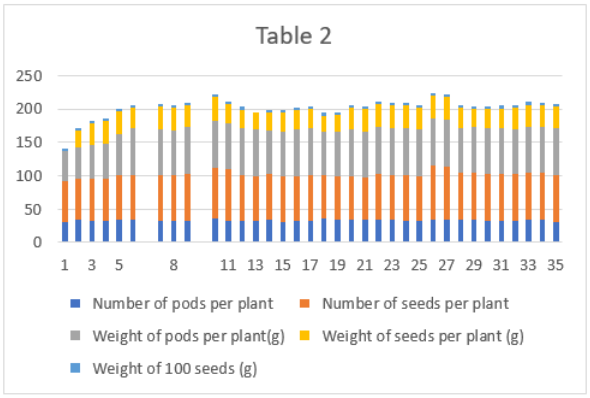


Fig 38. Graph of Yielding stage





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RESEARCH ARTICLE

Optimization Method in Turning Process of GFRP Composite

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ABSTRACT

The use of glass fiber reinforced polymer composites in engineering and manufacturing is common. This paper calculates the input parameters of dry turning GFRP composite material utilizing uncoated or straight carbide inserts. The cutting parameters used in this experiment include cutting speed, feed rate, and depth of cut. Optimal cutting parameters are employed to achieve a better result. Compared to the regular conventional process, this procedure saves time and material. The Taguchi method in MINITAB 19 software was used to determine the orthogonal array or series of experiments. The given input parameters are optimized considering surface roughness as a single response. SNR (Signal-to-noise ratio) and ANOVA are used to study the effects of these variables.

Keywords: Glass Fiber Reinforced Polymer (GFRP)Composite, Turning Parameters, Surface Roughness, Taguchi Method.

INTRODUCTION

Glass fiber reinforced polymer materials are used in many engineering sectors, including aviation and automotive. The machining process for fiber-reinforced polymer composites is very different from that for metals. One of the major issues we face is the surface roughness of the component. Taguchi's methods are widely employed in engineering design [1].It is a good approach to finding output performance and machining conditions. Taguchi parameter design is a simple, methodical way to optimize the design for performance, quality, and cost. The robust design uses methods like an orthogonal array, signal-to-noise ratio, and ANOVA.

Asilturk *et al* .,[2] conducted experiments on hard turning operations in lathe by the orthogonal array of L9 method. Abhang *et al* .,[3] carried out the experiment on a steel turning operation on the basis of Taguchi method. For analyzing the significance of each parameter, they used the analysis of variance method known as the ANOVA

method in their experiment. Yildiz [4] proposed the optimization approach can be applied to two case studies for multi-pass turning operations to illustrate the effectiveness and robustness of the proposed algorithm in machining operations. Pontes *et al .,*[5]discussed the study on the applicability of radial base function (RBF) neural networks for the prediction of Roughness Average (Ra) in the turning process of SAE 52100hardened steel, Taguchi orthogonal array is used as a tool to design parameters of the network. This paper reflects the ensure sustainable consumption and production patterns (SDG-12). Also promotes sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all (SDG-8).

Experimentation

The study included three independent input variables cutting speed (v, m/min), feed rate (f, mm/rev, and depth of cut(d, mm) with three levels each. Machining time is constant for each run, i.e 120 seconds. Here a standard L9 orthogonal array is used. The various factors and their levels are shown in table 1.

- The work piece is made of glass-reinforced fiber polymer (GFRP) and is 30mm in diameter and 150mm in length.
- This experiment used Taegu Tec SNMG 120412 uncoated carbide inserts as cutting tools.
- The turning process was done on a robust CNC lathe.
- Talysurf surface roughness tester was used to measure the surface roughness-Ra.
- S/N ratio for 'lower the better' type option was used for analysis.

RESULTS AND DISCUSSIONS

Show in Tables and Figures 2 and 3.

CONCLUSIONS

Several conventional strategies have been utilised to solve machining optimization problems, but they are not consistent and have issues when applied to the turning process, which has many variables and limitations. The Taguchi method is used to solve the aforesaid issues. The Taguchi approach is accurate since it is experimental. The feed rate, followed by cutting speed, is the main factor influencing surface roughness (from table 4). The optimal parameter combination obtained is 100 m/min cutting speed, 0.08 mm/rev feed rate, and 0.1 mm depth (from figure 2).

- Confirmatory surface roughness value at this condition is 2.08 μm.
- The method could be useful in predicting surface roughness as a function of cutting parameters.
- The regression equation for predicting surface roughness is Ra= 1.49-0.0075v+0.009d+19.23f
- The R^2-value (coefficient of determination) is obtained as 95.12.
- The difference between ANOVA predicted values and experimental for surface roughness are found to be within 10% of the experimental values. So the Taguchi experimental analysis was done correctly.

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Table 1. Input Factors and their Levels

Factors	Level 1	Level 2	Level 3
Cutting Speed	70	90	100
Feed Rate	0.08	0.12	0.14
Depth of Cut	0.1	0.4	0.8

Table 2. Experimental design of L9 orthogonal array& Results

v	d	f	R_a	SN Ratio
m/min	mm	mm/rev	μm	
70	0.1	0.08	2.24	-7.005
70	0.4	0.12	3.1	-9.8272
70	0.8	0.14	3.6	-11.1261
90	0.1	0.12	3.61	-11.1501
90	0.4	0.14	4.12	-12.2979
90	0.8	0.08	2.76	-8.8182
100	0.1	0.14	3.00	-9.5424
100	0.4	0.08	2.20	-6.8485
100	0.8	0.12	2.56	-8.1648

Table 4. Analysis of variance for S/N ratios

Source	SS	MS	F	P	C%
VC	9.9544	4.9772	21.63	0.044	34.623
d	0.2828	0.1414	0.61	0.619	0.983
f	18.053	9.0265	39.23	0.025	62.792
Residual Error	0.4602	0.2301			1.6
Total					100

Figure 1. Cutting Tool & GFRP Composite work piece

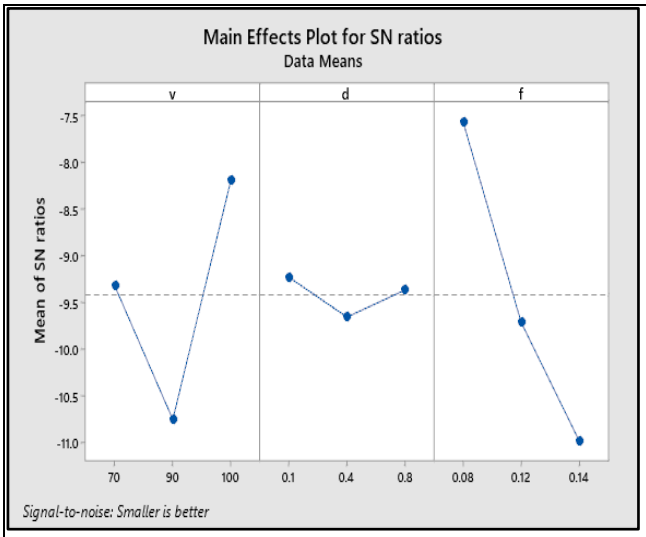

Figure 2. Main Effect Plot

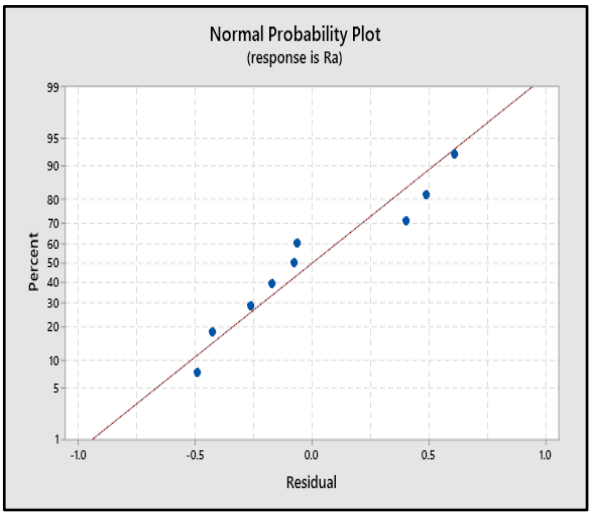

Figure 3. Probability Plot

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RESEARCH ARTICLE

Supercritical Fluids as an Alternate Green Media and Their Important Applications

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ABSTRACT

A supercritical state is an intermediate state of matter where it is difficult to discriminate whether it is a liquid or a gas. It has properties of intermediate range between liquids and gases. It has lesser density than liquids but greater density than gases. It has better solubility than liquids which is why they are used as replacements for many organic and inorganic solvents. Some popular SCF are H_2O (Water), CO_2 (Carbon Dioxide), Xe(Xenon). They play an important role in caffeine extraction, vanilla powder extraction, drugs preparation, extraction of biologically active compounds, pharmaceuticals, nutraceuticals, metallurgy. The most important analytical technique involving SCF is supercritical fluid extraction method, where supercritical CO_2 plays a major role. It is a green technology and a very cost-efficient method. It plays a vast role in chemical industries and research activities.

Keywords: Supercritical fluids, Extraction, Nutraceuticals, Drug preparation, Carbon dioxide.

INTRODUCTION

Matter is anything and everything present around us which occupies space and has some mass. Some observable physical properties of matter are mass, volume, colour, density, melting point, boiling point and some chemical properties are heat of combustion, chemical stability, flammability.[1] Matter is characterized by its properties and classified into various states. The two fundamental properties are intermolecular distance between constituent particles and molecular kinetic/ thermal energies of constituent particles.[2]. The variation in intermolecular distance and thermal energies gives rise to various states of matter. On a broader classification, there are three states of matter namely solid state, liquid state and gaseous states.[3] However, variations in temperature and pressure gives rise to some intermediate state of matter which are a connecting link between two major states of matter.

Solid State Liquid State Gaseous state

Increasing Thermal Energy

Decreasing Intermolecular Forces

A supercritical fluid is an intermediate state of matter between liquids and gases. As the name depicts, this state is exhibited when the temperature and pressure exceeds above the critical point(A point on phase diagram beyond which no definite phase boundaries exist) in phase diagram.[4] It is also referred as fluid due to its ability to flow. Its fluidity is greater that those of liquids but lesser than those of gases. A great variation in properties is observed on transition from either state to supercritical state. When a substance is heated at any temperature above its critical temperature and exposed to any pressure above its critical pressure, a new state of matter comes to existence referred as the supercritical state.[5] The corresponding liquid and the gaseous phase are quite indistinguishable from each other. This intermediate state has diffusivity like that of gases and solubility like that of liquids. supercritical fluids are getting popular due to its ongoing substitution with organic solvents in chemical industries and pharmaceutical industries and analytical methods. The motion of the SCF articles are much more similar like that of gases. They too exist in state of random motion and continuously collide with each and the walls of the container. They completely occupy the container in which they are sealed. The densities of SCF are quite nearer to that of liquids thus it exhibits a better dissolving effect. The reason behind such depiction of properties is due to its typical formation. When the sample is provided with a temperature high beyond the critical temperature, its kinetic energy becomes exceedingly high enough to overcome all intermolecular forces of attraction and repulsion existing between particles of liquid. When the sample is provided a pressure i.e. compressed high beyond the critical pressure, the molecules of gas come too close and settle into each other.[6] These collective changes in state of both the phases gives rise to a new intermediate state of matter. The supercritical state thus can neither be unitedly termed as liquid or as a gas.

The planets beyond the asteroid belt, i.e. the outer planets like Jupiter, Saturn are rich in supercritical matter content. The planetary surface holds very high temperature and pressures thus giving rise to existence to supercritical fluids majorly CO_2 on planetary surfaces.[7,8] The planetary surfaces are greatly prone to erratic atmospheric cyclones. The outer surface of the gas giant is rich in CO_2 (96%) and N_2 (4%) and the interior Atmosphere is rich in H_2 and He. All these entities are present at conditions beyond their critical parameters in the state of supercritical fluid. According to theoretical planetary models, it is believed that planets are composed of an ocean of supercritical fluids which undergo phase transition to denser liquid on proceeding deep and finally high-pressure water in the form of ice at the core.

They also occur in hydrothermal vents. These are places in deep seas where hot mineral rich fluids gush over from the sea bed. When this fluid meat cold water, it leads to formation of hard and rocky chimneys that can grow dozens of meters tall underwater.[9] The fluid also produces small particles of sulfide minerals which appears like smoke. Which is blue in color. The fluid was found to have temperatures 320 ℃ and very high pressures. Thus, giving rise to supercritical fluids.

Properties of supercritical fluids

The supercritical fluids are liquid-vapour species taken into conditions beyond critical point. The supercritical fluids resemble to liquid and gases in some of the properties. However, the properties exhibited are of intermediate range between that of liquids and gases. The various properties of supercritical fluids are mentioned below;

Density

Density is referred as mass per unit volume of a substance. The density varies inversely with temperature and directly with pressure. The densities of supercritical fluids are lesser than the liquids and are greater than those of gases. This property enhances its solvation tendency which makes it a better choice for various analytical techniques. It can easily dissolve substances better than gases and are quite easily recoverable which makes it beneficial over

Liquid-Liquid extraction methodologies. This is basic principle behind the supercritical fluid extraction method (Important technique used for purification of solid and liquid matrices) and supercritical fluid chromatography used for separation of Non-volatile and non-polar substances.

Diffusivity

It can be defined as the rate of diffusion. More particularly, it can be termed as the rate at which energy in the form of heat or matter such as gases or supercritical fluids transmit from one place to another. The molecular collisions are the driving force behind diffusion in matter. The rate of diffusion varies directly with temperature and inversely with mass of molecules and pressure. With rise in temperature the kinetic energy of particles increases thus their movement increases as a result of which their diffusivity also rises.[17,18] However, with rise in pressure the molecules come closer with decrement in volume and their diffusivity reduces. The diffusivity rises with decrease in mass of molecules as the smaller molecules travel faster. Steric factors also play important role in determining diffusivities. Molecules with simple shapes, elongated and less voluminous molecules how better diffusivities in supercritical fluids. The diffusivities of supercritical fluids lie between 10^{-1} mm^2/cm- 10^{-2} mm^2/cm. Due to their greater extent of diffusivities, they play major role in analytical techniques as supercritical fluid extraction and supercritical fluid chromatography.[19]

Viscosity

Viscosity is an important phenomena taking place predominantly in liquids and also in gases. In liquids, viscosity arises as a result of frictional interaction between interlaminar layers of liquid due to molecular transference from one layer to other.[20-22] The viscosity in gases is due to momentum transfer taking place between molecules due to collisions. On heating, viscosity in liquids decreases however it increases in case of gases. This is probably due to effective momentum transfer in gases which becomes ineffective in case of liquids due to presence of dominant Cohesive forces. The dynamic viscosity acting in fluids is measure of force but the kinematic viscosity acting in fluids is the measure of velocity. On dividing dynamic viscosity with fluid density, we get the Kinematic viscosity(η_d / ϱ = η_k).[23] The dynamic viscosity is constant at low pressures (below 1 atm) and almost parallels with density with increase in pressure.

Applications of supercritical fluids

The Human evolution began with technologies involving normal atmospheric pressures. As humans evolved, techniques involving high pressures. One such technique led to development of a very commercially important state of matter with special characteristics referred as the supercritical State of matter.This methodologies and products are economical and sustainable. The various applications of supercritical fluids are listed below:-

Food industry

SCFs are now used in food industries for several applications because of its advantages properties. The essence and aroma from bulk materials are extracted by using SCF without degrading their values. In particular, different SCFs are used for extraction of caffeine from coffee beans, extraction of aroma and flavors from herbs and spices, and so on. The low temperature extraction is the key factor with SCF that prevent the material degradation [24].

Dry cleaning

There are many things that need to be cleaning without the use of water. SC CO_2 is one of the best solvent for these kind of applications. The low surface tension, viscosity helps to remove the dirt particles, oils etc. and make the cleaning process easy. Another advantages with SC CO_2 cleaning is after removal of dirt particle, the solvent molecules also go away easily without much effort that reduces the labour and effort.[25]This process has been applied to the cleaning of semiconductor wafers as well as to the removal of photosensitive resins and residues following lithographic steps.

Supercritical Fluid Chromatography

There are many biological samples, and other samples that need to be separated at low temperature as they are not thermally stable. For this kind of situation SC CO_2 is one of the best way to separate these components. SC chromatography is not much different that of high performance liquid chromatography (HPLC) [26]. The only basic difference here is instead of any normal solvent, this method uses, pressurized CO_2 as mobile phase. The lower viscosity and surface tension of SC CO_2 helps for easy separation of samples. This methodology used specifically in pharmaceutical industries for separation and purification of active pharmaceutical ingredients.[27] The normal CO_2 are injected through the opening valve and then they are subjected to suitable temperature and pressure to meet the triple point of CO_2 and converted to SC CO_2 for separation and purification.

Supercritical Drying

Supercritical drying (SCD) process involves the conversion of liquid to gas by the method of sublimation. Many biological samples that are sensitive to heat undergoes these SCD for sampling and analysis. Furthermore, many chemical samples that are sensitive to heat are dried by the method of SCD. The SCD method also known as lyophilisation.[27] The materials after drying by SCF became very porous in nature because the liquids those were present before were get away by direct vaporisation leaving a porous space.

Recovery of Enhanced Oil

Enhance oil recovery is a process where the remaining crude oil is extracted from oil well. There are many other techniques used for enhanced oil recovery apart from SCF. However, SCF technique is a unique methodology where SCF is inserted into the oil wells and the remaining oils are extracted from the oil bed. This technique is a good technique because the surface tension and viscosity of the SCF is very low that helps in the recovery of heavy oils. Many oil exploration companies are using this methodology to extract heavy oil in a profitable way [28].

Refrigeration

An ideal refrigerant would be something which have good thermodynamic properties, and non-reactive to the components of the equipment. SC CO_2 is one of the best SCF to be used in refrigeration system.[29]. Furthermore, SC CO_2 has several other good properties that helps to be used as a suitable candidate for refrigeration. The environmental aspect of SC CO_2 is demanding to be used as refrigerant. The efficiency of this fluid is also nearly same to the currently used refrigerant.

CONCLUSIONS

From the above we may conclude that supercritical fluids are of many types and each SCF has their own beauty and limitations. Furthermore, different types of SCF have a wide range of physical properties which are greatly varied with the nature of the substance from which it is made up of. The most important applications of SCF are green extractions of valuable and delicate chemicals at low temperature without compromising on the quality and essence of desired product. The above mentioned applications are very few examples of SCF and there could be many more usage and applications in the modern industrial age. Moreover, SCF is one of the best alternate green solvent having tremendous potentials in both research and academia.

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Table 1: Critical constants for various supercritical fluids[10,11]

Supercritical Fluid	Molecular Mass(g/mol)	Critical Temperature (K)	Critical Pressure (MPa)	Critical Density (g/cm³)
Carbon Dioxide CO_2	44.01	304.1	7.38	0.469
Water H_2O	18.015	647.096	22.064	0.322
Methane CH_4	16.04	190.4	4.60	0.162
Ethane C_2H_6	30.07	305.3	4.87	0.2
Methanol CH_3OH	32.04	512.6	8.09	0.272
EthanolC_2H_5OH	46.07	513.9	6.14	0.276
Acetone CH_3COCH_3	58.08	508.1	4.70	0.278

Table 2: Critical Constants for some more commercially valueable supercritical fluids[12,13]

Supercritical Fluid	Critical Temperature T_c (K)	Critical Pressure P_c (bar)	Compressibility Factor Z_c
Carbon Dioxide CO_2	304	74	0.274
Water H_2O	647	221	0.235
Ethane C_2H_6	305	49	0.099
Xenon Xe	290	58	0.287
Ammonia NH_3	406	114	0.244

Table 3: Comparison of Various properties of Various states of Matter[14]

States of Matter	Density (kg/m³)	Viscosity(μPa·s)	Diffusity (mm²/s)
Gases	1	10	1-10
Supercritical Fluids	100-1000	50-100	0.01-0.1
Liquids	1000	500-1000	0.001

Table 4: Critical Densities of various Supercritical Fluids[15,16]

Supercritical Fluid	Critical Density (g/cm^3)
Carbon Dioxide CO_2	0.469
Water H_2O	0.322
Methane CH_4	0.162
Ethane C_2H_6	0.2
Methanol CH_3OH	0.272
Ethanol C_2H_5OH	0.276
Acetone CH_3COCH_3	0.278

REVIEW ARTICLE

A Systematic Review on Histone Deacetylase Inhibitors and Their Therapeutic Interventions on Cervical Cancer

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ABSTRACT

The histone and DNA collaboration is vital for gene expression in eukaryotes. In recent years, the role of epigenetic modifications on the carcinogenesis process has gained a lot of interest. Histone acetylation and deacetylation mediated by histone acetyltransferases (HAT) and histone deacetylases (HDAC) respectively performs an imperative role in epigenetic regulation, thus control the gene expression. Interestingly, HDAC inhibitors (HDACi) have the potential to arrest cancer cell cycle, differentiation, and cell death and also disable angiogenesis. For instance, the adverse effect of Human papillomaviruses (hpvs) which are considered to be the major human carcinogens, contributing for 4.5% of the patients diagnosed with cancer across the globe can be restricted by the use of HDACi. High-risk (HR) HPV types, primarily HPV16 and HPV18 promote the development of cervical cancer. Hdaci could deregulate the effect of HR-HPV oncoproteins by specifically arresting multiple cellular targets. It is intriguing to reveal the detailed molecular basis of the role of HDAC inhibitors as a possible involvement in cervical cancer treatment persuaded by HPV.

Keywords: Histone, gene expression, acetylation, deacetylation, cervical cancer.

INTRODUCTION

The long eukaryotic DNA is enfolded around histone proteins. It becomes a dense chromosome. The negatively charged DNA backbone and very positively charged histones exhibits an ionic interaction between them that results into a compact nucleosome structure and limits it's access to the transcription mechanism . The dense nucleosomes can be separated by neutralising the positive charge of lysine residues on the surface of histone. This neutralization is carried out by histone acetylase. This improves the accessibility of RNA polymerase II , leads to expression of the target gene [1-6]. Further by the action of HDAC (histone deacetylase) the lysine residue on the surface of histone reacquire the positive charge. As a result it restores the dense chromatin structure that are difficult to access by RNA polymerase , and there by reduce the gene expression. Both the processes of histone modification (acetylation and deacetylation) are regarded as a type of post translational modification and are important regulatory system for gene expression. In many eukaryotes it is generally termed as epigenetic control of gene transcription [7-9]. The imbalance between activities of histone acetylase and deacetylase can lead to certain divergent expressions of genes that eventually leads to instability of chromatin structure and epigenetic illness. Therefore, exact controlling of HAT and HDAC activity is essential for accurate and appropriate expression of several genes related to cell proliferation, cell death and signal trans duction. As a consequence of the suppression of of HAT or HDAC intrinsic enzyme activity leads to an variance between HAT and HDAC activity [10-14]. By inhibiting HAT activity the appropriate expression of the gene of interest can be restricted. Further, the expression of the target gene remains uninterrupted by inhibiting HDAC activity. Along With this, regulation of HDAC action by the HDAC inhibitors became the target of anti-cancer drug development strategies and cures for human illness resulting from cardio vascular , metabolic and neurodegenerative disturbance [15-18]. Based on major homology with yeast HDACs, total HDACs found in human are categorised into four classes. Within these groups, HDACs of Class I and II have the most important part in lysine deacetylation of histone N-terminal tails and the interaction of HDACs with multiple partners is carried out by different domains. Both HDAC3 and Class iia HDACs interrelate with N-CoR (nuclear Receptor corepressor) and SMRT (silencing mediator for Retinoic acid and thyroid hormone receptors). These two are closely linked corepressors [19-22]. Thyroid hormone receptors or nuclear Receptor corepressor and Silencing mediator for Retinoic acid interact with the sequence-specific DBD of BCL6, that controls activation and differentiation of B cell, Inflammation , cell cycle regulation and represses the process of transcription. In the solitary state both HDAC3 and HDACs of Class iia are catalytically quiescent but the enzymatic activation of HDAC3 occurs when it binds with SMRT / N-CoR irrespective of the presence of HDACs of class iia [23-28]. In contrast, when the Class iia HDACs binds to the SMRT/ N-CoR it now no longer display any important improvement in lysine deacetylase activity. The N-CoR/SMRT corepressors offer a structural hyperlink among inactive Class iia HDACs and active HDAC3 [29-34]. Hence, the action of HDACs those belongs to class iia and the significance of these comments stays uncertain. The current study emphasizes the importance of critical proteins in maintaining human cell physiology and thus aligns with the objectives of one of the United Nations formulated Sustainable Development Goals (SDGs); SDG3 which ensures healthy lives and promotes well-being for all at all stages.

Chromatin remodelling with histone modifications

The genome human contains a set of DNA present Inside 23 chromosomes pairs Including 6,469.66 megabases coding 20,000 no. of genes. When DNA taken from a solitary cell of human is strethed, it will be about six feet long [35-38]. The diameter of human cells is about 100 μm where as the diameter of nucleus of the cell is approximately 30 μm. Still, all the DNA present in each cell present in an area having only 6 microns diameter as the DNA exists in the cell nucleus in the form of dense chromatin. The chromatin creates a structure like "beads on string" called the nucleosome. "Beads" refers to histone octameric proteins, "thread" refers to a dsDNA molecule [39-44]. About 147 base pairs turns around each octameric histone forming nucleosome structure with a diameter of 11 nm. With 6 nucleosomes composing the chromatin fibres of 30 nm of compacted nucleosomes, the "beads-on-a-string" structure provides a much compressed secondary solenoid shape. The tightly coiled chromatin fibres subsequently combine to create a chromosome [45-51]. Mostly, the alkaline histone tail links with DNA.The positive surface charges of histone is due to lysine and arginine residues and it binds to the phosphate component of the negatively charged DNA.

Mainly 5 distinct variety of histones such as H1, H2A, H2B, H3 and H4 have been known so far. H5 is homologous to H1 and are called as linker histones and the core histone comprises of H2A, H2B, H3 and H4 where both H1 and H5 are linked to Histone with a chromatin solenoid construction and H2A, H2B, H3 and H4 are considered as key histone proteins which forms a rope like structure after binding to the DNA building. Modification of histone is possible using acetylation/deacetylation of lysine residues via HAT/ HDAC that controls Histone and DNA interaction. Histone Modification by acetylation disturbs the smoothness of nucleosome for the activity of RNA polymerase to attain precise genetic expression [15-24]. The process of Deacetylation induces Closed chromosomal conformation which ultimately leads to suppression in target gene expression. So the gene is said to turn on or off depending on changes in the histone protein that determines exposure of DNA, i.e. It is called epigenetic regulation.

Classes of HDACs

Based on occurrence of Preserved deacetylase domain and its existence Dependency on histone deacetylase (hdacs) and sirtuin (SIRT) family like definite cofactors HDACs are separated into two different families [6-12]. On the basis of sequence similarity with yeast deacetylase the members of Family histone deacetylase are divided into 3 major classes such as Class I , II and IV. HDAC1, 2, 3 and 8 comes under Class I HDAC whereas Class II HDAC includes HDAC4, 5, 6, 7, 9, and 10 . HDAC11 is the only member of Class IV HDAC .yeast deacetylases are zinc-dependent amide hydrolases. Depending on the composition of domain the Class II HDACs are again divided into class iia and iib HDAC [10-18]. Sirtuin Proteins (SIRT1, SIRT2, SIRT3,SIRT4,SIRT5,SIRT6,SIRT7) comes under Class III HDAC .They become catalytically active by the action of NAD(nicotinamide adenine dinucleotide) Cofactors. So far, 18 mammalian HDACs are classified into above four different classes. As compared to other classes the Class I hdacs shows extreme homology to Rpd3(yeast HDAC) and comprises of a fully preserved one Deacetylase domain.it is universally expressed and mainly found in Cell nucleus, where it exhibits strong deacetylase activity to histone [11-16]. They Suppresses target genes by forming a complex with the relative Corepressor regulated by inositol phosphate and also act as catalytic subunits. Recent studies have shown that class i hdacs Deacetylates non-histone proteins like AMPK (ampactivated protein kinase) and subunit of cohesion complex SMC3(Structural maintenance of chromosomes protein 3) and transcription factors to regulate their action. Both HDAC1 and 2 take part in complex formation with mitotic deacetylase complex (MiDAC), nucleosomes remodeling and deacetylase complex (NuRD), transcription regulatory protein Sin3A and CoREST (corepressor of REST) while recruiting HDAC3 to the corepressor complex SMRT / NCoR (review by Ayer). HDAC8 works independently without creating a huge complex [21-26]. Mihairowa, Show, Seto, and Yoshida Outlined numerous Class I HDAC complexes With a thorough debate. Maximum homology is shared between Class II HDAC with yeast HDA1 and its C-terminus contains a conserved deacetylase domain.

The N-terminal of class iia HDAC (HDAC 4, 5, 7, 9) host an adapter domain providing a site for the binding of MEF2 which is a DNA binding transcription factor. In response to different controlling cues successive three or four sites of phosphorylation serve as regulatory signals for 14-3-3 proteins, that can frequently move back and forth between both nucleus and cytoplasm. HDAC 6 and 10 of HDAC Class iib contains an additional tail like projection at c-terminal which is called as, tail domain. But these 2 classes of class iib HDACs are as well different from each other [11-15]. HDAC 6 contains two deacetylase domain. Along with this its C-terminal exhibits a ubiquitin binding zinc finger domain. Where as HDAC10 contains single deacetylase domain and its C-terminal a repeat domain is present which is rich in leucine. HDACs of Class iia rebuild huge structures Using complex SMRT/NCoR - HDAC3. In fact, Class iia hdacs show minimal enzyme activity [21-15]. In class IHDAC, Tyrosine residue is conserved in the catalytic site .On the other hand, in class iia, tyrosine replaces histidine. Therefore, Class iia HDAC may play a role Deacetylase with low or possible enzyme activity Presents a specific target that remains undiscovered. Little is known about HDACs of class iib. HDAC6 plays an important role in acetylation of cortactin, Alpha-tubulin, IFNαR and chaperone .it also has role in the regulating liver metabolism and autophagy. Mihairowa and shaw and Seto and Yoshida explained the outline of the class IIH DAC. Class IV hdacs consists of only HDAC11. It shows homology to Hos3 of yeast .It also has a catalytic domain similar to HDACs of class I and II and also associated to interleukin 10 and CDT1(chromatin licensing and DNA replication factor). Till date HDAC11 has not been fully studied. Homology has been seen between Class III HDACs and Sir2 (Yeast Silent Information regulator 2) which is necessary for

silencing transcription process. From bacteria to humans they are mostly preserved proteins in many Organisms. Class III HDACs contains DHS-like NAD / FAD binding domain which is a unique feature of HDAC. Seven Sir2-like protein (SIRT17) named situins are present in human [31-35]. Exclusive features like Momo ADP rybosyltransferase activity is exhibited by situins. SIRT1 exhibits strongest deacetylase action. Fascinatingly, SIRT5 displays both lysine demalonylase and desuccinylase action. Nucleus, cytoplasm or mitochondria may contain these proteins. Mitochondria contains SIRT3,4, 5, Nucleus contains SIRT1,2,3, 6,7 and cytoplasm contains only SIRT1 and 2 . SIRT5 is well studied [21-25].

Structures and catalytic action of HDACs

So far, 248 HDAC structures are available in PDB. Out of all these structures approximately hundred human HDACs are available there. *Aquifex aeolicus* bacteria contains histone deacetylase-like protein (HDLP) which is the first resolved HDAC structure. It possesses α / β-deacetylase folding of an already known arginase [1-15]. The Metallic arginase enzyme uses manganese ion as a catalyst Cofactor, HDAC Ancestor for common iron enzymes. Primarily, Zinc ion position in Class I, II, and IV HDACs is regulated by 1 Histidine, 2 aspartic acids and 2 active water molecules [15-25]. The acetamide carbonyl group acts as a substrate. It restores the water molecule of acetylated lysine, interrelates with OH group of tyrosine through H- bond.To facilitate substrate binding, tyrosine residue may undergo changes in conformation from a "out" to a "in" configuration.By the action of a neighbouring nucleophile of histidine via the His–Asp chargerelay system, deprotonation of another water molecule takes place [21-26]. It seems to be the common method for polarising and activating water molecules as nucleophiles [18-23]. Two histidine recidues are found near the active site. Second histidine of the intermediate functions as the proton to amine fractions and leads to the formation of Acetate and lysine [12]. For more information on this process, see a review by Lombardi et al. In Class iia, traces of tyrosine will be replaced by histidine, which appears to be important and a tetrahedral intermediate is created. Therefore, the Enzyme action of members of the iia class is lower compared to other classes [18]. HDACs of Class III are NAD-dependent enzymes and they display catalytic rifts between Rossmann fold domains and zinc binding domain. Sirtuin family proteins have conserved cleft residues that produce a tunnel for NAD+ and acetylated lysines, as well as big substrates like succinated lysine residues and malonated lysines [23-28]. The break down of nicotinamide starts the catalytic reaction. Cleavage occurs by the adding acetamide oxygen of the actylated lysine,by generating a intermediate named C1'O-alkylamidate. Activation of 2'-OH group of the first generated intermediate is carried out by the action of HIS-residues present on the active site through deprotonation [29-35]. Now 1', 2'- cyclic tetrahedral carbon intermediate is formed by the interaction of reactive oxygen with the intermediate C1'O-alkylamidate. Next, after the water molecule Attack 1', 2'- cyclic tetrahedral carbon intermediate which leads to generation of deacetylated lysine, 2' O-Acetyl ADP-Ribose. 2'O Acetyl ADP Ribose converts spontaneously into 3'O acetyl ADP-ribose [36-45].

Yeast HDACs of Class I and II

Class II HDA1 and Class I Rpd3 of yeast HDACs plays a significant role in transcriptional repression Of target gene expression. A multiprotein-Rpd3 complex is formed by the association of Class I Rpd3p with Some subunits such as scpho23p, scsap30p, scsin3p, scsde3p [42]. The assembly of dimeric HDA1 with two non-catalytic subunits such as HDA2 and HDA3 forms the heterotetrameric HDA1 Complex. Now the H2B and H3 histone subunits are deacetylated by the heterotetrameric HDA1 Complex. These 2 complexes takes part in transcriptional suppression when they are employed to particular promoter loci by proteins with sequence-specific DNA-binding domain. In the future, modification of adjacent nucleosomes takes place at lysine residues on histone surface. It also deacetylates the N-terminal histone tail by: Non-specific DNA binding mechanism. Both HDA1 complex and human hdacs of class II are closely related [44]. The HDA1 dimer of HDA1 complex is related with definite promoter sites in yeast and only shows the activity of catalytic deacetylase whereas subcomplex HDA2 – HDA3 is associated with nonspecific locations of DNA. For in vivo and in vitro deacetylase activity both HDA2 and 3 are required. HDA1 contains C-terminal argonaute binding protein 2 (ARB2) at C-terminal and deacetylase domain at N-terminal. ARB2 has important role in methylation of histone, assembly of heterochromatin and sirna generation [48]. Formation of homodimer is facilitated by newly identified domain ARB2 and then tetramers of H3-H4 or dimers of H2A- H2B permits histone binding (dimer or H3-H4 tetramer). Both HDA2 and HDA3 provides DNA-binding domain (DBD)

at N-terminal. Enzymes of family Rad54 contains helicase lobes of chromatin remodeling domains at C-terminal which is structurally homologous to DNA-binding domain. Along with this they also provide a coiled-coil domain (CCD) at the C-terminal which are used for the formation of subcomplex HDA2 – HDA3 (heterodimer) . In yeast sub complex HDA2-HDA3 performs as a DNA-binding scaffold protein for class II HDA1 HDAC complex. In humans homologues of HDA2 and 3 are unidentified . Human homologues of HDA2 and HDA3 have yet to be discovered. The Huber group postulated that both N-terminal DBDs of the two structural subunits of the HDA2–HDA3 complex act as unspecific DNA binding modules and anchors to position HDA1 in the vicinity of the H2B and H3 histone tails, on the basis of comprehensive structural and functional research. All HDA1 complex can form a large complex Containing both DNA and histone for global deacetylation of nucleosomes [54].

Unique features of class iia HDACs

As stated overhead, HDACs of Class II contains a C-terminal and / or N-terminal prolonged section. Fascinatingly, a nuclear localization sequence (NLS) is present in HDACs class iia at the N-terminal [48-52]. So they often present in both cell nucleus and Cytoplasm. In addition to the NLS a binding site for zinc ion is also present in catalytically active site of class II HDACs [51]. Many specific residues of class iia HDACs appear in the entry site to the catalytically active site or the binding domain of zinc ion. Relatively low Percentage of Catalytic Activity (approximately 1/1000 x) is seen in HDACs of class II than HDACs of class I [54-57]. It is caused by the replacement of catalytic Tyr remains by His remains. In fact, HDAC4(Class iia HDAC) won its deacetylase function when the Tyr is replaced by His remain. Therefore, it is not clear what role this can play.

HDAC-related diseases and inhibitors

The compact chromatin structure get affected by unbalanced activities of HAT and HDAC that ultimately leads to inappropriate expression of particular genes [48-51]. Accurate control of HAT and HDAC is necessary for controlled target gene expression those are related to various processes such as cell proliferation , signal transmission and death of cell.Cutaneous T-cell lymphoma/ skin lymphoma (CTCL) have been treated by using drugs (HDAC inhibitors) like SAHA (Vorinostat, Zolinza ™, Merck & Co, Inc., USA) and FK228 (Romidepsin, Istodax ™, Celgene Corp., USA).Recently, Belinostat was accepted by FDA for the treatment of external T cells Lymphoma (PTCL) in 2014 and Panobinostat (Farydak,) Novartis Pharmaceuticals) approved uses against multiple myeloma in 2015. Almost 10 years ago due to dose-limiting toxicity and indiscriminate, Greater Focus on Mixed therapies [48-57]. It involves other anti-cancer drugs Agents and their preclinical and clinical trials. The combined treatments includes DNA repair methods, radiation therapy, topoisomerases Inhibitors, epigenetic modifiers and immune checkpoints [41-46]. It shows important synergistic effects with the effect of inhibitors. Therefore, inhibitors of HDAC still appear to be promising tools. Many groups of anti-cancer drugs .The biological properties of HDAC inhibitors stays ambiguous [33-39]. However, this is one of the main issues for HDAC inhibitors dealing with partial effectiveness in treating a solid tumour as a single treatment with minimal resistance to these antibodies.

The limitations of HDAC small-molecule inhibitors

Identifying the catalytic activity of deacetylases is a key mechanism for the production of their inhibitors. Therefore, there are a number of competing HDAC inhibitors Targeted in the catalyst package Established and verified in the clinical and clinical phases .Amongst all these inhibitors, the first FDA-approved HDAC Inhibitors were SAHA (vorinostat), FK288 (Romidepsin) for the use in the medical field for cancer control. Valporic Acid and CI994 are presently being verified in Phase III clinical trials for their use in the field of cancer like cervical cancer, myeloma, lung carcinoma and ovarian cancer [10-18]. Some Other HDAC inhibitors like as MS275-SNDX-275, PCI24781 and mocentinostat were likewise included in Phase I or phase II clinical trials for blood cancer. Like other anti-cancer drugs inhibitors of HDAC shows only partial effectiveness and dose-limiting toxicity (dlts) along with some adverse complicacy like neutropenia, dehydration and anorexia [11-18]. Sever discomforting consequence is cardiotoxicity that involves ventricular tachycardia. In fact, before six patients were approved by the FDA, they died with Romidepsin. Certainly one of the most common problems related to presently accessible inhibitors of histone deacetylase is their low level of target HDAC selection over HDACs of other classes and cognate HDACs of similar classes with diverse tumor suppression activity [11,12]. Thus, improved HDAC isoform specification is probably one

of the most critical problems to deal with to reduce unintended deadliness. Generation of metal chelating inhibitors aim to inhibit the catalytical action of HDAC. It is an extensively used method as it is associated in preventing hydrolysis of an acetylated substrate by Designing small chelating molecule [3,4]. Because metals, particularly zinc-binding sites, are largely conserved, a significant percentage of metalloprotein inhibitors may induce cross reactivity. Histone deacetylases, arginase, and HDAC-related deacetylases proteins that behave like deacetylases are only a few examples of metalloenzymes. Therefore, for a given reason to better understand the precise function of Zinc binding region HDACs and its adjacent working pockets It is important to overcome the deficiency of specificity linked with non-metal chelate inhibitors or gaining synergistic result with metal chelating moiety [5,6].

The N-terminal domain as an alternative drug

Target for class iia HDACs

The N-terminal domain (NTD) is a functionally unique adapter domain of HDACs those belongs to the transcription factors (TFs). The regulatory signals mediated from this helps in distinguishing the enzymes from the histone deacetylases. N-terminal domain of HDACs those belongs to Class iia comprises of binding sites for Mef2 (myocyte Enhancer Factor-2) members of transcription factor Family. It also contains interaction sites for conserved serine residues [7-9]. It leades to Phosphorylated in a signal-dependent method by causing transport of enzymes across nucleus and repression of enzyme target. But more evidence proposes that some of the tfs such as Runx2 (Runx family transcription factor 2), serum response factor and calmodulin binding Transcription activator are the partners of class iia HDAC. Class iia HDACs are unphosphorylated at rest and reside in nucleus. Here they are recruited to their target genes via interactions with the TFs, allowing them to perform their activity as transcription-repressor. This shows that the class iia HDAC NTD could be used as a potential target for class iia anti-HDAC therapies. Phosphorylation of HDACs of class iia occurs by responding to particular signals. It leads to disruption of interaction between class iia HDACs and transcription factors. It causes the movement of transcription factors to the cytoplasmic area and their targets to be depressed. This process of phosphorylation involves kinases and extracellular signals [10-14]. It has been described thoroughly in previous reviews. As a result, inhibiting the function of class iia HDAC NTD is a target-specific therapy aimed at counteracting a subdivision of class iia HDAC functions those are abnormally regulated in cancer.

Advantages of targeting class iia HDACs

Interestingly, an alternative exclusive features of class iia histone deacetylases is the loss of their measurable enzymatic action. Even though they bear a surprisingly preserved catalytically active domain, they showcase minimum deacetylase interest contrary to acetylated histones [15-17]. So far, , there are no histones or any other proteins Substrate of class iia HDAC has been identified. In point of fact, their enzyme action rest on their mobilization For protein complex of SMRT / ncor and classi HDAC3. It's been postulated that the HDACs of class iia don't really function as histone deacetylases, but rather for repressor complexes it acts as adaptors. Class iia HDAC shows Tissue-specific expression. It has been exposed to use their function in repression of transcription in hypertrophy of the heart and blood vessels, differentiation of myoblasts, survival Nerve cell and neurodegenerative diseases. Thus, Class iia HDAC is now measured as a key regulator of a precise development and differentiation process . However, the majority of the research that have demonstrated their tissue selectivity have solely used in vitro experimental methods [18-23]. The Particulars can be found in the review by Verdin et al. N-terminal domain Inhibitors that targets HDACs of Class iia have received little research. This area of study is intended to lessen the chance of inhibitors having unwanted cross-reactivity with other HDAC classes. Another advantage of aiming class iia HDACs is that a peptidomimetic strategy for designing -specific inhibitors of class iia HDACs on the basis of complex structures with SMRT peptides is available [24-27]. According to structural and biochemical investigations Interaction occurs between the entrance of catalytic site of HDAC with peptide containing SMRT glycine–serine–isoleucine motif. HDACs of Class iia have a deacetylase domain containing zinc and a subdomain for binding zinc, as discussed above [28-31]. The structural zinc ion-binding area of the inhibitor-bound HDAC4 catalytic domain can assume two unique conformations, "closed" or "open," according to structural analysis. The "closed" conformation of the apo-structure may give a substrate pathway to the catalytic zinc ion at the active site, whereas the "open" conformation of inhibitor-bound structures shows a disorganized structural zinc ion-binding subdomain. Therefore,

the closed form is considered to be Important biological structures that do not affect Complex and SMRT-HDAC3 [32-35]. Fascinatingly, s a closed shape is displaed by the HDAC4- SPs (SMRT derived peptides) complex. SP-based inhibitors offers a stronger justification for the construction of biologically dynamic inhibitors of HDAC4, that may deliver excellent selectivity for histone deacetylases of class iia In comparison to certain other defined chemical inhibitors.

New biological approaches associated with class iia
HDACs and final comments

As previously indicated, the domains of HDACs belongs to Class iia combine with SMRT / N-cor-HDAC3 complexe to forms a large complex for particular gene repression and it also shows low deacetylase activity. HDACs Class II HDAC studies have informed that there is no increase in deacetylase activity of HDAC4 when a complex is formed by the interaction of HDAC4 and SMRT. HDAC4's deacetylase activity is not boosted whenever it establishes a complex with SMRT, according to studies on class iia HDACs. Depending upon the SMRT glycine–serine–isoleucine motif complex and crystal structure of catalytic domain of HDAC4, we recently discovered that SMRT-binding motif residues occupy the catalytic entrance site of HDAC4 [37-41]. This findings strongly shows that class iia hdacs instead of operating as enzymes for deacetylation of acetylated histones, they serve as bridging elements between transcription factors and SMRT-HDAC3 complex. Due to their relatively low enzymatic action, this is still essential to recognize genuine targets for class iia hdacs that are not part of the SMRT-HDAC3 complex in order to assess their physiological functions [42-47]. Furthermore, research into the interaction and inhibition of HDAC4/5/7 and SMRT/N-cor is essential to see how they affect the pattern of acetylation in the target gene. These methods will provide answers to basic inquiries about class iia hdacs.

From Histone to Enzymatic Acetylation/Deacetylation: The History

Professor Kossel, the father of modern biochemistry, pioneered the study of free histones by separating nucleic acids in sediments from histones in the supernatant [48-51]. Professor Albrecht Karl Ludwig Martin Leonhard Kossel was a Nobel Laureate for his work on the chemistry of nucleic acids and nuclear chromatin proteins. He had been a professor of physiology at Heidelberg Kossel University and the Research of Proteins [52]. In his studies on the nucleus, Kossel discovered a protein that was distinct from Miescher's protamine (which had previously been isolated from the nucleus of salmon sperm), and he termed it as histone [53-55]. Histone was first characterised as a nucleic acid-protein complex, which Kossel dubbed nucleoprotein, after discovering basic amino acids in calf-thymus histones [54]. The protamine was found in the nuclear proteins of sperm cells during the haploid phase of spermatogenesis and is required for condensation of sperm DNA and stability. Kossel, on the other hand, confirmed the presence of a basic amino acid composition in histone [54-57]. Before Kossel's study, it was known that histones had a significant arginine concentration, which varied depending on how they were chemically precipitated, and various investigations looked at histone amino acid composition [58-61]. Other experiments were conducted concurrently to better describe the amino acid composition of histones, and the occurrence of proline, alanine, and lysine in the N-terminal site of calf-thymus histones was confirmed [59,60]. As per the various histone chemical extraction procedures, the N-terminal alanine, lysine, and glycine residues in histones differed [57-60]. The histones of the calf-thymus contained proline end groups at first, and they were connected with a somewhat lysinerich portion [61]. Amino acids of histones were extracted more readily with lysine-rich residues using biochemical methodologies for calf-thymus histone extraction and were validated in both calf thymus and wheat-germ histone [62-64]. Furthermore, chromatin was defined as a nucleosome constituted of a histone octamer containing h2a, h2b, H3, and H4, with around 200 base pairs of DNA , resulting in a dynamic chromatin fibre [64]. Histone H1 was thought to be a changeable linker segment that steadies nearby nucleosomes collaboration [61-64]. This histone was identified as a core comprising two histone types H2a, H2B, H3, and H4 with a supercoiling of DNA around the core using crystallographic experiments [63].The chromatin from pea embryos was characterised as an RNA–DNA–protein complex that protects nascent RNA from rnase activity [64]. DNA was discovered to exist in minimum 2 different forms: DNA alone and DNA bound in the nucleus–histone complex [62-64]. The histones may then limit RNA production in the nucleus and histone repositioning led to enhanced messenger RNA production rates [60-64]. Furthermore, the suppression of RNA synthesis was linked to lysinerich histone fractions or a histone

complex, favouring the use of DNA as a primer for RNA synthesis [63]. A premature link has been discovered so far between histone-rich regions in lysine, histone modification, and RNA production [63]. The prefabricated lysine peptide chains might then be changed further by adding acetyl, methyl, or phosphoryl groups to the histones. The acetyl group has been discovered connected to the "-amino group of lysine residues at the amino group terminal in the polypeptide chain [37,62]. Early research on calf thymus nuclei confirmed a relationship between acetylated histones on RNA polymerase activities and modifications in histones through acetylation, as well as the possibility that DNA-histone binding might impact RNA synthesis rate [60-63]. Furthermore, chromatin DNA was ready for transcription through RNA polymerase, which stayed inactive because it was physically suppressed by histones, and when histones were released from chromosomal DNA, the genetic material was derepressed [60]. In human cells, the same result was obtained when acetylation of histone was accompanied by transitory changes in DNA linked to the histones, as well as changes in RNA polymerase activity and RNA production [48]. It was confirmed a rapid turnover of this N-terminal acetyl group in histone proteins and enhanced RNA production in metabolically active organs (i.e., hepatocytes, spleen, tumour cells, liver and thymus) in search of further scientific data [48,51]. This alerted scientists to the fact that histones may be modified by enzymes. Researchers used histones extracted from rat liver nuclei and chicken reticulocytes to show that modifications of histones were aided by the translocation of acetate from coenzyme A by an acetokinase [55-61].

Histone acetyltransferase was found in chromatin recovered from isolated nuclei of rats (Racey and Byvoet, 1971). Following that, distinct histone acetyltransferases were discovered in rat hepatoma cell lines or rat thymus nuclei , favouring acetylation in histone f2a1 rather than f3 or histone H4 rather than H3 [49-54]. The acetylation of this histone at its N terminus reduces the association of histone H4 lysine residues with DNA and increases availability to RNA production [48]. Furthermore, based on the acetylation state of chromatin on histone side chains, cellular functions were detected in various cells and at various stages of the cell cycle [36]. Furthermore, histone acetylation, which is extremely metabolically active, occurs in both normal and tumorous cells [38]. Those previous investigations established the underlying information that elevated level of cellular RNA transcription in proliferating and cancer cells were connected with high levels of histone enzymatic acetylation at lysine-rich chains. In parallel experiments, enzymatic histone deacetylation in the calf thymus revealed minor alterations in structure of histone by acetylation and deacetylation, shedding light on how to regulate chromatin and RNA production [42]. Then, in higher animals, histone acetylase and deacetylase enzymes became essential components for genetic control, and acetyl turnover by deacetylase activity occurred in active metabolic cells and tumours [42-51]. Furthermore, both free histone and chromatin-bound histone complexes showed histone deacetylase action [54]. A deacetylase was identified in mammalian cells, confirming that histone deacetylase is a crucial regulator of transcription in eukaryots [57-59]. In conclusion, histone acetylation and deacetylation were catalytic mechanisms that allowed RNA polymerase to stimulate or inhibit gene transcription (not transcriptional). This was thought to be an epigenetic signature, particularly in cancer [43-45].

In terms of vocabulary, a key idea evolved from histone modifications: "writers," "readers." And "erasers," The "writers" were enzymes (HAT, histone methyltransferase or kinases) that added acetyl, methyl, or phosphoryl groups to histones posttranslationally; the "erasers" were enzymes (HDAC, demethylase or phosphatase) that promoted contrary posttranslational histone modifications; and the "readers" were regulatory proteins that recognised domains that complemented specific posttranslational modifications: bromodomain acetylation, chromodomain methylation, and 1433 phospho-binding protein phosphorylation [40-47]. Several investigations have followed these previous researches, which have considerably benefited to current understanding and epigenetic therapeutics against malignancies focusing on inhibiting histone deacetylation enzyme activity. In humans, 18 HDAC isoforms have already been identified and classified into 4 categories [48]. Hdacs 1, 2, 3, and 8 are classified as class I; hdacs 4, 5, 6, 7, 9, and 10 are classified as class II; sirt 1–7 is classified as class II; and HDAC11 is classified as class IV. Class I, II, and IV hdacs are zinc-dependent enzymes, whereas class III hdacs are NAD+-dependent.

Statements and Declarations

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval and consent to participate

It is a review article. No ethics approval is required.

Consent to publish

Not applicable.

Human and animal rights

It is a review article. No animals were used in the study.

Availability of data and materials

Not applicable.

CRediT authorship contribution statement

All the authors have substantial contribution for the preparation of the manuscript. Gagan Kumar Panigrahi and Roshni Prinkit Bal conceived the idea. Data curation and writing: Roshni Prinkit Bal, Smruti Subhdarsinee, Annapurna Sahoo, Pradip Kumar Prusty, Simran Mallick, Tan Thakur, and Gagan Kumar Panigrahi. All the authors have read and approved the final manuscript before submission.

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RESEARCH ARTICLE

Novel MgO-Fe_2O_3 Composite Nano Adsorbent: Synthesis, Characterization and Adsorption Studies towards the Removal of Congored Dye from Water

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ABSTRACT

In this project, we have synthesized MgO-$Fe_2O_3$by varying weight ratio of Mg : Fenano composites through precipitation method using magnesium nitrate and ferric nitrate as salt precursors using polyethylene glycol as a stabilizing agent and NaOH as precipitating agents. Apart from this we have also synthesize pristine MgO, Fe_2O_3nanoparticles using the same synthetic method for comparison study. In order to determine the information on the crystal structure, formation, size, and morphology of the prepared nanocomposite were characterized by using XRD, FESEM and FT-IR analytical techniques. The prepared nanocomposites were used as absorbent for removal of Congo red dye from aqueous system. MgO-Fe_2O_3nanocompositematerials are found to be efficient adsorbent for removal of congo red dye as compared to individual MgO and Fe_2O_3 nanoparticles.

Keywords: Nanocomposites, Precipitation, adsorbents, Congo red

INTRODUCTION

Nanomaterials is described as the materials where a single unit is sized in between 1-100 nanometers in at least one dimension. It talks about material science-based approach to nanotechnology. Nanomaterials are given higher priority in research proposals[1,2]. Nanocomposites can be defined as the composite material of which at least one

phase has dimensions of less than 100 nanometers. It consists of solid or bulk material matrix with nano-dimensional phases of one, two or more nanomaterials. Arrangement of nanomaterials is random in nanocomposites. High surface to volume ratio of reinforcing phases of nanocomposites, differentiate nanocomposites from conventional composite materials. The reinforcing material can be made up of nanomaterials like nonaparticles, nanofibers, nanosheets. The matrix material is affected by proximity of reinforcement[3]. A small amount of nanoscale reinforcement gives a huge effect (i.e observable effect) on macroscale properties of the composites due to the large amount of reinforcement surface area. They have a huge range of applications on medicines, microelectronics, nanophotonics, sensors, food packaging, cosmetics. Nanocomposites are tools of nanotechnology which show a great change in all industrial fields. Metal Oxide nanomaterials can exhibit unique physical and chemical properties due to their limited size and a high density of corner or edge surface sites[3,4].1D Metal oxide nano nanomaterials such as nanowires / nanofibers, nanorods etc., have attracted a great deal of attention of recent research because of their large applications in various fields like catalysis, sensors, adsorption and environmental remediation like degradation of various contaminants from water [3].

Nanomaterials can be synthesized by various chemical methods like hydrothermal, co-precipitation and sol-gel. Among this method, we have used Co-precipitation method for highly low-cost adsorbent making. Among the several chemical methods the co-precipitation method is the simplest and low-cost method widely used for the synthesis of nano level materials[5]. This method can be carried out under very low temperatures and can give nanomaterials of both crystallinity and larger surface areas. In this process first the starting precursors were stirred and mixed together and again it was stirred to form a homogenous mixture. In this method it is important to maintain the purity of the precipitate, thermo gravimetric analysis shows that the precipitates contain undesired impurities which can increase the mass, this can be solved by digestion or by redissolving the precipitates again.

In the modernized society, the water pollution is a major global problem intimidating the life system which accounts for a large number of diseases and death by consuming contaminated water. There are various types of water contaminants such as inorganic pollutants like antimony, arsenic, barium, cadmium, chromium, fluoride, lead, mercury etc. and organic contaminants like acrylamide, phenol, benzene hexachloride, carbon tetrachloride and different organic dyes like congo red, methyl blue, methyl orange etc [5–9]. These organic and inorganic pollutants and their metabolites are toxic, carcinogenic, mutagenic, chromosomal fractures and responsible different respiratory disorders.Nowadays the adsorption is most prominent technique for removal of dyes due its easy and convenient operation and it can remove different type of pollutants [10,11].

Magnesium oxide (MgO) has pulled in extensive consideration for its novel properties and huge assortment of utilizations in the field of impetus, impetus underpins, stubborn materials, paints, harmful waste remediation, and superconductors. MgO nanomaterials have been investigated as a nontoxic and earth amicable adsorbent to evacuate natural poisons and dangerous metal particles from water[7,12]. Among the different systems for expulsion of natural poisons from waste-water, adsorption handle has been demonstrated as a powerful evacuation technique, because of its proficiency, effortlessness, and appropriateness. Subsequently, union of MgO with high surface region is of incredible enthusiasm for adsorptive materials. As of late, colossal endeavors have been made to integrate MgO with upgraded surface territory in shifting morphologies, for example, poles, wires, belts, tubes, etc. Among different blend techniques, compound strategies are the promising methodologies because of their straightforwardness, financially savvy, high return of definite item and low response temperature[12].

Thus, we have orchestrated huge scale MgO nanorods, various leveled nanostructures and nanoflakes by synthetic union defeats, for example, precipitation, reflux and aqueous strategies, individually. The orchestrated nanomaterials were connected as adsorbents to expel Malachite green (MG) and Congo red (CR) from fluid media. The adsorption tests, for example, impacts of materials sort, adsorbent measurement and introductory fixation variety were investigated in bunch tests.

MATERIALS AND METHODS

Materials

$Mg(NO_3)_2$. $6H_2O$,$Fe_2(NO_3)_3$. $9H_2O$, NaOH and Polyethylene glycol, Congo redwere purchased from sigma Aldrich. Ethanol is purchased from Merck chemicals Ltd, India. Double distilled water was used throughout the experiments. All the chemicals were used as such without any further purification.

Preparation of MgO nanoparticle

2.56g of $Mg(NO_3)_2.6H_2O$ and 2.56g of PEG and 25mL of ethanol was added to a beaker. The mixture was stirred in 50-60^oC till a clear solution appears. Then NaOH was added drop wise till the pH become 11-12 with continuous stirring for 6h to formed whitish precipitation. Then obtained precipitation was kept in air oven for 12hrs at 150^oC to dry followed by calcination at 550^oC to obtain desired product.

Preparation of Fe_2O_3 nanoparticles

4g of $Fe(NO_3)_3$. $9H_2O$ and 4g of PEG and 25mL of ethanol were mixed in a beaker. The mixture was stirred continuously in 50-60^oC till a clear solution appears. Then NaOH was added drop wise and made the pH of the solution in range of 11-12. Then obtained brown precipitation was kept in air oven for 12hrs at 150^oC to dry followed by calcination at 550^oC to obtain Fe_2O_3nanomaterials.

Preparation of MgO-Fe_2O_3 Nanocomposites

Different weight ratios of MgO-Fe_2O_3 were synthesized by hydrothermal method by taking $Mg(NO_3)_2$. $6H_2O$ and $Fe(NO_3)_3$. $9H_2O$ with PEG and alcohol in a beaker. Stirred the above mixture in 50-60^oC till a clear solution appears. Then NaOH was added drop wise so that pH of the solution is in the range of 11-12. Then obtained whitish brown precipitation was kept in air oven for 12hrs at 150^oC to dry followed by calcination at 550^oC to obtain desired product.

Adsorption Experiment

All the above nanoparticles and nanocomposites were taken as adsorbents for the removal of organic dyes such as Congo red (anionic dye) from aqueous solution. 100 ppm stock solution of Congo red was prepared. Then the adsorption of the dye was studied by taking 0.05 gm of adsorbents in 20 ml of dye solution taken in a 25 ml reaction bottle. During the adsorption process the bottle was kept under stirring using a magnetic stirrer. After that the solution was filtered and the UV-visible spectra of the residual solution was taken. Theλ_{max} value was recorded at 498 nm. The effect time for the adsorption of dyes on the surface of the adsorbents was investigated.

Characterization Techniques

Powder X-ray diffraction patterns of the samples were recorded in a PAN analytical X-ray diffract meter. It is used to analyses the phase of the sample. For measurement the sample powder was placed in the groove of sample holder and compressed with the help of another glass slide such that the samples should remain in the square of the holder, the excess powder was removed. Surface morphology, microstructure and particle size of the as obtained samples were studied by Nano Nova 450 *Field Emission* scanning electron microscopy (FE-SEM).The working voltage was kept at 15kV and 20 kV. It detects the signals from the interaction of the incident electron with the sample's samples. Area scanning mode was used for qualitative analysis (mapping) and X-ray scanning used to measure the elemental distribution (EDX). The IR spectra of the samples were recorded using a Perkin-Elmer infrared spectrophotometer with a resolution of 4 cm^{-1}, in the range of 400-4000 cm^{-1} region for sample dispersed in KBr pellets (10:90 ratios).

RESULTS AND DISCUSSION

Characterization of the Adsorbents

The phase analysis of the prepared nanomaterials was analyzed by XRD using CuKα radiation. Figure-1 shows the XRD patterns of the as prepared MgO, α-Fe_2O_3 nanoparticles and α-Fe_2O_3-MgO nanocomposite. The pattern (a) contains the characteristics peaks of MgO and can be index to cubic crystal structure according to JCPDS No: 45-0946. The pattern (b) contains characteristics peaks of hematite (α-Fe_2O_3) and can be index to rhombohedral crystal structure according to JCPDS No: 24-0072. The pattern (c) contains the characteristics peaks of both MgO andα-Fe_2O_3. The X-ray diffractograms reveal the well crystalline nature of the compounds[7].

FT-IR Analysis

Fourier transform infrared spectroscopy (FTIR) results were recorded using Perkin-Elmer FTIR (Spectrum RX-I) spectrophotometer. The spectra of nanomaterials were taken in the spectral range of 4000-400 cm^{-1} and the patterns are presented in figure 2. The characteristic peak at 436 cm^{-1} corresponds to Mg-O stretching frequency of MgO (figure 2a) and the peak at 535 cm^{-1} mention to Fe-O stretching vibration of Fe_2O_3 (figure 2b). The IR spectra of α-Fe_2O_3-MgO nanocomposite (fig-2c) show that presence of both Mg-O and Fe-O vibration peaks[7,12].

Surface Morphology

In order to understand the morphologies of our nanocomposites, FESEM analysis was performed. Fig. 3(a) and 3(b) shows the FESEM images of α-Fe_2O_3-MgO nanocomposite. This image indicates that there is formation of fine nanoparticles with average diameter range 50-80nm.Figures 3(c) and 3(d) shows the EDX elemental mapping and EDX spectra of α-Fe_2O_3-MgO nanocomposite respectively, in which presence of Fe, Mg and O is indicated.

Adsorption of Congo Red(CR) dye

Effect of the Adsorbent Dosage on the removal of CR: In order to study the effect of the adsorbent dosage and optimum dosage for the removal of CR, we have carried out adsorption experiments by varying the amount of MgO, α-Fe_2O_3andα-Fe_2O_3-MgO nanomaterials using 100 mg/L of a CR stock solution for 30 min of contact time with changing the quantity of adsorbents were ranging from 0.01 g to 0.1 g maintaining the solution volume of 20 mL is represented in Figure 4a. It is observed there is a continuous removal of CR with increase in adsorbent dose up to 0.05 g. for all three materials. This may be due to an increase in number of active sites of the adsorbent material with increasing amount of the adsorbent. Further increase in the amount of the adsorbent does not bring any considerable change in the adsorption, i.e., approximately straight line after 0.05 g thus 0.05 g was chosen as the optimum amount for all studies of the adsorbents. The highest percentage of removal obtained forα-Fe_2O_3-MgO nanocomposite among the three adsorbents.

Effect of the solution pH on the removal of CR: To investigate the effect of pH on the adsorption of CR dye, the pH ranges 2–8 was chosen. The pH of the test solutions was adjusted by using HCl and NaOH solutions. An amount of 0.05 g of each adsorbent were used in 20 mL of 100 mg L^{-1} CR solution of each pH with 30 min agitation time. From Fig. 4b, it is found that, there is no significant change in the percentage adsorption by increasing pH from 3 to 5 and reached maximum at pH 5 and then slightly decreased at higher pH. For all the materials. This is due to at higher pH, the adsorbents surface become negatively charged. Therefore, the adsorbents did not favour the adsorption of negatively charged CR dye due to electrostatic repulsion.

Kinetic Studies: The effect of contact time on the adsorption of CR by MgO, α-Fe2O3 and α-Fe2O3-MgO nanomaterials were studied for initial concentration of 100 mg/L of 20 ml CR solution. The contact time varied from 10 to 60 minutes. From the figure 6 (a), it is observed that maximum adsorption occurred within 30 min of contact time, thereafter the rate of removal became rather slow i.e. the adsorption reaches equilibrium after 30 min for all nanomaterials. The highest removal of CR is found to be 97.97 % for α-Fe_2O_3-MgO, 93.24 % for MgO and 84.62 % for α-Fe_2O_3 for 30 min contact time.

We have studied the kinetics of adsorption of CR by MgO, α-Fe_2O_3 and α-Fe_2O_3-MgO adsorbent and the experimental data obtained are applied to pseudo-first-order and pseudo-second-order kinetic model. Pseudo-second-order kinetic model was more preferable for adsorption of CR. The integrated form of pseudo-second-order kinetic equation is:

$$\frac{t}{q_t} = \frac{1}{k_2 q_e^2} + \frac{t}{q_e} \quad (1)$$

Where k_2 [g/(mg min)] is the rate constant of the pseudo-second-order equation and q_e and q_t are the amounts of solute adsorbed on the adsorbent at equilibrium and at time t, respectively. The values of q_e and k_2 can be determined by the slope and intercept of the straight line of the plot t/q_t versus t, respectively. The values of q_e and k_2 along with correlation coefficients of the pseudo-second-order model for the adsorption of CR for all materials is shown in table 1 and the pseudo-second-order plots of MgO, α-Fe_2O_3 and α-Fe_2O_3-MgO are given in Fig. 6b. The values of predicted equilibrium adsorption capacities(qe) showed good agreement with the experimental equilibrium uptake values. Similarly, correlation coefficients are always greater than 0.99, which also explains the good fit of the model. The maximum adsorption capacity (qmax) for the adsorption of CR onα-Fe_2O_3-MgO compared to other adsorbents is listed in Table 1. It is observed that the prepared α-Fe_2O_3-MgO is an efficient adsorbent for adsorption of CR from aqueous solution.

CONCLUSIONS

In this present study, we have synthesized MgO, α-Fe_2O_3nanomaterialsand α-Fe_2O_3-MgO nanocomposites by hydrothermal method. The obtained composites nanomaterials were calcined at 500^0Cto form desire product. FESEM images indicate the formation of fine nanoparticles with diameter around 50–70 nm. The XRD study represents the formation of mixed oxidesMgO-Fe_2O_3nanocomposites.The formation of nanocomposites was further confirmed by FTIR study. Then, the prepared α-Fe_2O_3-MgO composite nanomaterials were used as adsorbent for removal of carcinogenic organic dye such as CR from aqueous solution. From the adsorption study, it was found that α-Fe_2O_3-MgO nanocomposite was the most effective adsorbent for the removal of CR dye from aqueous solution as compare to pristine MgO and Fe_2O_3 nanoparticles. It is observed that the composites nanomaterials remove 98% of Congo red within 30 min of contact time.

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Table 1. Pseudo- second-order kinetic parameters for the removal of CR dye.

Adsorbents	K_2 (g mg^{-1} min^{-1})	q_e (mg/g) (Calculated)	q_e (mg/g) (Experimental)	r^2
α-Fe_2O_3	0.00832	37.17	34.8	0.998
MgO	0.00727	40.16	37.32	0.9984
α-Fe_2O_3-MgO	0.0075	42.37	39.25	0.9992

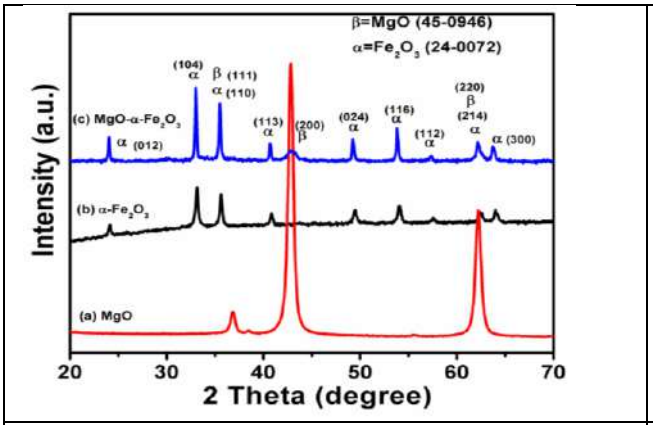

Figure 1. XRD patterns of (a) MgO, (b) α-Fe_2O_3 nanoparticles and (c)α-Fe_2O_3-MgO nanocomposite.

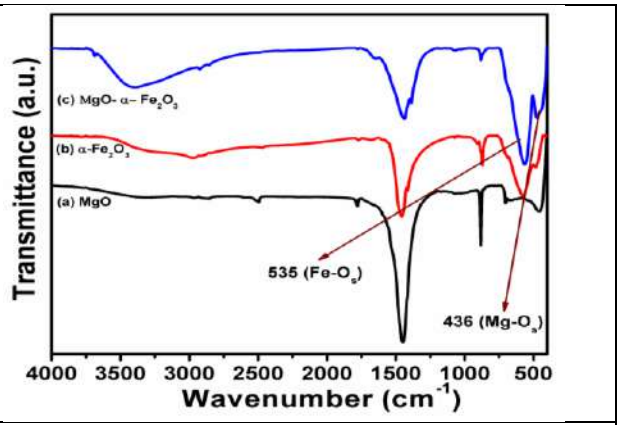

Figure 2. FT-IR patterns of (a) MgO, (b) α-Fe_2O_3 nanoparticles and (c)α-Fe_2O_3-MgO nanocomposite.

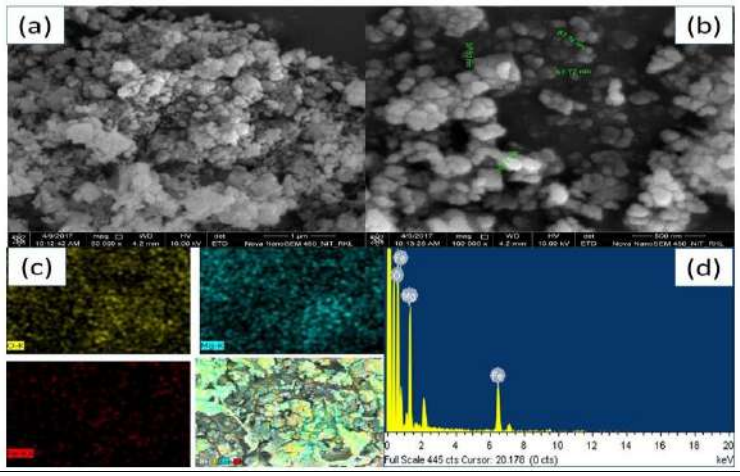

Figure. 3 FESEM image of (a) and (b) α-Fe_2O_3-MgO nanocomposite, (c) EDS elemental mapping and (d) EDX spectra of α-Fe_2O_3-MgO nanocomposite.

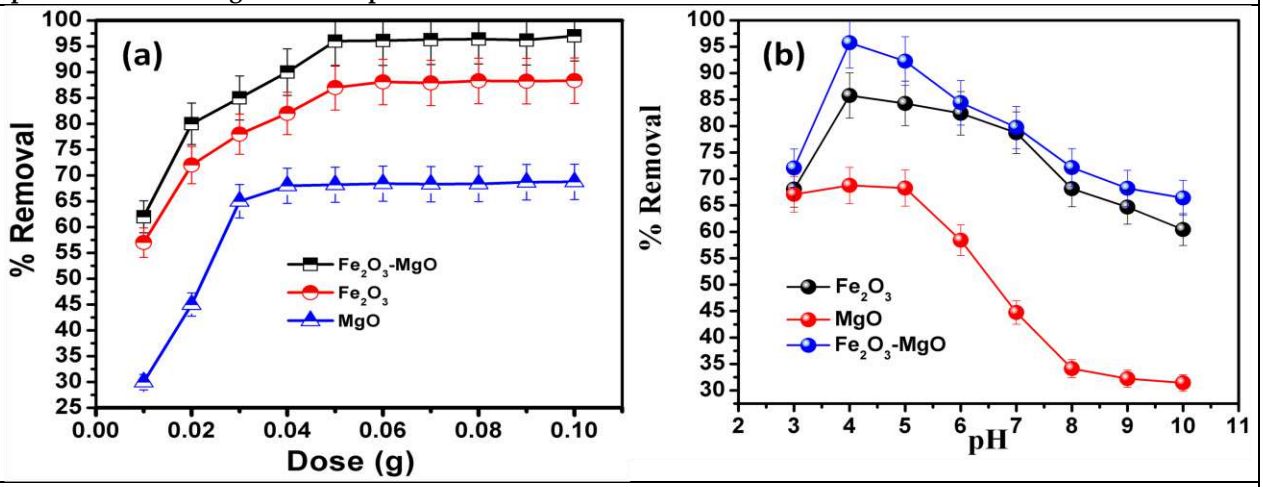

Figure 5 Effect of a) amount of adsorbent (dose), and b) pH on the removal CR dye byMgO, α-Fe2O3 and α-Fe2O3-MgO nanomaterials.

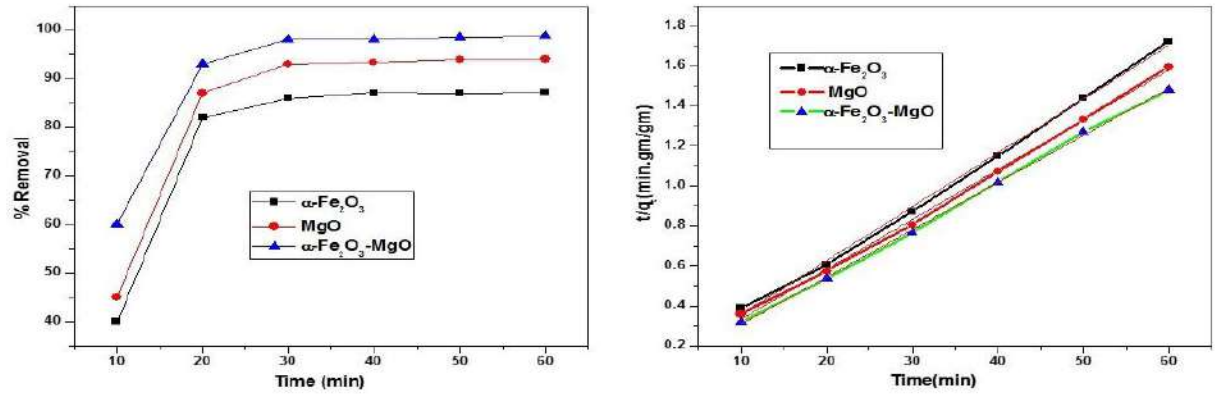

Figure 6(a) Percentage removal of CR dye as a function of time (min), and (b) Pseudo-second-order plot for CR removal by MgO, α-Fe_2O_3 and α-Fe_2O_3-MgO nanomaterials.

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REVIEW ARTICLE

A Review on the Fate of Bacterial Association during Vermicomposting of Industrial Wastes

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ABSTRACT

Vermicomposting technology is an emerging environmentally sustainable decompose process that obtaining with enriched material from various waste residues. This is a non-thermophilic process which undergoes oxidation in biological environment that is formed by certain species of earthworm. It leads to an enhanced soil conversion from one form to other means conversion of organic and inorganic waste to compost. By this process it enhance the microbial population in the soil as well as maintain the physico-chemical properties which increases the soil productivity. Different types of bacteria are found in vermicompost which depends on the environmental condition and types of used raw materials.A review work has been carried out here to identify the bacterial forms present in the industrial vermicompost sample which gives us an insight as to what are the constituents of this samples, what are the methodologies done by various researchers to incubate and detect the bacterial colonies in Industrial system which are interconnected by various physical, chemical and biological processes. As it's witnessed that the waste treatment systems such as theindustrial effluents are affected by various activities of microbe's specifically bacterial growths. Different culture analyses, qualitative and quantitative tests are performed by various researchers to evaluate the colonies, how the morphology and its proper characters are studied along with role of the earthworm with the bacterial species in the vermicompost enrichment. The beneficial potentials are studied which provides a better insight as to how the soil can be used for better agricultural and plant productivity.

Keywords: Earthworms, Vermicomposting, Bacterial species, Microbial diversity, Culture methods, Bacterial Identification, Inorganic waste vermicompost.

INTRODUCTION

General Overview of vermicompost, earthworms and microbes

Soil, is the basis of life form on earth and act as an abiotic agent that supports all kind of life that highly necessary for growth, survival and plant habitat. There is diverse form of micro floral activities observed in this soil. The most commonly found bacteria found in the soil include the genus like Bacillus, Pseudomonas and Streptomyces etc., which are bountiful producers of secondary metabolites that seem to possess various minerals and nutrients by different method like nitrogen fixation. Earthworm's major activity during vermicomposting is to breakdown the large solid soil particles and change the inorganic waste to enhance the organic matter availability by grinding and digesting them with the help of aerobic and anaerobic microbes (Jacoby et al., 2017). There is also an enriched nutritional soil due to the worm casts as they are themselves a rich source of nutritional micro, macro and enzymes (Lavelle and Martin 1992). Microbes are one of the most essential part of the ecosystem as a ubiquitous part of biodiversity's biotic part. Diverse microbes exists such as the bacteria, fungi, actinomycetes, etc. which are responsible for the biochemical degradation of organic matter (Emperor et al., 2015) and maintains ecological balance. The bio compost with inorganic waste, when combined with earthworms, is an excellent booster and improver for soil aggregation, soil fertility, plant nutrition, and beneficial microorganism development (Pereira et al., 2014). The soil quality is enhanced in terms of aeration and water holding capacity, which helps to promote plant development, restore microbial population, which includes nitrogen fixers, phosphate solubilizes and other macro and micro nutrients.

The soil's structural features are also improved, which aids in avoiding erosion and, as a result, improves crop yield and sustainability (Zhu et al., 2017). The physico-chemical properties of the soil are also observed to be improved as a result of the beneficial microbial communities' action (Pathma et al., 2012).The digestive activities of earthworms degraded the soil components and other industrial waste and improved as a result of better absorption of soil microorganisms with organic wastes from soil sources, and their population may grow during transit through the intestinal system. (Selvi et al., 2015).Microorganisms discovered biomaterials that were suited for their growth and product production. Micronutrients are generated as a result of interactions between microorganisms, soil components, and earthworms. Plant growth promoting microorganisms (PGPMs) are a category of microorganisms that includes *Azospirillum, Azotobacter, Phosphobacterium, Rhizobia*, and Cyanobacteria. Vermicompost improves soil aggregation, soil fertility, plant nutrition, and beneficial microbial development. Vermicompost is a nutrient rich preparation which is generally produced from various organic waste, inorganic wastes, industrial wastes, etc. through the combination of it with variety of earthworms and microorganisms (Dominguez et al., 2019; Dominguez et al., 2018; Ali et al., 2015). As the nutritional value of soil is increased manifold due to the addition of vermicompost an insight of its utilisation is being studied here in this review paper to describe the diverse bacteria obtained from the inorganic waste vermicompost and its nutrient status as a vermicompost and its significance in agriculture and waste management. This present work is relevant to the SDG no. 11- Sustainable cities and communities and SDG no.-15-Life on land.

Earthworm

The applications of the worms are seen since old times either as fishing bait or as a food resource providing protein and enzyme source for various food products, be it for animals or as it's utility as biodegradable cleansers. These worms convert waste into worm rich manure otherwise known as the worm-casts which are highly nutritious biologically derived and beneficial both in the field of biological sciences as well as in agricultural production. Several species such as *Eisenia foetida, Eudrilus eugeniae, Perionyx excavates, Lumbricus rubellus, Eisenia Andrei, Dendrobaena veneta, Dichogaster bolaui, L. terrestris, Allolobophora caliginosa, and A. terrestris* etc. are involved in vermicomposting. Out of which *Eisenia foetida, Eudrilus eugeniae* are mostly used as ancient species for vermicomposting.Vermicomposting is utilising the worms for production of compost which is a type of composting method. It is also otherwise known as worm farming whose recent advances are seen both on a small and large scale levels with three major mind goals which is proper waste utilisation, producing vermicompost, and vermiculturing.

Earthworms and Vermicomposting

Large scale production is seen by production of various worm beds which have different equipment to harvest vermicompost and to separate the worms. Continuously there is an in-vessel flow system systems designed to produce vermicompost. Generally they are surface-feeders but to incorporate a casting harvest mechanism on the bottom of the system, below the active feeding area the additional settings of the food and the additional bedding are added to the top layer, to encourage their work moving from the down to the upwards.In the castings, some worms and egg cases will be left, which can be utilised to start indoor plantations. Curation of casting is a necessary process before using it in outdoor applications. Castings should be put into potting soil as soon as possible after harvesting for the optimum effect on indoor plants. Outdoor plants must be exposed to aerobic conditions in order to dry out and avoid the growth of mould due to damp circumstances.

Quality of the Vermicompost

The results of the vermicompost obtained from the inorganic wastes seems to possess fine percentage of microorganisms in association with the earthworms, nutritious excretory materials having tons of nitrogenous and other end products which is obtained after the metabolism of the earthworms and leads to the castings in the form of vermicast. The casts obtained are seen to possess high moisture content, high carbon content due to the presence of inorganic sulphur, carbon, phosphorus in its constituents and rich oxygen conditions provide an extraordinary favourable microenvironment for wide range of decomposing microorganisms.

Industrial wastes which are agro-based

Typically, any industrial waste that will be used to make vermicompost seems to be of either organic or inorganic origin from wastes that may be further processed to undergo degradation by bio-means. As long as it doesn't have any harmful qualities for earthworms, that is. When industrial wastes are collected from agro-based companies, a large source of plant substrates is created, as well as a loss of resourceful material. Due to in situ burning in the fields or land disposal in the adjacent areas, these wastes are now either severely underutilised or entirely unutilized. These agro-industrial wastes might be successfully exploited for resource recovery using vermicomposting technology for use in sustainable land restoration techniques, both individually and collectively. The accompanying Fig.1 depicts a wide range of agro-based industrial wastes recovered after processing for use as vermicomposting.

Bacterial diversity in association with earthworms in vermicompost

The gut microflora of Earthworm determines the ability to enhance the plant rich soil. Indirectly the processing of the soil texture and fertility is enhanced by the earthworms as they form the litter and affecting the activity of the soil microbes (Petersen and Luxton1982; Lee 1985; Edwards and Bohlen 1996). Microbial interactions with the earthworms are of great interest but too complex. Most bacteria which is ingested by the earthworms are the rhizobium bacteria such as *Pseudomonas, Rhizobium, Bacillus, Azosprillium, Azotobacter*, etc. which are associated with the soil with rhizobium, which are seen to get activated due to the formation of gut microflora of the worms. Therefore, this vermicompost idea increases the activity of earthworms which indirectly influences the population of plantgrowth-promoting Rhizobacteria (PGPR) (Sinha et al.,2010). Free living soil bacteria and the earthworm microbes are seen to be associated with one another. List of vermicompost bacteria and their beneficial traits are depicted clearly in the following fig.2:

Earthworms such as *L. terrestris, Allolobophora caliginosa, and A. terrestris* have been shown to contain microbial communities in vermicompost that comprise different bacteria such as actinomycetes, filamentous fungus, and yeast, according to another research (Parle 1963a, b). Khambata and Bhat (1953) found that an oxalate-degrading *Pseudomonas oxalaticus* was isolated from *Pheretima posthuma* in vermicompost. Citernesi et al., 1977 found anaerobic nitrogenous-fixing bacteria such as *Clostridium butyricum, Clostridium beijerinckii, and Clostridium paraputrificum in E. foetida*. Contreras, 1980. Researched *Streptomyces lipmanii and Streptomyces spp. E. lucens* reported by Contreras, 1980. From Kristufek et al., 1993, *Actinobacteria L. rubellus* was isolated. Devliegher and Verstraete, 1997 discovered fluorescent pseudomonads *L. terrestris*.

Bacterial isolation from industrial wastes vermicompost

A study done by Satpathy et al., 2020 proved to identify various bacterial specimens from the vermicompost produced from industrial wastes, cow dungs, and other component from organic vermicompost. The physico-chemical characters and the qualitative and quantitative studies for the studying the bacteria isolated from vermicompost samples showed around 8 bacterial species which includes the *Actinomyces israelli, Micrococusluteus, Azotobacter, Bacillus cereus, Enterobactor, Pseudomonas aeruginosa, Bacillus subtillis.* This microflora was seen in the earthworm gut as well as indicated it's identification a better experience towards better crop production and to effectively manage plant diseases.Similar studies done by Pathma et al., 2013, where a total of one hundred ninety three bacterial species were studied that were studied for its fertilising potential. This research focused on the straw and goat manure-based vermicompost produced by the earthworm *Eisenia foetida*. The bacterial sequencing when done showed the abundance of three major genera which 15 percent of *Pseudomonas*, 57 percent of the *Bacillus*, 12 percent belonging to the genera *Microbacterium* and the rest included smaller percentages of 5 percent , 3 percent and insignificant percentages of *Acinetobacter, Arthobacter, Chryseobacterium*, *Pseudoxanthomonas, Panibacillus, Stenotrophomonas, Rhodococcus, Cellulmonas, Enterobacter and Rheinheimera*. Thus, this study concluded the *Bacillus* genera as the majorly found bacterium in the taken sample followed by the bacterium of the genera *Pseudomonas* and genera *Microbacterium*.

A research carried by Namlı et al., 2020 performed a study on the vermicompost preparation from the by-products wastes obtained from the agro-industrial wastes of the sugar industry. This experiment concluded that the nitrogen-fixing bacteria were affected which affected the total nitrogen nutrient content in the vermicomposting done.Another study carried on by Vasanthi et al., 2014 when the vermicomposting was done on the sugar factory wastes using various species of earthworms like the Epigeic Earthworm. *Azospirillum* enhances the soil fertility along with accelerated plant growth promoting activity by this bacterial growth by addition of this industrial vermicompost. Thus, concluding the bacterial presence abundantly in all forms of vermicompost types which includes its sample collection either from organic wastes, industrial wastes, municipal wastes, sewages and inorganic wastes. But the studies related to the vermicompost samples in relation to the inorganic wastes is very few and needs a better experimentation as well as hypothesis for its implementation.

Functionality of industrial waste vermicompost

Vermicomposting is one of the beneficial aspects of nature whose essentiality can't be explained as its significance is globalised in the major sector or needs of human life which is in the food development and agriculture. There are several factors on which vermicomposting depends but a few are enlisted below:

Bacterial role in industrial waste vermicompost

Pathma et al. (2011b), soil is the infinite life's spirit, promoting different microflora. Bacillus, Pseudomonas, and Actinomycetes, among other soil microorganisms, develop the secondary metabolites that act against the co-existing phytopathogenic fungi and human pathogenic microorganisms.Edwards and Bohlen (1996), the behaviour of earthworm gut microflora is likely to affect the ability of earthworms to increase plant nutrient availability. Earthworms indirectly impact the dynamics of soil chemical processes by commentating the litter and regulating the behaviour of the soil microflora. *Pseudomonas, Rhizobium, Bacillus, Azosprillium, Azotobacter*, and other plant growth-promoting rhizospheric bacteria are swallowed by earthworms with rhizospheric soil, and they may be activated or enhanced owing to the gut's optimal micro-environment, according to Sinha RK et al. (2010). The population of plant growth-promoting rhizobacteria (PGPR) rises as a result of earthworm activity. Mariangela Hungria (2018), was reported that *Azospirillum* is a genus of plant-growth-promoting bacteria (PGPB) that has been extensively studied. Plant benefits from *Azospirillum* inoculation have been attributed primarily to its ability to fix atmospheric nitrogen, but also to its ability to synthesise phytohormones, especially indole-3-acetic acid. According to Vivas et al. (2009), vermicompost included a high concentration of Actinobacteria and Gammaproteo bacteria, whereas conventional compost contained a high concentration of Alphaproteobacteria and Bacteriodetes, the bacterial taxonomic groups' characteristic of non-cured compost.

Future prospective

There is ample database about the vermicompost, it's mechanism and the earthworms in its relation. But detailed pathogenic and worm relationship and it's mechanism of action is yet to be done. A number of studies targeted it's mechanism as a pilot study but its population analysis, and as a bioreactor from vermicomposting samples are very rare. Generally this paper highlights the comparison of bacterial growth between the vermicomposting from organic samples and the vermicompost produced from industrial waste. This review stressed the need of thorough study of such waste product composting by-products for it's the a major waste being formed and whose analysis will be highly beneficial for the better waste management into usable forms and will further help in better soil management, reduce soil pollution as well as greater soil manures discovery. Understanding the variety of microorganisms in soil and vermicompost will lead to improved extraction and assessment of micro biome-derived advantages in vermicompost, which will be a critical step in the development of commercial and field applications to promote sustainable agriculture and soil health. Future research on the impact of the microbial community in vermicompost soil is essential since it can lead to improved plant growth promotion and disease suppression, which would include both fungal and bacterial communities in the soil. Vermicomposting is a bio-oxidative process in which the earthworm interacts extensively with microorganisms, speeding up the stabilization of organic materials and improving crop plant development and yield.

CONCLUSION

Although the review studies are generally similar to those in previous vermicomposting studies, the material supplied for the starting sample is an important distinction of our study. The study started with an industrial substrate vermicompost sample about which information is very rare as the experimentation performed here is lacking w.r.t inorganic manure decomposition of the industrial wastes. Generalised studies are done on the inorganic wastes. Additionally a diversified and increased bacterial samples were obtained in the vermicompost sample culture of the media analyses by various other researchers in the organic samples conclude the various bacterial presence and its possession of greater genetic diversity during vermicomposting. This bacterial diversity will further lead to various functional aspects of the soil.

Various studies also claim these microbes to be a rich source in maintaining the soil and support plant growth as a study done on *Actinomycetes* proved to suppress the pathogenic growth thus, this culture can prove to be useful in keeping the various plant diseases at par (Dilip et al.,2013).Similar studies done on Micrococcus spp. provided as insight as to use to this bacterial agent to prevent the various environmental stressors such as desiccation and starvation in environmental and host-associated ecosystems. Thus, proving it be a great agent to be used during the soil erosion control conditions. *Azotobacter* and vermicompost are a common and significant agents used in crops as biofertilizers as it lead to normalising nutrient deficit soil and well as in reclaiming the deficit irrigation (Shirkhani et al.,2016).

The research backs up the presence of a group of bacterial strains in vermicompost made from various concentrations of industrial and organic wastes. The bacterial strains discovered in their investigations utilizing phenotypic studies such as colony shape and microscopic analysis will aid our research using inorganic waste vermicompost samples. According to other research, all of these bacteria are helpful since they increase the nutritional quality of vermicompost as well as soil aeration and fertility. Finally, vermicomposting evaluations on various types of inorganic wastes will aid in determining the destiny and functioning of various pathogens during the breakdown of these polluting substances. Extensive research investigations are urgently needed since this discovery will assist bridge the gap between studies and solve one of the most pressing environmental concerns.

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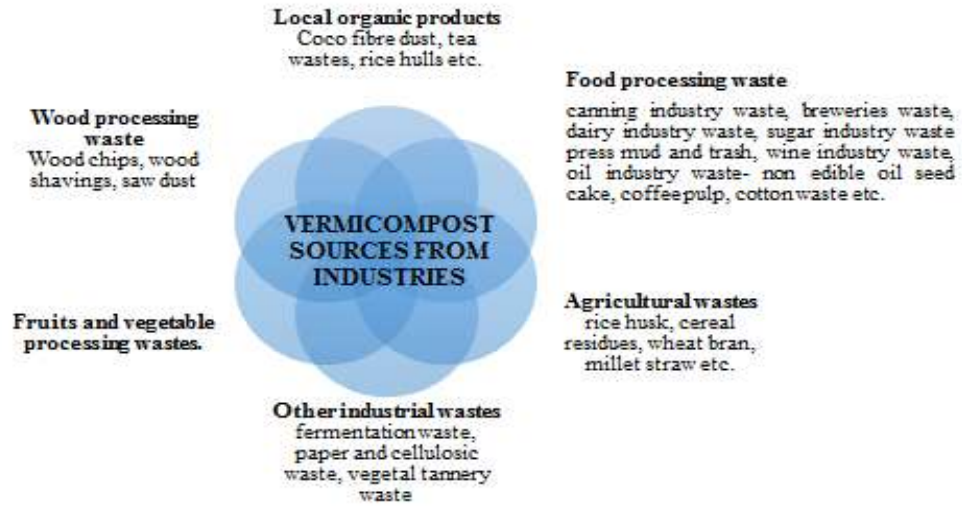

Fig 1. Various Vermicompost Sources

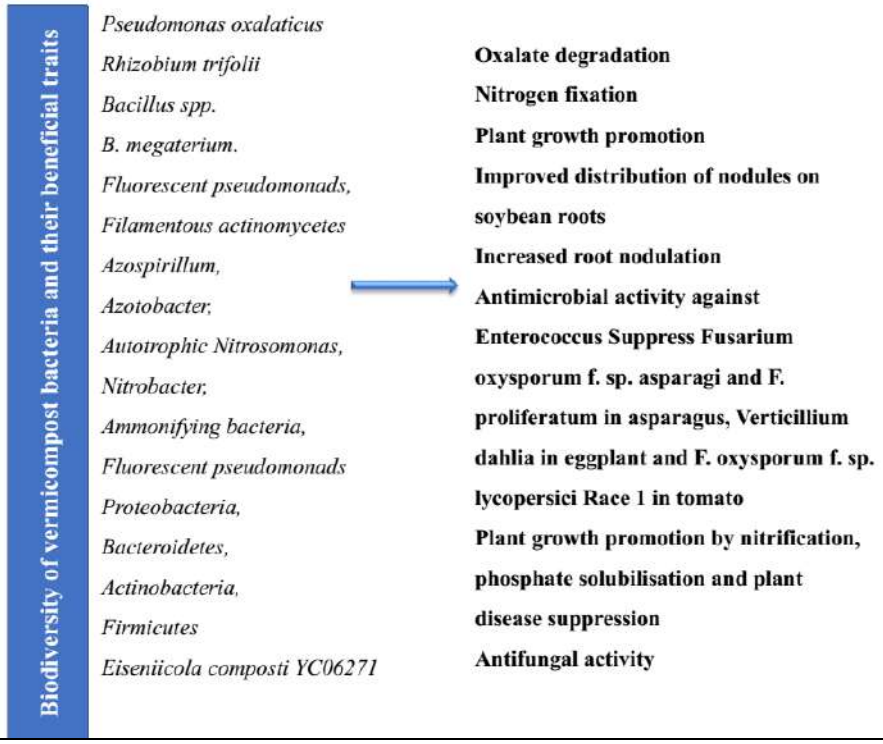

Fig 2. Diverse vermicompost bacteria and their beneficial traits (Pathma et al., 2012).

RESEARCH ARTICLE

Green Synthesis of MgO Nanomaterial using *Azadirachta indica* leaf Extract for Adsorptive Removal of Congo Red Dye from Water

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ABSTRACT

Green Chemistry is the design of chemical products and processes that reduce the generation of hazardous substances. Synthesis of nanoparticles is used as a bio-based substances that has been proposed as a cost-effective and environmentally friendly. It isalternative of chemical and physical methods that is used for the preparation of Magnesium oxide(MgO) nanomaterials by using Neem (*Azadirachta indica*) leaf extract. After that the synthesized nanomaterial is used for the removal of Congo red (CR) dye from water. Formation of MgO was confirmed from the XRD analysis. FESEM study was revealed the formation on fine nanoparticles from the adsorption studies, it is confirmed that CR adsorption is pH dependent and maximum adsorption occurs at pH=4.

Keywords: *Azadirachta indica*, Magnesium oxide, Nanoparticles, Congo red, Adsorption

INTRODUCTION

Magnesium oxide naturally occurs in three different mineral forms Carnallite, Magnesite and Dolomite are the ores of magnesium metal. As the mineral known as magnesium oxide, MgO is the main source of magnesium. MgO crystallizes in a cubic cell with a rock-salt structure. The crystal structure can be described as an FCC lattice of Mg ions with O ions occupying all the octahedral holes or vice versa. MgO can also be obtained in various polymorphs. MgO nanoparticle size ranges from 1-100 nm. Also, MgO can be used to as vehicle for targeted drug delivery as well as coating for nanoscale anti cancerous drug and for magnetic data storage. Apart from these MgO nanoparticles are also used in industries coatings, plastics, nanowires, nanofibers, and textiles and in specific alloy, water purification and catalyst applications[1–5].

Green Chemistry is the design of chemical products and processes that reduce or eliminate the use and/or generation of hazardous substances. The synthesis of nanoparticles using bio-based substances has been proposed as a cost-effective and environmentally friendly alternative to chemical and physical methods. Plant-mediated synthesis of nanoparticles is a green chemistry approach that connects nanotechnology with plants. The extract obtained from leaves, barks, and seeds are widely exploited for catalyzing a synthesis. The present scenario, where much effort are being paid towards searching green alternatives for conventional synthesis method has driven the research to a new scale where exploiting nature in more judicious way has shown a bright future for green synthesis[6].Congo red (CR)is a benzidine based anionic dye. It is generated from textiles, printing and dyeing, paper, rubber and plastics industry, among others. CR is known to metabolize into benzidine, which is a known human carcinogen[7–12]. Therefore, it is very important to remove residual Congo red from water sources before discharge to receiving water bodies. Treatment of wastewater containing dyes is conventionally done by several physicochemical and well as biological methods including coagulation-flocculation, advance oxidation, adsorption, ozonation, photo-chemical degradation, fungal decolorization, etc. However, adsorption is the most popular method due to its low operational cost, low maintenance and simplicity[13–16]. Under the adsorption treatment method, Iron oxide nanomaterials rank as the most widely used materials due to their stability, functionality, extremely high surface area and regener ability.

The Sustainable Development Goals (SDGs), also known as the Global Goals, were adopted by the United Nations in 2015 as a universal call to action to end poverty, protect the planet, and ensure that by 2030 all people enjoy peace and prosperity. The 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 3 (Good Health and well-being), 6 (Clean water and Sanitation),11 (Sustainable cities and Communities) and 12 (Responsible consumption and Production) and 14 (Life below water). Here our main objectives are to synthesize MgO nanoparticles using chemical free *Azadirachta indica* (Neem) leaf extract. Then the prepared nanomaterial characterizes using XRD, FESEM, FTIR analytical method. Then these nanomaterials use for the removal of CR dye from water.

MATERIALS AND METHODS

Materials

All chemicals were analytical grade and thus used as received without doing any further purification. $Mg(NO_3)_2$ and Ethanol were purchased from were purchased from Merck, India. For all adsorption experiments, distilled water (DW) was used.

Preparation of plant extract

Fresh leaves of *Azadirachta indica* leaves were collected from the campus of CUTM BBSR and were washed meticulously with water to remove any dirt and impurities and are then rinsed with distilled water to remove ionic impurities. The washed leaves were then cut and crushed using mortar and pestle, distilled water is added in 5:1 ratio. This solution is gently heated to about 60-80^{o}C for 10 minutes and cooled down at room temperature. The solution is filtered and centrifuged for 5 minutes at 4000 rpm. The obtained plant extract is ready to use. Extract can also be stored for 2-3 days if required.

Preparation of MgO nanomaterial

To prepare MgO nanomaterial, firstly 0.1 M $Mg(NO_3)_3$ solutions are prepared using DW. After complete homogenization of the solution, leaf extract is added drop wise to the solution using a burette with constant stirring

in approximately 1:1 ratio for about 15 min. After complete formation of precipitate, solution is kept for undisturbed again for 45 min and then it is centrifuged for 5 min at 4000 rpm. The precipitate obtained is washed thoroughly with DI water and alcohol for removal of ionic impurities followed by Acetone to remove any organic impurities. Formed precipitate is then oven dried followed by combustion at 400^{o}C for 12-14 hours. The overall synthetic procedure is shown in Fig. 1.

Characterization

The prepared samples were characterized by X-ray diffraction (XRD; Riguka, Ultima IV). The XRD system has a wide-angle Theta, Copper X-Ray tube with high intensity (1.54Å wavelength). The scanning was carried out at 2Θ, from 5° to 60°. The performed adsorption studies were carried out using UV Spectrometer (UV-VIS; Hitachi Inc., U-3900). FTIR Technique (Perkin-Elmer FTIR (Spectrum RX-I)) was used for analyzing chemical bonds with the 400 to 4000 cm^{-1} range at room temperature. The morphological feature was determined by field emission scanning electron microscopy (FESEM, Nova-450).

Adsorption Experiments

To study the effect of pH a set of adsorption experiments were carried out for CR adsorption by changing the pH from 2 to 10 on MgO surface. In the equilibrium adsorption tests, 0.05 g of MgO nanomaterial was added to 50mL of 100 mg/L CR solution in 100 mL blue capped bottles. All the adsorption experiments were performed using an orbital shaker (Remi RS 12 plus) with continuous shaking (250rpm) at room temperature. The adsorbent after adsorption was separated out by centrifugation. Then the adsorbent free solution was collected for analysis. The final concentration of CR after adsorption was measured by UV-vis spectrometer with maximum wave length at 498 nm. The equilibrium adsorption capacity ($q_e$in mg/g) was calculated using equations 1 and % removal (%R) was calculated using equation 2 .

$$q_e = (C_o - C_e)V/m \quad (1)$$

$$\%R = (C_o - C_t)/Co \ X100 \quad (2)$$

C_o and C_t (mg/L) are the initial concentration and final concentration at time t respectively. C_e (mg/L) is the concentration at equilibrium. V is the volume (L) of solution and m is the mass (g) of the adsorbent. All the adsorption experiments were repeated three times and the average value of the data were considered for final results.

RESULTS AND DISCUSSION

Characterization

Fig. 1 reveals the XRD patterns of MgO nanomaterial. The XRD pattern of MgO contains characteristics peaks at at 2θ=37.05°, 43.42° and 62.1° belong to the plane (111), (200), and (220) respectively are index to cubic structure of MgO according to JCPDS no. 45-0946 [17]. FESEM analysis shows the formation of MgO nanoparticles (Fig. 2). The nanoparticles were irregular shape with particle size range from 50 to 90 nm. The larger nanoparticles may be due to the aggregation of the smaller ones.

Adsorption studies of CR dye

The pH is the important parameter for adsorption experiment because the adsorbent and adsorbate substance change their properties with different pH of the solution. Hence, we have performed CR adsorption on MgO surface with changing the pH of the solution from 2 to 9 where other parameter are fixed (dose=0.05 g, time=60 min, concentration= 100mg/L and volume of the solution= 50mL). The pH of the CR solution was maintained using 0.1M NaOH and 0.1M HCl. The obtained experimental results were presented in Fig. 3. From this figure, it is found that, removal efficiency lower at higher pH of the solution. And the maximum adsorption occurs at pH=4 and 5. This result is explained with CR structure and surface properties of adsorbent at different pH. CR is a negative dye and it

exists in anion form. Hence for better adsorption it requires positive surface. At lower pH surface has more positive ions so higher adsorption of CR occurs through electrostatic interaction and lower adsorption occurs at higher pH due to electrostatic repulsion.

CONCLUSIONS

An environmentally friendly and cost-effective method was used for the preparation of silver-magnesium oxide α-MgO nanomaterials using Neem (*Azadirachta indica*) leaf extract. Then the synthesized nanomaterial used for the removal of Congo red dye from water. From the XRD analysis, the formation ofMgO was confirmed. FESEM study was revealed that the formation on fine nanoparticles. From the adsorption studies, it is confirmed that CR adsorption is pH dependent and maximum adsorption occurs at pH=4.The beauty of this work is its full fill the SDGs number 3 (Good Health and well-being), 6 (Clean water and Sanitation), 11 (Sustainable cities and Communities) and 12 (Responsible consumption and Production) and 14 (Life below water).

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Fig. 1 Synthesis MgO nanomaterials by using Neem-leaf extract

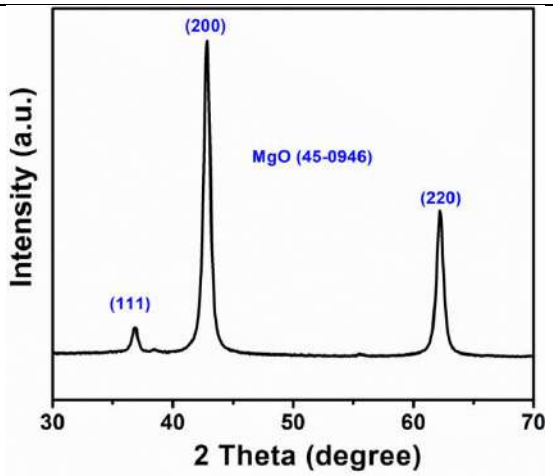

Fig. 2. XRD of MgO nanomaterials

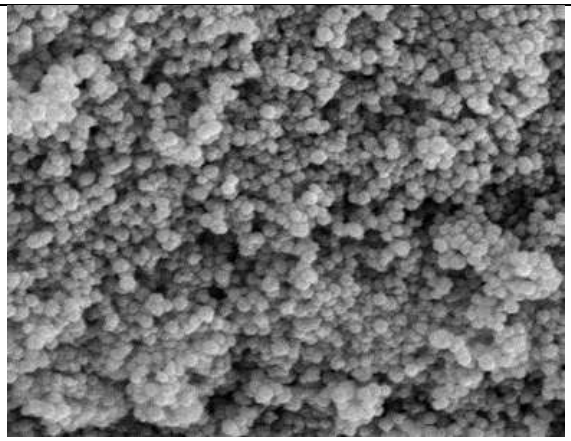

Fig-3 FESEM image of MgO nanomaterials (resolution 1 μm)

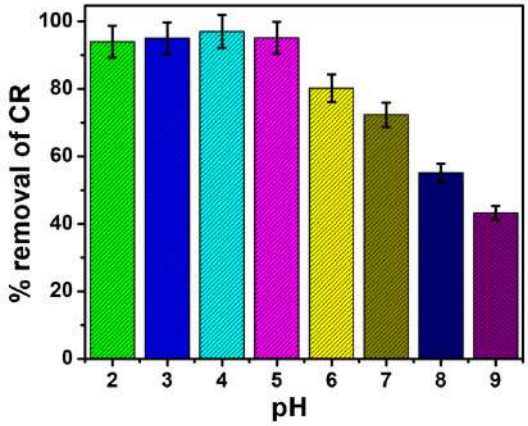

Fig. 4. Effect of pH on the removal of CR dye on MgO surface

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REVIEW ARTICLE

A Review on the Effect of Biofertilizers on the Growth, Yield and biochemical parameters on Green gram (*Vigna radiata)*

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ABSTRACT

India is an agricultural based country. A major part of the Indian economy is sustained on agriculture. It gives employment and socioeconomic status was increased. To enrich the soil quality bio fertilizers are used in agriculture. For the production of crop they are play an important role. As they are ecofriendly they don't have harmful effect on the environment. They are cost effective and pocket friendly as compared to other chemical and synthetic fertilizers. They are also renewable source of energy. Bio fertilizers are able to maintain the long-term fertility in the soil. They are inoculants of microorganism that helps in improving of production in agricultural system. A review was done to know the effect of different bio fertilizers on growth and yields of green gram .

Keywords: Bio fertilizers, Green gram, agriculture, production, micro organisms.

INTRODUCTION

Pulses are important in our daily food life as they are contain high protein . Pulses are important sources of nutrition of the people in the world and pulse crops are included in a cropping system for improving the cropping intensity, soil health and fertility status of the soil . Pulses are important crop in our agricultural system (Dixit.2008) . In pulses a good amount of lysine is present .They have useful in different cropping as they have vary in maturity periods . On an average pulses contain 22-24 % protein against 8-10% in cereals. In India pulses is the important crop due to its importance in food as it full fill the nutrition requirement in the body. From "puls pulits " a Latin word the word " Pulse" is derived. Generally they are the dried seed of leguminous crop which belongs to the family *Leguminosae* .The pulses are used as food from ancient time due to its high value nutrition . Like pinto, red beans , navy beans every dry beans is a pulse , but every legumes are not pulses like soybeans and peanuts etc. The

consumption of pulses is increased globally for its high nutrition of value. Pulses are help in decreased the cholesterol in body (Goud.2007).

Green gram (*Vigna radiate)* is commonly known as mung bean .By consumption of 100 gram of green gram it gives 30 calories , 3 grams protein , 6 grams carbohydrates and 2 grams dietary fibres . It is free from raffinose or other oligosaccharides and also free from flatulence causing agent. It is remedy for edema , fever ,headache , anxiety believed by Chinese (Khan.2002) . For arsenic it also has a good binding capacity and also it removes the mineral toxicity .It is also rich in linoleic acids .Also other antioxidants are present in green gram . Green gram Starch has content of sparsely branched amylose of a relatively high molecular weight . highly branched amylose , highly branched amylopectin and moderately branched intermediate fraction (SubbaRao 1986) .Due to this constitution of green gram it was highly recommended indiets. It was also show in some research that it is also a good source of essential fatty acids , minerals , and tocopherol.

Low fertility of soil decrease the production in agricultural system. Due to high demand of pulses the use of synthetic and artificial fertilizers was increased . Due to use of artificial fertilizers the health problem was increased in the body . So, the use of biofertilizers was more in the agriculture .It is a challenge for the farmer that to stop the use of expensive chemical use in the crop field(Bhat 2005)It is important that bio fertilizers have no negative impact on environment as well as in our health. For healthy environmental conditions it is necessary that the organic fertilizer used should increase and expensive synthetic fertilizers used should decrease . They are low cost plant nutrient fertilizers for non polluted environment. The objective of use of bio fertilizer to increased the microbial activity and also increased the nodulation in green gram plant.

The production of bio fertilizers occurs in the anaerobic process. Nearly 7000 tons of bio fertilizers are produced from 70 to 80 units in India. Bio fertilizer are alternative of the chemical fertilizers which is a harmful product for the nature. The use of synthetic fertilizers has led to the pollution of soil ,water, and air. The use of synthetic fertilizers can lead to destroy the ecofriendly microorganism and useful microorganism and insects. It increased the diseased in the soil (Ghosh .2007) . It is cost effective for the farmer and when it was required in bulk quantities it can also be produced in farm it self.

There are different types of bio fertilizers are used in agriculture. They are Nitrogen fixing bio fertilizer -*Rhizobium, Actinobacteria , Azotobacter* are the examples of nitrogen fixing bio fertilizer.

- Phosphate solubilizing bio fertilizer -*Bacillus Spp , Pseudomonas Spp .* and *Aspergillus Spp* are examples of Phosphate solubilizing bio fertilizer.
- Phosphate mobilizing bio fertilizers – Examples are Mycorrhiza for Phosphate mobilizing bio fertilizers .
- Plant growth Promoting bio fertilizer- Examples include of these types of bio fertilizers is *Pseudomonas Spp.*
- Sulphur oxidizing bio fertilizers– *Thiobacillus Spp.* are included under Sulphur oxidizing bio fertilizers.
- Potassium mobilizing biofertilizer -*Bacillus Spp.* are the examples of Potassium mobilizing biofertilizer.

Application of Bio fertilizers

The form in which bio fertilizer are form was liquid, granular and powder forms which is used in soil , compost , seed , seedling and plant leaves . By using the instructions and warning mentioned on the bio fertilizers package the bio fertilizers should used . Mostly there are three ways of using the bio fertilizers i.e.

Inoculation to seed - The seed was mixed with the bio fertilizer and before applied on the field it should be dried.

Seedling root dip – The seedling was sowed in the bed of water for 8 to 10 hours.

Field application - The bio fertilizeris through the soil where the crop was planted .

Effect of bio fertilizers

To increased the productivity the chemical fertilizers play an great role as compare to bio fertilizers , but it have a great impact on the environment as it polluted the air , soil and water. Due to the application of synthetic fertilizers the health problem was also increased . The fertility power of the soil also decreased by application of the chemical

fertilizers. So the indiscriminate use of chemical fertilizers can reduced and the application of bio fertilizers was increased. The use of bio fertilizers is a step forwarding towards organic farming . Organic farming is now a demanding agricultural system because of the demand of safety and healthy food in India as well as World.

As a biological cell bio fertilizers have the potential to fix the atmospheric nitrogen to nitrates. A bio fertilizer contains living cells that specially help the root system. By providing nutrient it also help in seed germination .In soil it can also produce fertilizing substance. Due to application of bio fertilizers the crop yield can increased up to35 to 40 %. Also the improvement of soil texture, pH and other physical properties of soil can increased by application of bio fertilizer. It also prevent from plants to pathogenic fungi. Bio fertilizers destroy the harmful pathogen present on soil through that the plant can disease free(Rokhzadi 2008) .

Bio fertilizers contains different types of microorganisms which are organic products and help to increase the fertility power of soil by nitrogen fixing . They have the ability of converted the important unavailable sources to the available sources through the ecological processes. Bio fertilizers are decay the area by which the number of microorganism can increase and the microbial process are increased , through which the nutrient are available in the soil are uptake by the plant .These biofertilizers are not affected the other beneficial microorganism.

The review was done with bio fertilizers *Rhizobium leguminosorum, Bacillus megaterium ,Bacillus mucilaginosus ,Azotobacter spp.* The impact of these bio fertilizers on growth and yield on Green gram was reviewed with the root length ,shoot length, no of leaves per plant and fresh weight of green gram plant , no of pods and no of seeds per plant. Hence to increased the productivity of soil the bio fertilizer should be used. In a sustainable agriculture it is important to use of the biofertilizers. The use of the nodule bacteria and endophyticactinoxycetes in a attractive way for the plant growth and yield productions enhancement. Under the effect of biofertilizers The plant should significantly promoted with the shoot ,root length growth and also the fresh weight and dry weight was increased. The yield was also increased with the application of biofertilizer.

Biofertilizers are maintain the soil health with reducing the environmental pollution. Biofertilizers are the substances containing living microorganism which are applied to the seed ,plant surface or on the soil, colonize the *Rhizosphere* or the interior of the plant and promotes the nutrition level for the development of plant(Karwasra 2006). As they are ecofriendly and highly balanced they are effective by supplying many nutrients to the soils .By using the atmospheric nitrogen they enhanced the nutrient level of the plant. On the soil they trap the atmospheric nitrogen and convert them to plant usable forms .Also the phosphate form which is unusable by plant was converted by which the plant growth was increased . The nutrient cycle was boost by application of the biofertilizers . They also enhanced the immunity and protected them from the pests and parasites. There are many elements of traditional farmer knowledge that, enriched by the latest scientific knowledge, can support productive food systems through sound and sustainable soil, land, water, nutrient and pest management, and the more extensive use of organic fertilizers.

Some examples of biofertilizers

Rhizobium -In general *Rhizobium* is more effective than other biofertilizers. In association with legumes *Rhizobium* fixes the atmospheric nitrogen. With a symbiotic association with the *Rhizobium* bacteria the formation of root nodules was increased which gives the better result on the growth and productivity. The population of *Rhizobium* bacteria was depended on the presence of leguminous plant. In the absence of legumes the *Rhizobium* was decreased

Mycorrhizae – It is different in structure found inside and out side of the plant root. With a favorable parameters of the host plants ,these are found in a specific number. The parameters are included soil type ,presence of chemicals on the soil and the absence of beneficial microorganism on the soil.

Azotobacter -It is a common soil bacteria. Extensively in Indian in Indian soil *Azotobacter* chroococcum was found. The organic matter in the soil was important factor for the growth and decay of bacteria.

Phosphate solubilizing bacteria- For capable of solubilizing inorganic phosphorous from insoluble compounds phosphate solubilizing bacteria(PSB) biofertilizer is a beneficial bacteria. As a phosphate biofertilizer phosphate

solubilizing bacteria has been introduced. As a main essential macronutrients phosphorous is applied the soil for the improvement of the soil.

Root length

In the seedling stage the highest root length was found in*Rhizobiumleguminosorum*i.e7.51 cm while the lowest is 5.18 which is grow in control. In the flowering stage the highest root length is 7.90 cm which is found in the application of *Bacillus mucilaginosus* while the lowest root length i.e 5.79 cm in the flowering stage was found in control in which no bio fertilizers was used. In the yielding stage the highest root length was found in the application of *Rhizobium leguminosorum* i.e. 13.37 cm while the lowest is the 11.69 which is grow in the control medium.

Shoot length

In the seedling stage the highest shoot length was found in the application of *Rhizobium leguminosrum* i.e. 11.00 cm where as the lowest was found in the control i.e 8.20 cm in the control. In the flowering stage of green gram the highest shoot length was found11.80 cm in the application of *Rhizobium leguminosorum* and the lowest was found in the control medium i.e 10.23 cm . The highest shoot length was found in *Bacillus mucilaginosus* i.e. 13.63cm and the lowest shoot length was found in the control mediumi.e. 12.89 cm in the yielding stage.

No of leaves per plant

In the seedling stage the highest leaves i.e. 18 leaves was found in both the plant in which the *Bacillus megaterium* and *Bacillus mucilaginosus* was applied and the lowest leaves of 9 number was found in the control . In the flowering stage the highest leaves 21 was found in the green gram plant with the application of *Rhizobium* leguminosorum and the lowest was found in the control i.e.15 numbers of leaves. In the yielding stage of green gram plant the highest no of leaves was found in the application of *Rhizobium leguminosorum* with36 numbers of leaves and the lowest no of plant was found in the control i.e. 24.

Fresh weight of plant

In the seedling stage of green gram plant the highest fresh weight was found in the application of *Rhizobium leguminosorum*i.e.99.18 g/plant and the lowest is 91.15 g/ plantin the control . In the flowering stage of green gram plant the highest fresh weight was found in 103.13 g/plant with the application of *Rhizobium leguminosorum* and the lowest fresh weight of plant was found in the control i.e. 99.31g/ plant .In the yielding stage the highest fresh weight was found in the application of *Rhizobium leguminosorum* i.e. 141.28 g/plant and the lowest was found in the control i.e. 125.35g/plant.

Yield parameters

Also the effect of bio fertilizers on yield of green gram was found .The highest no of pods per plant was found 37.12 on the application of *Rhizobium leguminosorum* and the lowestno of pods was 34.25 i.e. found in the application of *Bacillus megaterium* . The highest no of seeds per plant was 79.61 and the lowest was61.33 . In the highest *Rhizobium leguminosorum* and in the lowest control was used.Thehighest weights of 100 seeds found in the application of *Rhizobium leguminosorum* i.e. 4.31 g and the lowest was 3.12 found in the control medium.

Graph showing biochemical parameters

The application of bio fertilizers also influence the chemical parameters of Mung bean plant . From the review it was found that the application of *Rhizobium* on mung bean was shown better result .The highest no of carbohydrate 2.45was found on the application of *Rhizobium* and the lowest 2.15 was found on the control medium in which no bio fertilizers was used . Total chlorophyll content was found best on the application of *Rhizobium*i.e.0.819 and the lowest was 0.789 on control medium . The highest number of protein was found on the application of *Rhizobium* i.e 3.1 and the lowest is 2.8 which is control .

CONCLUSION

The present review was deals with effectiveness of bio fertilizers on growth of green gram (*Vignaradiata)* . It was clear from the review that the application of biofertilizers was effective on growth of green gram .It was found from the review that the application of bio fertilizers was effective on the root length , shoot length , fresh weight , dry weigth , no of pods and also no of seeds .It was clear that the application of *Rhizobium leguminosorum* was more effective than other bio fertilizers. *Rhizobium leguminosorum* is more effective in the flowering stage and yielding stage than the seedling stage. Hence it is important that the awareness among farmer for use of bio fertilizer specific *Rhizobium leguminosorum* should increase. The application of bio fertilizers was enhance the growth of green gram plant and also enhance the productivity . It was clear that the application of microorganisms in the form of bio fertilizers show beneficial effect on green gram as well as leguminous plant .

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Table 1Effect of morphological parameters of green gram at seedling stage

Sl.no	Bio fertilizer	Seedling stage			
		Root length(cm/plant)	Shoot length(cm/plant)	No of leaves /plant	Fresh weight (g/plant)
1	Control	5.18	8.20	9	91.15
2	*Azotobacter spp.*	6.06	9.19	15	93.86
3	*Bacillus megaterium*	6.23	10.56	18	96.74
4	*Bacillus mucilaginosus*	6.95	10.90	18	99.13
5	*Rhizobium leguminosorum*	7.51	11.00	12	99.18

Table 2 Effect of morphological parameters of green gram at flowering stage

Sl.no	Biofertilizer	Flowering stage			
		Root length(cm/plant)	Shoot length(cm/plant)	No of leaves /plant	Fresh weight (g/plant)
1	Control	5.79	10.23	15	99.31
2	*Azotobacter spp.*	6.56	10.36	18	101.25
3	*Bacillus megaterium*	7.33	10.45	20	102.19
4	*Bacillus mucilaginosus*	7.90	11.35	18	102.28
5	*Rhizobium leguminosorum*	7.56	11.80	21	103.13

Table 3 Effect of morphological parameters of green gram at yielding stage

Sl.no	Bio fertilizer	Yielding stage			
		Root length(cm/plant)	Shoot length(cm/plant)	No of leaves /plant	Fresh weight (g/plant)
1	Control	11.69	12.89	24	125.35
2	*Azotobacter spp.*	12.05	12.68	32	129.86
3	*Bacillus megaterium*	12.48	13.60	27	138.69
4	*Bacillus mucilaginosus*	12.96	13.63	30	139.49
5	*Rhizobium leguminosorum*	13.37	13.58	36	141.28

Table 4 – Effect of different bio fertilizers on yield parameters of green gram

Sl no.	Treatments	Number of pods per plants	No of seeds per plant	Weight of 100 seeds (g)
1	Control	35.32	61.33	3.12
2	*Azotobacter spp.*	36.48	67	3.45
3	*Bacillus megaterium*	34.25	76.98	3.56

4	*Bacillus mucilaginosus*	34.59	78.20	3.89
5	*Rhizobium leguminosorum*	37.12	79.61	4.31

Table -5 Effect of Biochemical parameters by application of bio fertilizers

Sample	Total carbohydrate content	Total chlorophyll content	Total protein content
Control	2.15	0.789	2.8
Rhizobium	2.45	0.819	3.1
Azotobacter	2.39	0.798	2.9

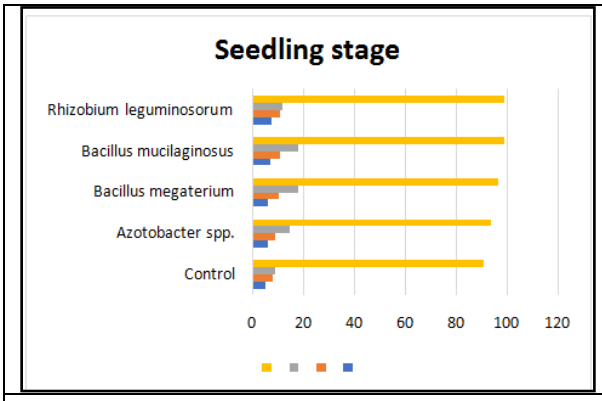

Fig. 1. Graph of seedling stage

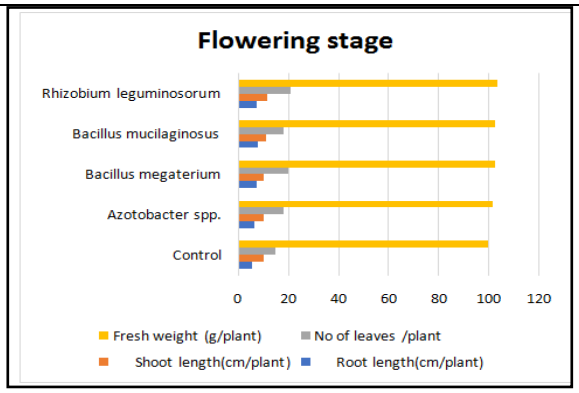

Fig.2. Graph of flowering stage

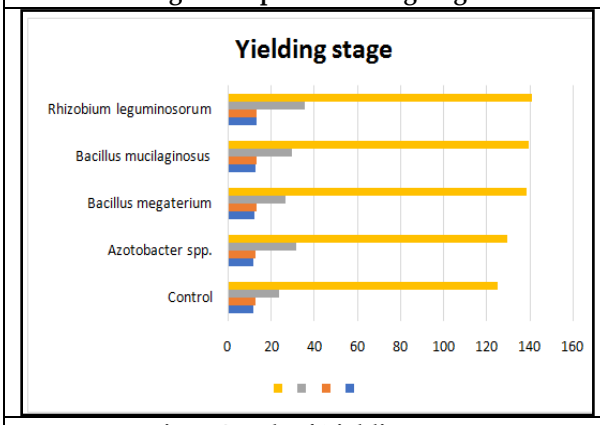

Fig.3. Graph of Yielding stage

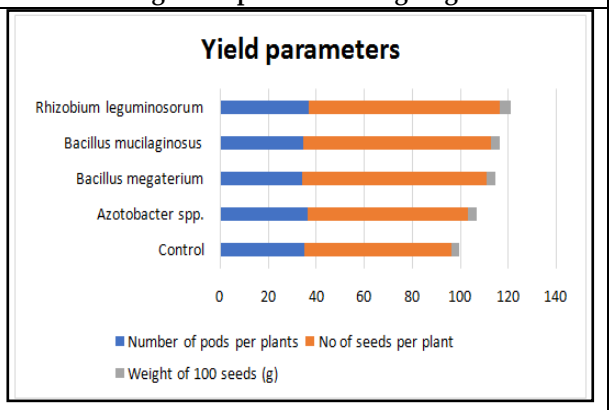

Fig.4. Graph of Yielding parameters

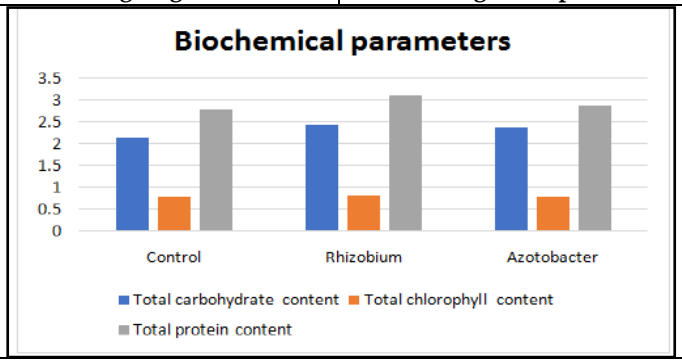

Fig.5. Graph showing biochemical parameters

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RESEARCH ARTICLE

Band gap engineering in ZnO Nanostructures / Microstructures

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ABSTRACT

Zinc oxide (ZnO) nanostructures, a II-VI semiconductor compound, recently paid much attention to the research community due to its exciting properties, that promoted it as a suitable material for develop diversing sustainable applications. Band gap change in ZnO is an observed phenomenon that is very interesting from the fundamental point of view. In this report, a simple chemical bath deposition approach has been adopted to prepare ZnO nanostructures using zinc nitrate hexahydrate ($Zn(NO_3)_2 \cdot 6H_2O$) and hexamethylenetetramine (HMT) ($(CH_2)_6N_4$) salts as starting material and demonstrated the successful synthesis of ZnO nanorods. The synthesis has carried out by varying the precursor concentrations from 10mM to 500mM, keeping the other synthesis parameters constant. The effect of precursor variation on the morphology and crystalline characteristics of the ZnO nanostructures has been investigated by using X-ray diffraction (XRD) and field emission scanning electron microscopy (FESEM) techniques. The optical absorption as well as band gap engineering study are carried out using UV-Visible spectrophotometer. The FESEM image revealed that by varying the precursor concentration, the morphology of ZnO nanostructures can be tuned from nanostructure to microstructure. Similarly, XRD results show that the prepared ZnO samples are highly crystalline in nature having hexagonal wurtzite structure.From the UV-visible spectroscopy study, low precursor concentration synthesized ZnO materials which are in the nanostructured state exhibit band gap widening while higher precursor concentration synthesized ZnO materials which are in the form of microstructure phase, exhibited band gap narrowing with respect to the bulk ZnO materials. The degree of band gap change was dependent on the precursor concentration of the ZnO materials. From UV-visible spectroscopy, it was found that the mechanism for band gap tuning was due to the shifting of the valance band maximum and conduction band minimum of the materials.

Keywords: Sustainable, ZnO Nanorods, FESEM, Band gap tuning, wurzite structure.

INTRODUCTION

The wide application of ZnO nanomaterials make it a considerable study for recent research. It has been extensively used in UV-blockers, antimicrobial, antibacterial, antifungal, cosmetics, sunscreen etc. Also, ZnO is outspread in the area of additives to different products and personal care like ointments, lotions, glass, paints, pigments, batteries, food nutrition etc. Controlled structure and morphology of ZnO nanomaterials rises several applications in the field of optical properties such as absorption, reflection, refraction, transmission and emission etc. The variation in optical properties of ZnO functionalized materials is due the inter electronic transition between valency band to conduction band in terms of highest occupied molecular orbital (HOMO) to lowest occupied molecular orbital (LUMO). [1-3]One can verify these optical properties through different spectroscopic analytical techniques, that are crucial to be explored more about several characteristic properties of a nanomaterial. With regards to that, especially semiconducting metal oxide containing nanomaterial exhibit brilliant optical tendency related applications such as optoelectronics, cosmetics, sunscreens etc. ZnO show unique optical characteristics due to its wide band gap of 3.4 eV and large exciton binding energy of 60 meV which has been directed it further for the next generation electronic devices. [4,5]Various methods have been employed in order to synthesize the ZnO nanomaterials such as oxidation, sol-gel, hydrothermal, co-precipitation, flow injection, electrochemical, aerosol / vapour phase, sonochemical deposition, supercritical fluid deposition, solvothermal, microemulsion, pyrolysis, precipitation, chemical reduction, chemical bath deposition, gas condensation etc. However, chemical bath deposition technique is a very simple and cost-effective technique in order to prepare ZnO nanomaterials. In this report, we have fabricated ZnO nanorods with different precursor concentration from 10mM, to 500mM, by keeping other synthesis parameter constant and investigated the morphological, structural as well as optical properties. Most importantly, band gap tuning of ZnO nanostructure to ZnO microstructure has been investigated. This emerging technology can be employed for getting affordable and clean energy in solar cell / light detecting devices.

EXPERIMENTAL

The ZnO nanorod synthesis was carried out using simple and cost-effective chemical bath deposition techniques in which, different ZnO nanorods sample were fabricated with varying the precursor concentration, keeping all other parameters constant. In to aqueous DI water, equal concentration of $Zn(NO_3)_2.6H_2O$ and HMT salts were dissolved in order to prepare the mixture of solution. Then transferred the whole chemicals in to a beaker along with volume make up to 100 ml. Subsequently, stirred the sample with the help of a magnetic stirrer. Later on, cleaned Si wafers were dipped in the solution containing beaker and covered properly with Aluminium foil and kept it in oven for 3hrs under 100^0C temperature. After 3hrs completion, the sample containing beakers are removed and the supernatant liquid is decantated through dropper and again kept the beaker in oven under 60^0C Temperature for drying process. The ZnO nanorods samples were fabricated with different precursor concentration at 10mM (Sample S1), 50mM (Sample S2), 100mM (Sample S3), 200mM (Sample S4) and 500mM (Sample S5) respectively for further ananlysis. In order to understand the details about structural properties of prepared sample like crystal lattice and different lattice parameters, we have used X-ray diffraction (XRD) (Philips X'pert),where X-ray diffractometer equipped with a monochromatic CuK_α radiation source (1.54178Å). The morphology of samples was investigated using by field-emission scanning electron microscope (FESEM) techniques. UV-Visible study has been carried out using UV-1700 Spectrophotometer, M/s Shimazdu for measurement of absorbance of ZnO nanorods with different precursor concentration.

RESULTS AND DISCUSSION

The morphology of ZnO nanomaterials with different precursor concentration were investigated by using FESEM measurement. Fig. 1(a) shows the FESEM images of ZnO nanorods, where precursor concentration was chosen 10mM and Fig. 1(b) represent the growth of ZnO with 500mM precursor concentration. FESEM result predicts, with increasing

the precursor concentration, the growth rate of ZnO nanostructures increases and due to the availability of more nucleation centre on the surface of the substrate, the agglomeration of number of nanostructures evolves into microscopic structures.XRD analysis was performed on ZnO nanomaterials grown by chemical bath deposition technique. It was observed that, all the diffraction peaks for ZnO nanorods samples corresponds to hexagonal wurtzite ZnO (JCPDS No. 36e1451). Fig. 2(a) and 2(b) represents the XRD figure for 10mM and 500mM for structural analysis purpose. XRD results shows that all concentration of ZnO nanorod sample are highly crystalline by nature along with hexagonal wurzite structure. The presence of several peaks in the XRD reveals that the nanostructures/ macrostructures are polycrystalline by nature.**[1]**

In order to understand the effect of different precursor concentration on band gap modification of ZnO nanomaterials, UV-Visible absorption measurements were carried out for each sample of different precursor concentration like 10mM, 50mM, 100mM, 200mM and 500mM. The corresponding UV-Visible spectra were represented in below Fig. 3(a).The optical absorption measurements were recorded in the wavelength range of 200-800nm. The prepared powder samples exhibit characteristic absorption peaks for the corresponding ZnO hexagonal wurzite structure. From the below Fig. 3(a),it was observed that,a strong absorptionedge observed in the range of 350nm to 375 nm range, i.e., related to the excitonic band edge absorption of ZnO, shows a red shift with increasing precursor concentration. Energy band gap was one of the most physical properties of any material, especially semiconducting material, which affect their optoelectronic action.Fig.3(b)to Fig. 3(f) illustrates the band-gaps for the ZnO material by varying precursor concentrations from 10mM to 500 mM respectively. The optical band gap values for ZnO material with different precursor concentration from 10mM to 500mM were calculated from Kubelka-Munk plot. For absorption coefficient α, $(\alpha h\upsilon)^2$ is shown as a function of photon energy ($E=h\upsilon$) for all the spectra described below and tabulated in Table 1.[6]. The redshift in band gap was observed in the range from 3.93 eV to 3.65 eV for sample S1 to S5 respectively. Also, it was observed that, band gap energy of nanosized / nanostructured materials are larger than that of micro sized / microstructure materials. This reduction of band gap was due to transfer of charge between conduction band/valence bands to 3d level electrons of Zinc. Besides that, due to quantum confinement effect in nanorods samples, the higher band gap value observed for Sample S1, S2 and S3 nanostrcuture samples [7,8]. The above Fig. 4.represent the variation in the band gap of ZnO with increasing precursor concentration from 10mM to 500mM. As shown in Fig. 4., a clear reduction in bandgap of ZnO was observed, when the synthesis precursor varies from 10 mM to 500 mM concentration.

CONCLUSION

ZnO nanomaterials with different precursor concentration were successfully synthesized using simple and cost-effective chemical bath deposition techniques and characterized by XRD, FESEM and UV-Visible spectroscopic analysis. FESEM results shown that the morphology can be tuned from nanostructures to microstructures by varying the precursor concentration. The structural analysis also confirmed the improvements in crystallinity in microstructure samples.UV–Visible spectroscopy exhibits a tuning in bang gap of the ZnO material by varying the precursor concentration.

ACKNOWLEDGMENTS

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Table-1. Absorption band gap of ZnO sample with different precursor concentration

Sample Name	Concentration(mM)	Band gap Energy(eV)
S1	**10**	**3.93**
S2	**50**	**3.89**
S3	**100**	**3.82**
S4	**200**	**3.79**
S5	**500**	**3.65**

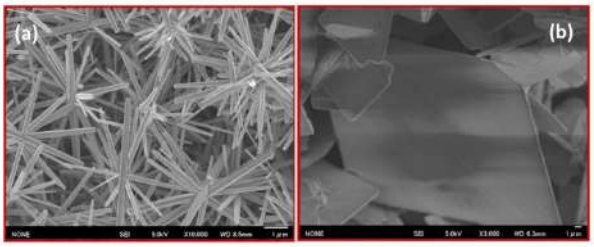

Figure- 1: FESEM image of ZnO material with (a) 10mM concentration and (b) 500mM concentration

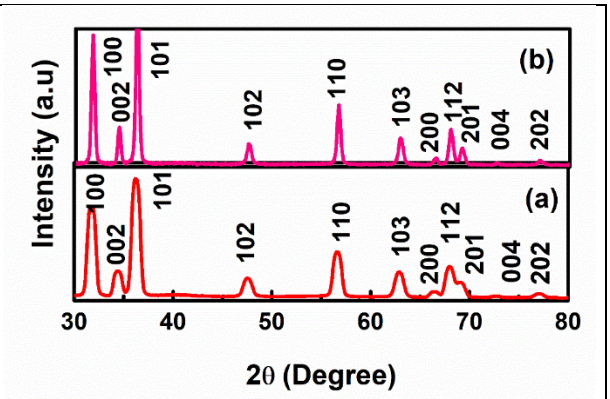

Figure- 2:X-ray diffraction patterns of ZnO material of different concentrations deposited on Si substrate(a) 10mM and (b) 500mM.

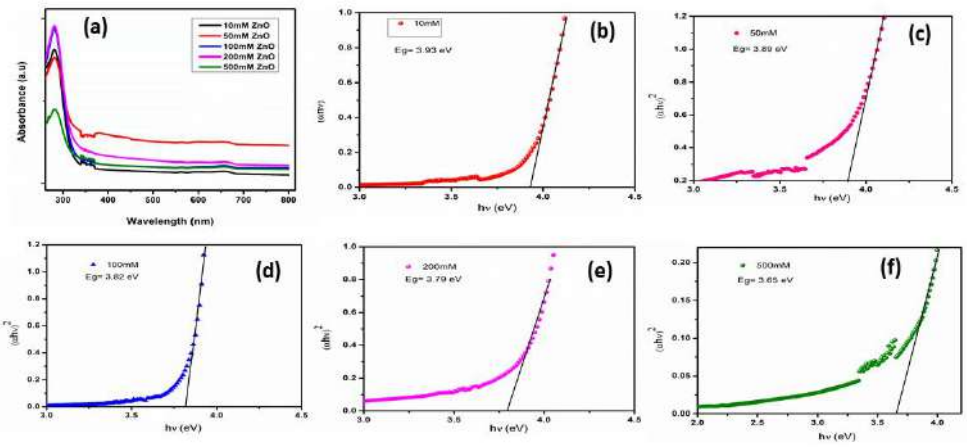

Figure- 3:(a) UV-Visible absorption spectra of ZnO nanomaterial with different precursor concentration. (b)Tauc's plot of ZnO material with 10mM concentration. (c) Tauc's plot of ZnO material with 50mM concentration. (d) Tauc's plot of ZnO material with 100mM concentration. (e)Tauc's plot of ZnO material with 200mM concentration. (f) Tauc's plot of ZnO material with 500mM concentration.

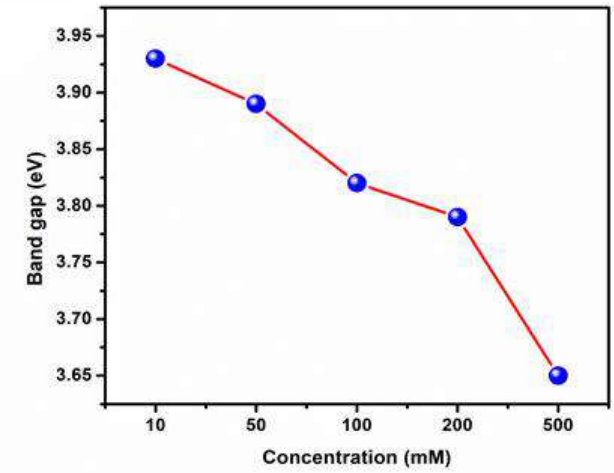

Figure- 4: Variation in the band gap of ZnO with increasing precursor concentration

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RESEARCH ARTICLE

The Potential of Phytomolecules towards Modulation of the Autophagy-Apoptosis Pathway: A Complement to Cancer Chemotherapy

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ABSTRACT

Bioactive plant compounds play myriad of functionalities primarily their applicability in treatment of several patho-physiological disorders including their involvement as cancer therapeutics owing to the astonishing anti-cancer properties of phytomolecules. Essentially phytochemicals alter autophagy and apoptosis, both of which are critical cellular pathways involved in the basic pathobiology of cancer development as well regulation. Therefore, phytomolecules-mediated pharmacological targeting of autophagy and apoptosis can be extensively explored in order to offer a complementary strategy to the conventional cancer chemotherapy. In this review, the molecular basis of the autophagic-apoptotic process is fundamentally highlighted, largely to understand its role in the progression of cancer and thus will pave way forward to unravel the potentiality of phytomolecules to target specific pathways resulting in limiting the cancer progression. In the current context, we also aimed to explore the latest developments and address the limitations being faced in the development of phytochemical-based anticancer drugs.

Keywords: Bioactive, anti-cancer, phytomolecules, apoptosis, autophagy.

INTRODUCTION

In this 21st century, the death toll from cancer has increased dramatically, mainly due to lifestyle factors, use of tobacco, carcinogenic agents, synthetic reagents, consumption of liquor, and malnutrition and other unraveled

factors (Bhatia *et al.* 2020; Khaltaev and Axelrod 2020; Sanford *et al.* 2020; Siegel *et al.* 2020). Delay in the treatment of cancer may also result in an increased patient fatality rate (Hanna *et al.* 2020). Nevertheless, with the increasing strategies towards healthy way of living, early detection, diagnosis, and operation may contribute widely in reducing the spread of cancer (Henley *et al.* 2020). Multifaceted cancer treatment strategies like chemotherapy, radiation therapy, hormonal therapy, immune- and surgical-treatment, palliative care, and combos are practized which usually have differential range of effectiveness depending on the types of cancer. Primarily the major aim of the maximum cancer treatment approaches is to initiate cell death in abnormal cells resulting in maintenance of the required number of healthy cells that are required by an individual (Schirrmacher 2019). Chemotherapy acts as the pillar for a wide range of cancer drugs. This helps to reduce tumor size and kill more cancerous cells or metastatic cells (Sak 2012; Alfarouk *et al.* 2015). The responses for treatment are varied depending on the class of cancer or perhaps same cancer (Sak 2012). Defiance towards various chemotherapeutic agents is the main complication in the treatment of cancer that finally reduces the effectiveness of cancer drugs, further leading to treatment failure and potentially having fatal effects (Alfarouk *et al.* 2015). Insolence towards chemotherapy may be due to the choice of procedures, as well as multidrug resistance, mutations in cell death, mutations in drugs, epigenetic and medication purposes, modification of DNA, tumor heterogeneity, pill release, and metabolism, and stress is brought on by a tumor microenvironment or other epigenetic causes like exposure to drug-response (Wang *et al.* 2019). Amid that procedure, the modification of autophagy and apoptosis, self-harm mechanisms developed by new medical innovations may be important reasons for resistance to chemotherapy (Thorburn *et al.* 2014). Autophagy, cellular regeneration is a conservative and evolutionary process that has emerged as an important factor in metabolism and a binding remedy. In a true sense, these approaches attempt at maintaining or restoring metabolic homeostasis through catabolizing unnecessary protein degradation and damage or acquisition of old organelle (Santana-Codina *et al.* 2017). The function of autophagy innumerous tumor treatments is complex; it can work as a means of endurance or traumatic demise to prevent or interfere with the cytotoxic effects of anticancer marketers (Santana-Codina *et al.* 2017). Autophagy acts typically like a plant suppressant in controlling active forms of oxygen (ROS) in cells and supporting genetic instability. In addition, the collection of evidence suggests that autophagy is associated with mutant stem cells. In these circumstances, autophagy incitement may be an important means of preventing tumorogenesis and initial boom. Still, autophagy can market the crash and lifestyle of present plants during their migration and for their epithelial to mesenchymal transformation. In addition, this process can be utilized by most cancerous stem cells to monitor the immune system and to create more cancer cells in order to resist anoikis (Rahman *et al.* 2020). Here, the prevention of autophagy will increase chemotherapy-precipitated cytotoxic. Thus autophagy, a two-dimensional sword acting on the context, will be able to block the early degrees of tumorogenesis. At the same time, it becomes an attack on the driving force of the tumor and metastasis in later tiers. The molecular operations that regulate the transition within particular modes of movement are very poorly understood (Kardideh *et al.* 2019). However, the interaction between apoptosis and autophagy may be used for multiple cancer treatments (Tompkins and Thorburn 2013; Thorburn 2014). Many cancerous cells emerge as they undergo chemotherapy using extinguishing certain apoptotic mechanisms, as well as sub-controlled pro-apoptosis signaling, suspended anti-apoptotic signaling, and apoptosis release and erroneous execution. Still, the useful dating between apoptosis and autophagy is complex and engraved with cellular stems. Therefore, controlling the essential features of autophagy and apoptosis methods may be a new treatment modality to improve the effectiveness of chemotherapy.

The potential role of phytochemicals within autophagy mutations and apoptosis are reviewed. (Deng *et al.* 2019). Phytomolecules play an important role in boosting immunity against a myriad of pathological disorders (Panigrahi *et al.* 2021a). Phytomolecules not only contribute in elevating the plant immunity against invading pathogens but also is involved in ensuring the fidelity of biological molecules (Jung *et al.* 2020; Panigrahi and Satapathy 2020; Panigrahi *et al.* 2021b). Reviewed inclusion autophagy or apoptosis prevention is a complicated technique that needs deep examination. However, better crosstalk technology between autophagy and apoptosis could make it work to deepen the development of the latest cancer-fighting techniques. Here, we have compiled the biological methods for autophagy and apoptosis in carcinoma. In order to cure cancer, we are willing to talk about different phytochemicals which alter the signals involved in autophagy and autophagy methods to improve cancer treatment outcomes. The current study emphasizes the importance of critical proteins in maintaining human cell physiology and thus aligns

with the objectives of one of the United Nations formulated Sustainable Development Goals (SDGs); SDG3 which ensures healthy lives and promotes well-being for all at all stages.

Autophagy Mechanism in Cancer

Autophagy is nothing but a cellular system which reduces or breaks down the number of unwanted cell components or compounds in contact with lysosomes; this process of cellular system is understood to carry out an important function in keeping the cellular aspect essential (Krishnan *et al.* 2020). We can maintain a live interlink to cellular defense over the cytostatic hyperlink in developing multiple cancer cells (Rahman *et al.* 2020; Rahman and Rhim 2017). This method is probably introduced during pre-autophagosomal structures and is often termed Phagophore Assembly Sites (PAS) (Rahman and Rhim 2017; Hurley and Young 2017; Rahman *et al.* 2020; 25). Phosphatidylinositol 3phosphate (PI3K), related to the endoplasmic reticulum (ER), plays a pivotal function within the inception of PAS development. AMP-activated Protein Kinase (AMPK), Mammalian Target Rapamycin (mTOR), and unc51-like autophagy activating kinase1 (ULK1) were confirmed in order to ease the genesis of phagophore during autophagy induction (Alers *et al.* 2012), with Vps34, Vps15 / p150, and Beclin1 as phagophore architecture monitors (Velazquez and Jackson 2018). While phagocytosis is formed, phagocytosis occurs. This process is succeeded by enlargement and closure of the lining of the throat (Rubinsztein *et al.* 2012).The mature esophagus is related to lysosomes, which are critical to the formation of autolysosomes (Kardideh *et al.* 2019). Next, autolysosomes contain decomposed internal loads in the form of acid hydrolases and deliver vitamins; special recycle metabolites and maintain cell stability. Therefore, the future of most carcinogenic cells depends on autophagy (Wei and Huang 2019; Huang *et al.* 2017). Autophagy concludes that cancer is banned or promoted under certain conditions. MTOR marks a crucial role in carcinogenesis or safety cells through autophagy insertion. But, chemotherapy drugs were intended to subdue carcinogenic cells using self-regulation mechanisms. Furthermore, inhibition of this regulation of cancer cell development and the impact of autophagy becomes a factor in cell abidance or cell demise (Jang *et al.* 2019). The metabolism of harmful cells is radically changed to maintain duplication and abidance under dangerous conditions of minor natural conditions. Autophagy also maintains the metabolic regulation of many cancerous cells. Although autophagy is known to keep most cancer cellular metabolism under control, the link between mobile cancer metabolism and autophagy is unknown. MTOR and AMPK are recognized as significant components of autophagy by balancing amino acids and blood sugar (Alers *et al.* 2012).Nevertheless, specific metabolites, ROS, a factor of expansion, palate, oxygen levels, the cost of ATP to ADP, the range of specific amino acids, and oncogenic cells alter the activation of autoimmune strategies. Moreover, what are they fixing? Well-balanced by incorporating these autophagy-related symptoms into multiple cancers (Singh and Cuevro 2011; Panda *et al.* 2015). Evidence, autophagy is often described as playing a "twin role" as it can prevent or promote the onset and development of multiple cancers (Patra *et al.* 2020; Rahman *et al.* 2020). In this study, emphasis is given to the twofold function of autophagy in tumorigenesis, and stress is laid on our current technology for activating cancerous cell autoregulation and metabolic processes to regulate tumor growth and development.

Phytochemical Modulate Autophagy - Apopstasis Sign in Multiple Cancers

Autophagy is an essential aspect in the treatment of cancer, especially in chemotherapy, to remove intracellular components and inactive organelles and cause lysosome degeneration. This autolytic process reinforces cellular defense in order to defend cells from different intracellular and extracellular stress and regulates redox homeostasis for genomic delivery and cytoplasmic stability. New evidence aid the twofold role of autophagy in cancer (i.e., as a tumor promoter and inhibitor in evolution). Nevertheless, implantation of autophagy in cancer is still a possible technique, as it produces planned cell death of type II. During the onset of cancer, autophagy regulatory authorities, such as mTOR and AMPK, negatively controlled by the tumor suppressor factor, trigger autophagy induction (Comel *et al.* 2014).Moreover, these activated autophagy controls are some cancerous substances that prevent autophagy and promote the formation of cancer (Choi *et al.* 2013). Carcinogens can also inhibit autophagy through the regulation of ROS regulation f ROS, thus promoting tumorigenesis (Ávalos *et al.* 2014; Filomeni *et al.* 2015). Because of their therapeutic activities, various phytochemicals have shown promise for multiple cancer treatments (Mitra and Dash 2018; Aung *et al.* 2017). In a few cases, the metabolites and artificial products from natural chemicals

showed a better effect of early chemo-preventive compounds than the original ones (Aung *et al.* 2017). Our model and emerging evidence suggest that phytochemical targeting Autophagy is a promising agent for the treatment of cancer in both ways or that it relies independently on the cellular pathways targeted to cancer cells.

Phytochemicals in Autophagy Signaling

Apigenin is a flavonoid spinoff which regulates many kinase pathways and inhibits the cell cycle in the G2 / M phase. Various studies have proven that apigenin can block cellular boom and cause autophagy in time and dose-dependent patterns in HepG2 cells. It was also found that autophagy can be mediated by blocking the PI3K / Akt / mTOR pathway in HepG2 cells (Yang *et al.* 2018). Allicin, which is a natural sulfur compound, works as an antitumor agent that causes the loss of autophagic life by blocking the signaling pathway of PI3K / mTOR. It also inhibits the secretion of p53 and Bcl2 and regulates the signaling pathway of Beclin1 and AMPK / TSC2 (Chu *et al.* 2012). Anthocyanins (ACNs) found in black soybeans bring about autophagy, but their underlying mechanism has not been determined yet. Aspalathin, which is a polyphenolic dihydrochalcone C-glucoside, plays an important role in preventing Dox-induced cardiotoxicity and reducing the expression of P53. Aspalatin introduced autophagy-related genes and reduced p62 with the help of AMPK seduction and Fox methods (Johnson *et al.* 2017). Berberine, which is an isoquinoline alkaloid, performs the anticancer activity of autophagy induction with the help of the AMPK / mTOR / ULK1 pathway. Celastrol is any other triterpenoid that is potent against human prostate cancer. Celastrol blocks AR signaling pathways, which begin to activate and slow down the production of miR101 (Guo *et al.* 2015). Cordycepin induces ROS in many cancerous cells and amplifies p53 and LC3I / II expression, thus regulating autophagy (Chaicharoenaudomrung *et al.* 2018). Cordycepin inhibitor renal cell carcinoma within the Caki1 cell line migrated by reduced expression of microRNA21 expression and Akt phosphorylation, as well as extended phases of PTEN phosphatase (Yang *et al.* 2018). Similarly, cordycepin induced autophagy using Bax activation in ovarian cancer cell lines, including SKOV3 and OVCR3 (Tang *et al.* 2019). Curcumin also increases ROS and DNA damage to cancerous cells. In addition, curcumin reproduced phosphorylation of ERK1 / 2 and p38 MAPK, blocked Akt and P54 JNK (Masuelli *et al.* 2017), and then induced autophagy in NSLCA549 cells (Liu *et al.* 2018). Evodiamine, which is a quinolone alkaloid, helps in mediating autophagy activation through the use ofthe regulatory expression of Beclin1 and Bax and lowering Bcl2 (Rasul *et al.* 2012). Fisetin, which is a naturally occurring flavonoid, is meant to abolishthe mTOR signaling pathway through Akt inhibition and AMPK activation, as well as spontaneously programmed cell death in many cancer cells (Suh *et al.* 2010). In addition, genistein has shown chemotherapeuticas well as chemopreventive effects on carcinogenic cells. Treatment of ovarian cancerous cells with the help of genistein has brought a significant reduction in Akt phosphorylation and stimulated autophagy, thereby playing a crucial role in the reduction of glucose absorption in cancerous cells (Gossner 2007). Ginsenoside F2 raises interest in anti-proliferation and initiates Autophagy in breast cancer cells. Conversely, ginsenoside F2 will increase Atg7 tiers, causing the genesis of acidic vascular organelles and accumulating GFP-tagged LC3II in autophagosomes (Mai *et al.* 2012). Hispolon, which is a phenolic compound, has shown apoptotic effects along with anti-tumor effects on cell lines of cervical cancer and has directly induced autophagy. It was found out that hispolon containing drug inhibits metastasis by upregulating lysosomes cathepsin S protease (CTSS) (Chen *et al.* 2012). Similarly, hispolon has been shown to chunk the ERK pathway and improve the conversion of LC3 and acidic organelles (Hsin *et al.* 2017). Yet another phytochemical by-product that produces autophagy is Three hroxydaidzein (3'ODI),and it has been found to drastically reduce αMS mediated melanogenesis in cancerous cells (Kim 2005). Toxicarioside O, which is an antiseptic product based on Antira toxicaria Lesch, has shown to have anticancer efficacy through the inclusion of autophagy with the following discount of the Akt / mTOR method (Huang *et al.* 2017). Falcarindiol (FAD) is a natural polyene that promotes autophagy in ER response, while αmangostin mediates autoimmune cell death through the activation of AMPK in human glioblastoma cells (Chao *et al.* 2011). The bioflavonoid quercetin has anti-cancer properties and anti-inflammatory properties. In the first case of hyperactive effusion lymphoma (PEL), quercetin reduces cytokine release. It inhibitsmTOR/P13K/Akt and STAT3 mediated pathways autophagy, over time leading to cell death of PEL (Granato *et al.* 2017). In breast cancer cells, rottlerine (Rott) major manifestations of LC3, Beclin1, and Atg12 are concentrated in specific autophagy. Silibinin (silybin) is a Chemoprotective flavonoid that may also show antidepressant effects in renal cell carcinoma (RCC). Silibinin enhances the expression of LC3II, not only the

best pressure of the controlling mTOR but also opens the way for AMPK (Li *et al.* 2015). Sulforaphane (SFN) is a compound of phytochemicals the thrown isothiocyanates (Uddin *et al.* 2020). Numerous studies have shown that autophagy with another stage of cell death in SFN-precipitated removes benign pancreatic carcinoma cells by releasing ROS without cytotoxic effects (Uddin *et al.* 2020; Naumann *et al.* 2011). Gintonin has been identified to stimulate autophagic flux using the Akt / mTOR / p70S6K.-Mediated pathway within the first astrocyte cerebral cortex. Ursolic acid (UA), a 5-cyclic triterpenoid, has proven effects on inhibiting G1-level binding and autophagy regulation initiated using beclin1 and Akt / mTOR methods (Shin *et al.* 2012). Tripchlorolide exists within the vascular triangle. A solution containing tripchlor gold has been shown to reduce the exposure of the PI3K / Akt / mTOR signature method (Chen *et al.* 2012). Tetrandrine is an alkaloid of bisbenzylisoquinoline isolated from the Chinese herbal medicine Stephania tetrandra S. Moore. Tetrandrine plays an important role in the development of human hepatocellular carcinoma, Wnt / βcatenin, an inhibitor mechanism, and reduces MTA1 exposure, which ultimately triggers autophagy (Zhang *et al.* 2018). N-desmethyldauricin differs in mediated autophagy Ulk1 / PERK / AMPK mTOR inhibition and calcium induction collection, leading to spontaneous cell death. Quinacrine has proven anti-cancer properties among many breast cancer cells with the help of enhancing the regulation of p53 and p21 and inhibiting the reproduction of topoisomerase (Mohapatra *et al.* 2012). The anti-proliferative activity of tangeritin initiates anticancer activity by modulating autophagy and inducing CYP1 enzyme and CYP1A1 / CYP1B1 proteins in MDAMB468 and MCF7 cells (Surichan *et al.* 2018). a few studies have shown that the treatment of licochalcone A activates the LC3II signaling pathway and suppresses the PI3K / Akt / mTOR autophagy signaling pathway in MCF7 cells (Xue *et al.* 2018). In addition, ophiopogonin B is available to initiate autophagy with the help of the signaling pathway PI3K / Akt / mTOR. The anti-cancer activity could be demonstrated using juglanin, which is usually derived from the green husks. Juglanin based solution reduces the G2 / M phase arrest and allows autophagy by controlling the signaling pathway of ROS / JNK in most breast cancer patients (Sun *et al.* 2017). Another naturally occurring compound of tetracyclic triterpene is Cucurbitacin B which is commonly used as an anti-inflammatory drug. Cuc B solution promotes DNA damage and enhances protein expression of γH2AX through ATM / ATR phosphorylation, and at the same time increases the ROS level of autophagy in MCF7 cells (Ren *et al.* 2015).

Phytochemical in Apopstasis Signaling

Angelica polymorpha Maxim, which contains angelicin, will increase cytotoxicity and induce apoptosis in a way that reduces the expression of apoptotic proteins, including BclxL, Bcl2, and Mcl1 in human SHSY5Y neuroblastoma cells. Because FAD-precipitated cell death is thought to be due to caspase-structured mutations, FAD is proposed to influence the interaction of other approved cancer drugs designed to kill multiple cancer cells (Lu *et al.* 2017). The effect of Alisol purple on autophagy by controlling the signaling pathways of CaMKK-AMPK-mTOR, the combination of calcium and increased ER pressure, leads to apoptotic cell death (Zhang *et al.* 2018). Luteolin is a Flavonoids found in many special flowers and is considered to play a critical role in hepatocellular carcinoma cells up to G0 / G1.Studies have proven that luteolin treatment induces apoptosis through increased caspase8 expression, which reduces Bcl2 at the mRNA stage, improves LC3BI conversion to LC3BII, and reduces SMMC7721 cell function. In the BEL7402 carcinoma cell line, oridonin-mediated apoptosis was modified to detect activation of caspase3 activity in addition to reduced Bcl2 expression and Bax regulation, which may inhibit cell proliferation (Zhang *et al.* 2018). The rott-containing solution in breast CSCs suppressed Akt phosphorylation and mTOR and increased AMPK phosphorylation, ultimately promoting apoptosis (Ling *et al.* 2012). Dozens of natural plants extracted from *Dioscorea nipponica* Makino, *Melandrium firmum* (Sieb. & Zucc.) Rohrb. and *Saussurea lappa* (Decne.) Sch. is found to lead to the destruction of anti-growth and apoptotic effects on human neuroblastoma cells. γ-Tocotrienol, a single isomer of vitamin E , was recognized by the vaccine Ang 1 / Tie2 and had its anti-cancer effect by initiating AMPK signaling, leading to a line of prostate cancer cells for apoptotic death cell. Triptolide removes apoptosis in many pancreatic cancer cells, causing Akt / mTOR / p70S6K to disable and modify the ERK1 / 2 pathway (Mujumdar *et al.* 2010). Kaempferol is a Flavonoid compound that results in ROS and p53 as well—signaling to alter p38 phosphorylation and caspase activation, thereby inducing apoptosis of many colorectal cancer cells. Myricetin is an herbal flavonoid found in a variety of fruits and vegetables. The previous record has suggested that myricetin reduces tumor cell proliferation by selling apoptotic mobile demise. Myricetin has anti-apoptotic and cytotoxic effects on prostate cancer

cells by blocking P1M1 and reducing the interaction between P1M1 and CXCR4 (Ye *et al.* 2018). Galangin apoptosis is induced in kidney cancer by increasing Bax and Cytc expression and reducing Bcl2 (Zhu *et al.* 2018). In the human breast cancer cell line, isorhamnetin inhibits tumor proliferation by inducing cellular cycle binding within the S-section and exhibits potent cytotoxic effects through the ROS-dependent apoptotic pathway (Wu *et al.* 2018). In H522 cells, Hesperet induces apoptotic cell death through casopase3/9, p53, and Bax expression, as well as dramatic control of Fas, FADD, and caspase8 (Elango *et al.* 2018). Cyanidin3glucoside (C3G) is an ACN found in fruit. C3G has anti-inflammatory properties and imports miR124 expression. At the same time, miR124 regulation reduced STAT3 regulation and inhibited C3G-induced angiogenesis in most human breast cancers (Ma and Ning 2018; 94). Benzyl isothiocyanate (BITC) is found in cruciferous vegetables. Bitcoin Mouse administration reduces the phosphorylation of PI3K / Akt / FOXO1 / PDK1 / mTOR / FOXO3a, suppresses the proliferation of many pancreatic cancer cells, and causes apoptosis (Boreddy *et al.* 2011). A few studies have shown that phenethyl isothiocyanates derived from glucosinolate (PEITC) promise anti-tumor retailers. PEITC-treated mice were found to show decreased expression of HER2, EGFR, and STAT3 and developed apoptosis with the help of split caspase three and PARP. NCTD inhibits cMet and mTOR as well as popular antitumor expression properties.

Phytochemicals Involved Both In Autophagic And Apoptotic Signaling

B-Elemene is a natural chemical compound collected in the health of intelligent medicinal plants, comprising Curcuma (Edris 2009). B-Elemenes performs cytoprotective function by converting LC3-I to LC3-II to form autophagy-forming autolysosomes and significantly reduces in vitro growth of many human breast cancer cells through apoptosis (Guan *et al.* 2014). Capsaicin is one of the few phytochemicals that works effectively using antitumor as a means of reducing PI3K / Akt / mTOR pathways. Capsaicin promotes autophagy employing mechanisms to improve autophagy signaling, LC3-II, and Atg5, and enhances p62 and Fap-1 degradation while enhancing caspase-3 relaxation (Lin *et al.* 2017a). Morus alba L. root extract containing oxyresveratrol altered pre-determined ROS accumulation and led to spontaneous and apoptoticmolecularr health loss using the Fmoleculare-3 pathway in human neuroblastoma cells (Kwon *et al.* 2015; 18). Gingerol contains the antioxidant 07b031025f5f96dfa8443f843db463b6 and anti-tumor homes (Shukla and Singh 2007; Baliga *et al.* 2011; 33) and inhibits the proliferation of many cell carcinogens that cause the spread of autopause-converting acac pathway. (Radhakrishnan *et al.* 2014). Simultaneous treatment with honokiol (Hono) and magnolol (mag) reduces the expression of cyclin A, D1, and cyclin-dependent kinase, which binds cellular cycle development and reduces the expression of p-PI3K, IP-Akt, and -Ki67 to U87MG and LN229 human glioma cells. . Each Hono-and Mediated magazine solution has the same anti-tumor effects as a cell-phone inhibitor; as a result, they result in autophagy and apoptosis in human GMB cells (Cheg *et al.* 2016). 6-Shogaol disrupts the integrated Akt / mTOR signal path; Akt blocking is beneficial for apoptotic molecular death. 6-Shogaol creates autophagy through Akt over expression inhibition and expresses anticancer interest in competition in most non-small cell lung cancers (Hung *et al.* 2007). Thymoquinone (TQ), the first component of black cumin, reveals amazing cytotoxic effects in many major cell carcinoma lines. In SASVO3 cells, TQ transformed into cellular cell death resolution due to the development of Bax expression and increased autophagic vacuoles and LC3-II protein expression following apoptosis and autophagy. In our previous post review, we found that gap-junction inhibitor, 18α- Glycyrrhetinic acid (18-GA), causes apoptosis and autophagy. 18-GA-added autophagy was developed to deliver Atg5, Atg7, and LC3II compounds for p62 degradation. 18-GA was modified in addition to deciding to suppress Bcl-2 / Beclin-1 interactions and Beclin-1 fragmentation, ultimately highlighting the proliferation of mitochondrial-mediated apoptosis in SH-SY5Y cells. 18-GA is also approved to open multiple MAPKs and bind to the cellular cycle, which ultimately activates apoptosis. 18-GA can also be used appropriately as a therapeutic target for the apoptosis autophagy pathway in neuroblastoma. Delphinidin is an anthocyanidin monomer with high anti-oxidant properties. In HER-2 top-notch breast cancerous cells, delphinidin enhances apoptosis and autophagy thru the mTOR suppression method and the use AMPK signaling method. Growing evidence has proven that epicatechin-three-Ogallate (EGCG) promotes autophagy and apoptosis in many types of cancer (Siddiqui *et al.* 2011; Grube *et al.* 2018; Stadlbauer *et al.* 2018). Previously, OxyR transformed into a decision to simultaneously suspend apoptosis and autophagy in NB. OxyR also reduced PI3K / Akt / mTOR signaling and improved cytotoxicity in a way that enhanced the autophagy range. OxyR delivered to

cell death has shifted in determining the indiscriminate occurrence of apoptosis induction due to changes within the degrees of PI3K / Akt / mTOR and p38 MAPK recreational cells in SH-SY5Y cells.

Saikosaponin-d is proposed to induce intracellular calcium accumulation and autophagy by activating the CaMKKβ-AMPK-mTOR pathway. However, ER type and UPR activation in the form of saikosaponin-d have been shown to induce apoptosis and autophagic momolecularеath (Wang *et al.* 2014). Isoliquiritigenin (ISL) inhibits the activity of ovarian maximum cancers molecular strains (OVCR5) and the ES-2 model. ISL was further introduced with autophagy to OVCR5 with cell cycle arrest in phase G2 / M, cleaved caspase-3, and accelerated LC3B-II and Beclin-1. Guttiferone okay (GUTK) away from garcinia yunnanensis Hu (Xu *et al.* 2008) has been modified in the decision to reduce Akt phosphorylation and block the mTOR pathway. GUTK is also a more effective ROS derived from JNK phosphorylation in EBSS, which introduces autophagy and apoptosis under adverse nutritional conditions.

CONCLUSION AND FUTURE VISIONS

With the increase in cancer every day, new methods are being developed to ensure that this deadly disease is cured. Conditions that need to be improved requiring cancer pills are strongly associated with the complexity of many types of carcinoma. Autophagy and apoptosis are among the most important cellular mechanisms associated with cancer advancement and policies. In addition, crosstalk takes place through signatory mechanisms, entailing those concerned with autophagy and apoptosis. Numerous cancer models grow into drug-resistant chemotherapy because of the defects in the signature pathways, especially the apoptosis process. As a substitute for cellular genetics, autophagy may be experimented with to increase the different targets of cancer drugs. In addition to research, each in vitro and in vivo, however important in the advanced knowledge of cancer organic disorder, will activate the full potential for designing autophagy apoptosis pills targeted for exploitation. Researchers have always been fascinated with the use of commercial flowers and their emergence as a powerful source of cancer treatment. In reality, a growing number of evidence points to the growing ability of cancer-fighting phytochemicals that regulate many manifestations involving autophagy and apoptosis. The anti-cancer outcome of phytochemicals was considered as specific and to be different from most cancer cells that have been implicated in autophagy exchange and cell death. Thus, many phytochemicals point to a promising source of cancer pills. High levels of phytochemicals that use their anti-cancer properties in vitro and in vivo by controlling suicide strategies (i.e., berberine, lycopene, sulforaphane, curcumin, and resveratrol) are recently studied under analytical investigation for multiple varieties of cancers. Because autophagy creates a normal state for cancer patients, identifying this necessary cellular approach will not always be helpful. Similarly, a few phytochemicals targeting specific signaling pathways can be distributed between single-cellsystems; for that reason, we set the stage for the development of many completely phytochemical-based cancer cells. This suffering may, nonetheless, be settled by in vitro as well as in vivo studies in alter phytochemical-mediated autoinfection. Similarly, a unified system of pharmacokinetics and calculation method can be used to enhance the understanding of the antitumor consequences of phytonutrients. While the analytical packages of phytonutrients are inhibited with the help of bioavailability, improvements may be achieved through the use of nanotechnology-based distribution of drugs. Mainly elicited from the highlights of this study, the strengths and phytochemical challenges centered on autophagy and apoptosis can slow down new processes and strategies to develop new cancer treatment programs to treat certain types of cancer. Finally, difficult conditions in advance in addition to the possible guaranteed desire to improve the anti-cancer effect in addition to speeding up the translation process strengthen nanomedicine or an accurate technology for Autoinfection-based cancer treatment. Nanoparticle-Based Drug Delivery Systems (NDDS) are widely applied in diagnostic therapeutic, in addition to many cancer speculations due to their unique cancer-focused function and coffee-toxic environments. However, due to complications of diagnosing a negative patient, mutagenicity, and multidrug resistance (MDR), the NDDS is now being challenged in a sensational trial. Indeed, the mixed purposes of nanoscience and the current, bioactive compounds are far more appealing than the recent rapid development combined with conventional medicine to enhance clinical outcomes. Therefore, it will put pressure on developing novel treatment strategies to critically

evaluate early predictors and carcinogenic mechanisms, thereby targeting phytochemicals in the path of autophagy apoptosis.

Statements and Declarations

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval and Consent to Participate

It is a review article. No ethics approval is required.

Consent to Publish

Not applicable.

Human and Animal Rights

It is a review article. No animals were used in the study.

Availability of Data And Materials

Not applicable.

Credit Authorship Contribution Statement

All the authors have substantial contribution for the preparation of the manuscript. Gagan Kumar Panigrahi and Abhijeet Pattjoshi and Ipsita Sahoo conceived the idea. Data curation and writing: Abhijeet Pattjoshi, Ipsita Sahoo, Annapurna Sahoo, Subhashree Sadangi, Shraban Kumar Sahoo, and Gagan Kumar Panigrahi. All the authors have read and approved the final manuscript before submission.

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RESEARCH ARTICLE

Development of Synthetically Elegant Inhibitors against Pathogenic Gram-Negative Bacteria: *Salmonella typhimurium* and *Escherichia coli*

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ABSTRACT

Many of the Gram-negative bacteria are known from decades. These are highly abundant in nature. These harmful Gram-negative bacteria are known for causing serious life-threating diseases such as: neurological disorder, gastroenteritis, and many more. These bacteria can sustain in the host body quickly due to the presence of additional protective cell wall which defends from invasion of exogenous toxic agent. Therefore, developing new molecules with appropriate three-dimensional geometry and shape that can easily penetrate the preventive cell wall of such noxious bacteria is a huge demand. We report herein, a small organic molecule, PA-P-Amide which having unique molecular scaffold of prerequisite properties that can easily penetrate through the protective cell wall of the bacteria. We also successfully demonstrated antibacterial activity of PA-P-Amide molecule against pathogenic gram-negative bacteria such as: *Salmonella typhimurium* and *Escherichia coli*.

Keywords: Gram-negative bacteria, *Salmonella typhimurium, Escherichia coli,* infected diseases, antibacterial activity, small organic molecule, pathogenic bacteria,

INTRODUCTION

Gram-negative bacteria such as: *Salmonella typhimurium* and *Escherichia coli* are known for causing serious life-threating diseases. These bacteria can infect a broad range of animals. [1, 2] These bacteria have a additional

protective cell wall that protect the bacteria from toxic effect of exogenous agent.15 The cell wall of these bacteria is made up of lipopolysaccharide coat (LPS) which strictly prevents the foreign invasion. The presence of this additional cell wall in gram-negative bacteria enables to survive in any adverse environment. However, most of the gram-positive bacteria devoid of such protective cell wall and therefore, they have poor resistivity in hostile environment than gram-negative bacteria.

Among gram-negative bacteria, *Salmonella* is a most toxic pathogen that infect thousands of lives worldwide even today. [1, 2, 16] These *Salmonella* species can cause a broad spectrum of diseases such as: neurological abnormalities, gastroenteritis, and life-threatening Typhoid fever in human being.[5, 7, 11-13] Therefore, *Salmonella* has been a cause to longstanding worldwide health problem and became a reason for significant mortality globally.[6, 11-13] *S. Typhimurium* belongs to *Salmonella* and it infects a wide variety of hosts; but however, there are few class of *Salmonella* such as: *S. Typhi*, *S. Pullorum*, and *S. Gallinarum*are exquisitely host-restricted.[6] Furthermore, *Salmonella entericaserovar typhimurium* is also a primarily responsible for food-borne disease as well.[8,] In addition to this, there are another category of gram-negative bacteria, called *Escherichia coli* which are found in the environment, foods and intestines of people and animal. This is a highly diverse group of bacteria. It has been known in the literature that most of *E. coli* are not harmful, rather helps to keep our digestive track healthy. However, there are few varieties of *E. coli* are highly responsible for causing a broad spectrum of infections such as: diarrhea, food poisoning, pneumonia, urinary tract infections etc. There are different categories of E. coli such as: enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), enteroinvasive *E. coli* (EIEC), enterohemorragic *E. coli* (EHEC) and entero aggregative *E. coli* (EAEC) which are responsible for causing diarrhea.[14]

In day today life these bacteria some way or other impact our lives, even if these are pretty small living organism in the earth.[1] Among many gram-negative bacteria, *Salmonella* and *E. Coli* are two major pathogens that infect thousands of lives worldwide even today. [1, 2, 16] These bacteria are existed in different shape such as: spheres, spirals and rodsin nature and are having wide range of size varies from 0.4 to 3 μM. The varying shape is due to the presence of actin-like bacterial cyto-skeleton.[3, 4] Among many of these gram-negative bacteria, *Salmonella* species are found to be highly toxic pathogen. According to the recent findings, *Salmonella* species are responsible for causing wide spectrum of diseases starting from neurological abnormalities to gastroenteritis to life-threatening Typhoid fever in human being.[5, 7, 11-13, 20-21] Therefore, *Salmonella* has been a cause to longstanding worldwide health problem and became a reason for significant mortality globally.[6, 11-13] The bacteria *S. Typhimurium* is a wild in nature which infects a broad range of hosts. However, this specific bacterium belongs to *Salmonella* species. In addition to that, there are few class of *Salmonella* such as: *S. Typhi*, *S. Pullorum*, and *S. Gallinarum* are exquisitely host-restricted.[6] Furthermore, the bacterium *Salmonella entericaserovar typhimurium* causes food-borne disease as well.[8] In addition to this, there is a highly diverse group of gram-negative bacteria called *Escherichia coli* which are mostly found in the environment, foods and intestines of people and animal. It has been known in the literature that most of *E. coli* are not harmful, rather helps to keep our digestive track healthy. However, there are few varieties of *E. coli* are highly responsible for causing a broad spectrum of infections such as: diarrhea, food poisoning, pneumonia, urinary tract infections etc. There are different categories of E. coli such as: enterotoxigenic *E. coli* (ETEC), enteropathogenic *E. coli* (EPEC), enteroinvasive *E. coli* (EIEC), enterohemorrhagic *E. coli* (EHEC) and enteroaggregative *E. coli* (EAEC) which are responsible for causing diarrhea. [14-16, 18-21]

Considering the life-threatening pathogenic effect of gram-negative bacteria, it has been a continuous endeavour from wide spectrum of scientific community to develop novel antibacterial agent. Till today, Most commonly used antibacterial agents are the derivative of quinolones and fluoroquinolones compounds.[9] It is always been a huge challenge for synthetic chemist to develop molecule with well-defined architecture that can strictly inhibit pathogenic gram-negative bacteria. The poor rate of progress is attributed to the protective cell wall of the gram-negative bacteria which demands a precise molecular structure. Therefore, to overcome this difficulty, herein we have developed a new scaffold with stringent architectural component inbuild into the benzene core. We have demonstrated potential antibacterial activity of this molecule against gram-negative bacteria.

RESULTS AND DISCUSSION

There are numerous coupling reagents (DCC, HATU, HBTU, EDC, SOCl2 etc.) available now a days to convert acid to corresponding amide or ester. But all these amide or esters coupling reagents such as: 1) DCC, 2) HATU, 3) HBTU, 3) EDC are highly expensive and therefore, difficult to afford them for academic research. But on the other hand, thionyl chloride (SOCl2) is another robust alternative for the synthesis of an amide or ester from acid. Furthermore, it is comparatively much cheaper than other coupling reagents. This reagent is pretty simple to handle and moreover, it affords high yield. Therefore, this reagent became central to many of the organic transformation for industrial uses. In light of these potential advantages, wehave utilized the thionyl chloride (SOCl2) as a coupling agent to generate a new variety of molecular scaffolds which might inhibit toxic pathogen like Gram (-ve) bacteria such as: *Salmonella and E. coli*. (Scheme 1).

In search of an ideal molecular scaffold for the precise installation of n-propylamine unit in order to have amide-based molecules, we intended to start with semi-rigid backbone like phthalic acid (PA). We envisioned that benzene ring in PA will provide rigidity along with pi-pi stacking interaction with hydrophobic region of the toxic pathogen which in turn could provide good binding efficacy. In addition to that the ester functionality may help in making hydrogen bonding interaction with hydrophilic part of the pathogen. The remaining butane tail may provide flexibility to the core structure and along with that it may enhance the possibility of cell permeability nature of the molecule. Consequently, synthesizing this kind of molecule may inhibit pathogens. Having these anticipations in mind, we wanted to install the ester moiety into a rigid system, Phthalic acid (PA). Therefore, we persuaded to synthesize compound, PA-P-Amide (Scheme 1) with an intention that this compound may show better inhibition property towards pathogen. In the beginning, the precursor compound, phthalic acid (PA) converted to corresponding acid chloride, PA-Cl by treating with thionyl chloride under room temperature for 3 hours (Table 1). The mixture of water and tetrahydrofuran was chosen as the solvent system to carry out the reaction. Minimum amount of water was taken to solubilize the precursor compound, phthalic acid.

The resulted acid chloride, PA-Cl was further treated with n-butanol in the presence of triethyl amine as a base to get the desired product, PA-P-Amide. Reaction kinetics was completely monitored by thin layer chromatography (TLC) techniques. But surprisingly, TLC result analysis showed no new product formation, rather mostly precursor, PA was observed on TLC (Figure 1). We anticipated that the phthalic acid does not convert to corresponding acid chloride due to high transition state energy barrier which may require high temperature rather than room temperature. Therefore, to overcome this challenge we further executed the reaction in the reflux condition keeping all other parameters unaltered. TLC result shows very mild product formation (Figure 1) which is negligible. This experiment clearly indicating that, not only temperature but also protic solvent like water and methanol plays a role in inhibiting the reaction. In presence of methanol, we observed almost the similar results like water. Therefore, we turn our attention to start the reaction using only aprotic solvent like THF.

To overcome this problem, we designed two experiments in parallel by using THF as solvent. In the first experiment, the reaction was carried out at room temperature in presence of THF as a solvent and kept all other parameter constant. However, in the second experiment the reaction was carried out in reflux condition in presence of THF as a solvent without altering any other parameters. TLC analysis clearly shows new product formation (Figure 1, TLC-4) in both cases. The intensity of product spot observed for refluxed reaction is much brighter than room temperature reaction. These results clearly reveal that the reaction must be carry out in aprotic solvent at refluxed condition to get the optimum product formation. With this optimized reaction condition, we observed up to 90 % of product yield (Table-2). The products were further purified by column chromatography in 1% methanol and chloroform system. The desired product, PA-P-Amide formation was further confirmed by UV-Visible spectroscopy study (Figure 3) by comparing with commercially available starting material. This data clearly showed the formation of product. Elemental analysis data also support the product formation.

Again, to cross verify the product formation we carried out the base hydrolysis reaction (Scheme 2) with sodium hydroxide solution in water as a solvent and isolated the hydrolyzed products using column chromatography techniques. After column purification of crude product, we observed two kinds of material. One material is solid and another one is liquid. The solid material expected to be phthalic acid and liquid material may be n-propylamine. The solid material obtained after hydrolysis was analyzed by comparing the TLC with commercially available starting material. The TLC result clearly shows, the hydrolyzed product is a starting material (Figure 2). It was further confirmed by comparing melting point with the starting material. The melting point of the starting material (207 ^{o}C) was found to be same as that of isolated product (207 ^{o}C). This indicated that the hydrolyzed product is PA (Scheme 1). The liquid material obtained after hydrolysis was analyzed using TLC with reference to commercially available n-butanol compound. TLC result clearly showed both have the same retention time. This result indicated the second hydrolysis product may be n-butanol. It further confirmed by determining the boiling point of the liquid material which was similar to n-propylamine. This result confirmed that the resulted hydrolysis product is a n-propylamine. Therefore, these results strongly support the formation ester derivative, PA-P-Amide.

The antibacterial activities of PA-P-Amide against pathogenic bacteria i.e., *Salmonella typhimurium* and *Escherichia coli* were checked. A standardized concentration of both the inoculums were evenly spread on the surface of two different agar plates. A 500 μM concentration of PA-P-Amide was loaded into both the bore wells and incubated for 24h at 30±2^{o}C temperature. The results clearly showed a very strong inhibition zone of diameter 30.2 mm size against *Salmonella typhimurium* after incubation with PA-P-Amide for 24 hours (Figure 4a). This result clearly reveals that, PA-P-Amide has potential antibacterial activity against *Salmonella typhimurium*. However, the antibacterial activities of PA-P-Amide was found to be relatively lesser for *Escherichia coli* than *Salmonella typhimurium* which is evident from the inhibition or clearance zones of both the pathogenic strains (Figure 4 a & b). This antibacterial activity could be due to the presence of well-balanced hydrophobic, hydrophilic and long chain hydrocarbon molecules. Owing to these well-balanced properties of PA-P-Amide, might be proficient to cross the bacterial cell membrane resulting in the inhibition of the bacterial strain growth.

MATERIALS AND METHODS

The chemicals and solvents were purchased from Spectrochem Ltd and Sigma Aldrich. All the chemicals were directly used without further purification. Normal phase column chromatography purification was carried out by using MERCK silica gel 60 (particle size: 100-200 mesh). Reactions were monitored wherever possible by thin layer chromatography (TLC). Silica gel G (Merck) was used for TLC and column chromatography was undertaken on silica gel (100–200 mesh) in hexane, hexane–ethyl acetate or chloroform. UV and visible peaks of synthesized organic compound was measured in chloroform as a solvent in the range of 200-400 nm. The walelength (in nm) was taken in X-axis and absorbance in the Y-axis. It shows maximum absorbance at 243.6 nm wavelength. Melting points were recorded in a Fisher-Johns melting point apparatus.

Test organisms

The test bacterial cultures including *Escherichia coli* (MTCC No.- 614), *Salmonella typhimurium*(MTCC No.-3224) were collected from IMTECH Chandigarh. All the bacterial cultures were maintained in nutrient agar slants. The slants were kept in refrigerator for use during further experiments.

Antimicrobial Assay

A standardized concentration of inoculums with fixed volume was spread evenly or swabbed on the surface of gelled agar plates. A hole which ranges from 6 - 8 mm in diameter was punched with a sterile cork borer aseptically in plates. A fixed volume (50 μl) of the sample solution was then introduced into the bored agar well and incubated at optimum temperature (Bacteria - 30±2^{o}C for 24 hrs) depending upon the test microorganism. [17]

Synthesis of PA-P-Amide

Phthalic acid (5g) was taken in a round bottom flask (RBF). To this solid mass, thionyl chloride (6.5 ml) was added dropwise over a period of 1o minutes at 10-15 ^{o}C. The temperature of reaction mass was raised to 70-80 ^{o}C and stirred it for 3 hours. Slowly cooled the reaction mass temperature to 0-5 ^{o}C and added THF (50 ml) into it. To this ice-cold solution, triethylamine was added slowly over a period of 1h. Then n-propylamine (6.4 ml) was added into the reaction mass at 0-5 ^{o}C. Slowly raised the reaction mass temperature to room temperature and stirred it for 12h. TLC was checked and reaction was found to be completed. The organic layer was dried over anhydrous Na_2SO_4, filtered and evaporated. Finally, the crude compound was purified using column chromatography.

CONCLUSION

In conclusion, to our knowledge, it is a very unique example where PA-P-Amide molecule strongly inhibit the growth of pathogenic gram-negative bacteria like *Salmonella typhimurium* and *Escherichia coli*. We have also thoroughly studied the mechanism of inhibition of this molecule towards these two pathogenic bacteria. This molecule may open up new doorway for the treatment of diseases, causing by these bacteria. This may inhibit pathogenic bacteria present in food and potentially good for food security, which relate to SDG 2 and 3. To our opinion, this work may provide new insight to design potential molecule of tunable property with respect to protective cell wall of the bacteria which will enhance the cell permeability of the molecule. Thereby, it will inhibit the pathogenic gram-negative bacterial growth.

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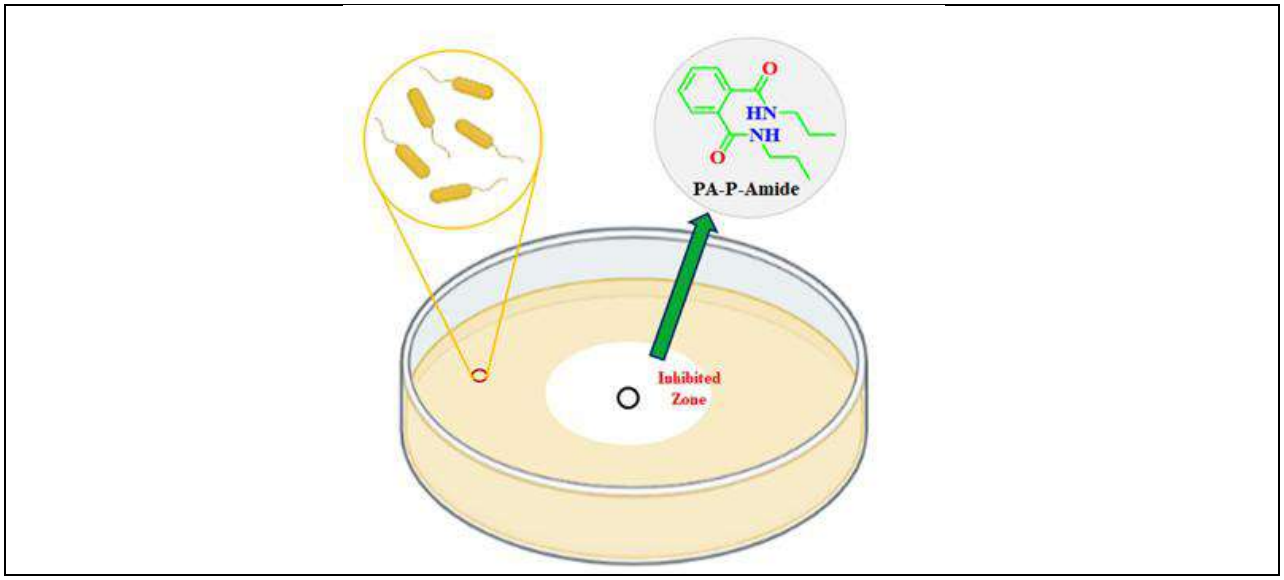
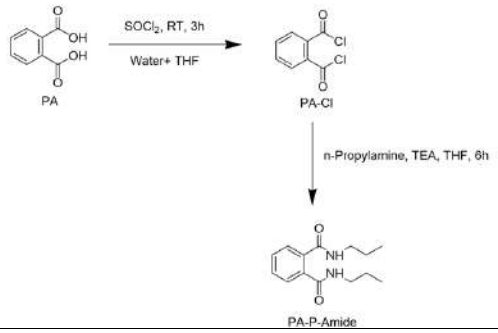
Table 1: Chemicals used for the reaction

Chemicals	Molecular Weight in g/mol	Quantity	Moles
Phthalic acid $\{C_6H_4(COOH)_2\}$	166.13	5 gm	0.03
Thionyl Chloride ($SOCl_2$)	118.97	6.6 ml.	0.075
THF(C_4H_8O)	72.11	100 ml.	0.09
n-propylamine(C_3H_9N)	74.121	6.04 ml.	0.81

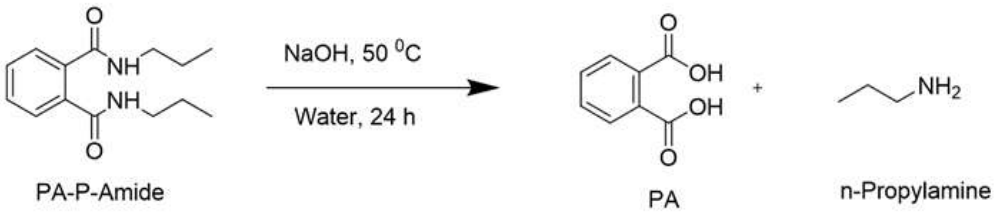
Table 2: Reaction analysis in different solvent system

Solvents	Temperature	TLC Analysis	Yield	Remark
Water + THF	Room Temp. (RT)	No new spot observed	0%	The reaction was not progress in aqueous medium.
	Reflux Condition	No new spot observed	1%	
Methanol +THF	RT	No new spot observed	2-3%	The acid was not converted into acid chloride in methanol solvent.
	Reflux Condition	No new spot observed	10%	
Tetrahydrofuran	RT	New spot observed (not clear)	40%	In RT the rection progress very slowly and is taking long time. Yield is less. But in refluxed condition the rection progress very fast and observed quantitative yield.
	Reflux Condition (70-80° C)	New clear spot observed	90%	





Scheme 1: Synthetic scheme for the synthesis of PA-P-Amide



Scheme 2: Base hydrolysis of PA-P-Amide

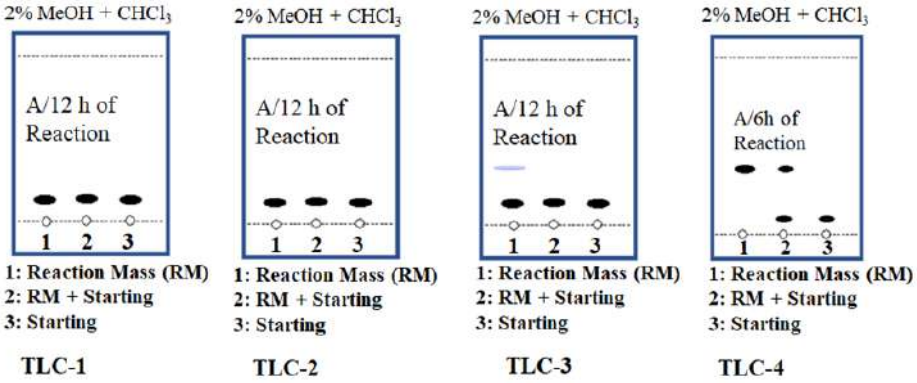


Figure 1: TLC-1-Reaction carried in water+ THF solvent mixture at room temperature; TLC-2-Reaction carried in water as solvent at reflux condition; TLC-3-Reaction carried in methanol as solvent at reflux condition; TLC-4-Reaction carried out in THF at reflux condition

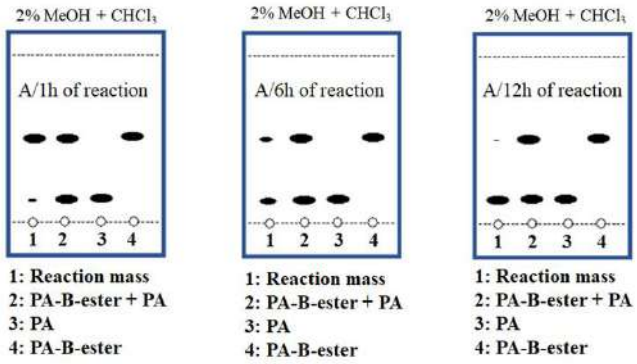


Figure 2: Monitoring the reaction kinetics of PA-P-Amide hydrolysis reaction (scheme-2): after 1, 6, and 12 hours of reaction time using TLC.

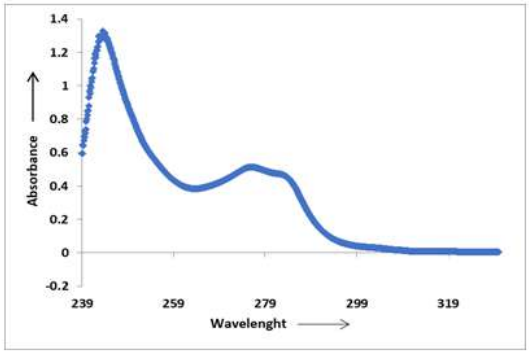
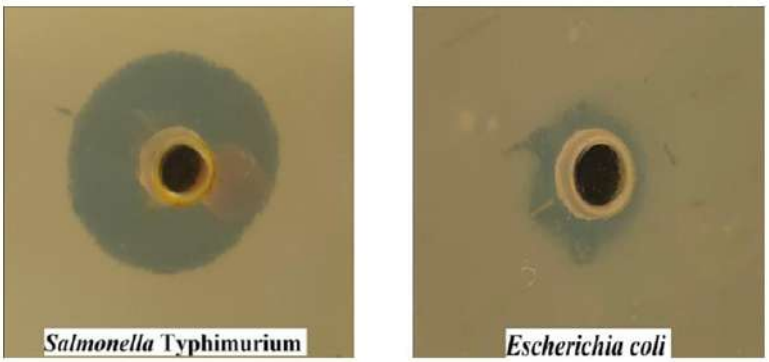


Figure 3: UV-VIS Spectra of the compound, PA-P-Amide



(a) **(b)**

Figure 5: Antibacterial activities of PA-P-Amide against pathogenic bacterial stains: (a) Staining of PA-P-Amide against *Salmonella Typhimurium*, (b) Staining of PA-P-Amide against *Escherichia Coli*.

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RESEARCH ARTICLE

Understanding of Carbon Dioxide Dissolution in Aqeous Methyl Diethanolamine through Molecular Dynamics Simulation

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ABSTRACT

Carbon dioxide is one of the most important constituent of our atmosphere. However, due to the increasing percentage of this gas it causes a serious concern for survival of mankind. There are various sources from where CO_2 gas can be obtained. With every passing days the amount of CO_2 released to atmosphere is getting increased. Due to the global concern, many scientists all over the world are working on how to reduce the effect of CO_2 and how to control of CO_2 amount. In this regard in this manuscript we have calculated the efficiency of aqueous methyl diethanolamine for CO_2 absorption by using materials studio software. The results shows that 0.4 m mol of CO_2 can be adsorbed by the proposed aqueous solution. The results are encouraging and is matching within the error limits with the experimental results published in literature.

Keywords: Carbon dioxide, Ethanol amine, Gas absorption, Efficiency, Gas sweetening.

INTRODUCTION

From the beginning of the civilization, the atmosphere exists and it is and was necessary for the growth and survival of mankind and other living beings. Among several other gas that make the atmosphere, CO_2 plays an important role. It is used for plant photosynthesis and have many other applications [1-5]. However, due to rapid industrialization, increase in vehicles, and many other human activities, the rate of CO_2 release to atmosphere is increasing on every passing day. Due to these human activity, million tons of CO_2 are releasing to the atmosphere that causes several disease and problems to the population and environment [6-8]. Since past few decades, a lot of scientific research is going on to capture the CO_2 from the chimney and from the atmosphere. In this regard several initiatives are also being taken by many governments to reduce the carbon foot print from earth. In this regard, we have explored the possibility and efficiency of CO_2 capture by aqueous solution of methyl diethanolamine [9-13].

Computational Details

To calculate the dissolution capability of aqueous solution of methyl diethanolamine using materials studio software, first of all all the components such as water, methyl diethanolamine, CO_2 and piperazine were drawn and then geometrically optimized for their stable structure [14-18]. After that suitable force field such as compass has been used for several other calculations. A three dimentional data structure was prepared by combining water, methyl diethanolamine, CO_2 for absorption investigation are depicted in Figure 1. The density data of the above mentioned materials were utilized from literature to construct the Amorphous cell [18,19]. Different ensembles were used for MD simulation calculation [9,20]. The NPT and NVT ensembles were the two important ensembles and are used for all possible combinations. All the calculations were conducted at room temperature because it is easy for comparison as well. All the different interactions were calculated from variety of calculations that are helpful for the CO_2 absorption. The cohesive energy density also have been calculated for all the studied materials followed by absorption efficiency.

RESULTS AND DISCUSSION

An example of Amorphous Cell containing all the above materials is depicted in Figure 2. To prove that we have used correct methodologies, we have calculated the absorption efficiency of CO_2 in aqueous Methyl diethanolamine and piperazine solution. The results shows that 0.5 mmol of CO_2 can be absorbed per gram of aqueous solution. The Methyl diethanolamine alone has the potential to absorb the CO_2 through hydrogen bonding interactions. However, the efficiency is low that is the reason why we have incorporated piperazine into the mixture. The mixture has more efficiency in absorbing the CO_2 due to the increase in interactions between CO_2, water, methyl diethanolamine, and piperazine [21]. Although there is a good agreement between the values of CO_2 absorption for both calculation and literature, the observed deviations could be due to some inconsistent parameters choosen during our calculations. During the absorption process there is a possibility that CO_2 get interacted with piperazine, methyl diethanolamine, and water. Most likely the hydrogen bonding is playing a major role for CO_2 absorption apart from van der Waals interactions and there weak interactions. The radial distribution curve as depited in figure 3, says that the distance between the diethanolamine and CO_2 gets increased as they separated from each other [22]

CONCLUSION

As discussed in the above work, the CO_2 absorption efficiency of aqueous methyl diethanolamine in presence of small amount of piperazine has been investigated. The results shows that only a 5 % addition of piperazine to the aqueous amine solution drastically increases the CO_2 absorption upto 0.4 mmol of CO_2 per gram of sample. The calculated value of CO_2 is almost nearly equal to the experimentally investigated values by the several researchers. The little deviation from the CO_2 amount from literature could be attributed to the assumption during the MD simulation calculation. This work will surly encourage to many researchers to investigate the CO_2 absorption by many solvent theoretically to have a preliminary idea about the efficiency of absorption.

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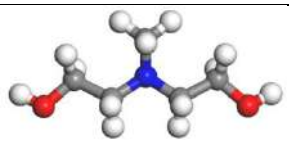
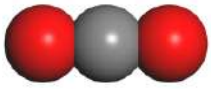
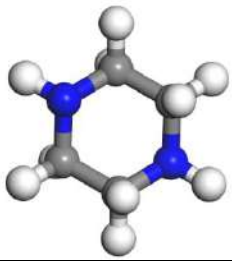
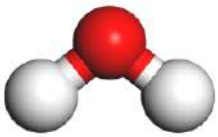

Methyl diethanolamine	CO_2	Piperazine	Water

Figure 1: Geometry optimized structures of all the materials used for calculation.

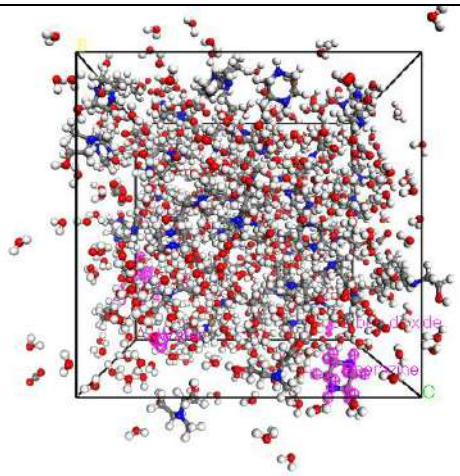

Figure 2: Bulk arrangement of all the above mentioned materials used for CO_2 absorption prepared in Amorphous cell module of Materials Studio software

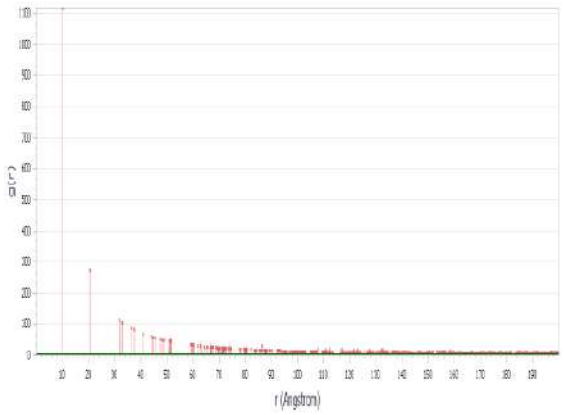

Figure 3: Radial distribution function between methyl diethanolamine and CO_2 during absorption.

RESEARCH ARTICLE

Effects of Bavistin(fungicide) on Morphological Aspects of Haematological Parameters of Amur Carp

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ABSTRACT

Bavistin is a type of fungicides which helps in the growth of plant and at the same time it also imparts toxicity to the soil and water. Due to its toxic effect in water an aquatic organism also suffers. Therefore, an attempt is made to study, the harmful effect of bavistin in amurcarp in the present study. The morphological examination is done in the zoology lab of centurion university of technology and management. In this examination we have taken the total number of 6 fishes for 30 days, in which 3 fishes were kept in the aquarium and feed daily and were observed and 3 fishes were kept at different concentration treated with bavistin and were feed daily and observed. The concentration of Bavistin were 2 ppm, 3ppm and 4ppm.Then the blood was collected from the tail vein of fishes. 2ppm concentration of blood was collected from the fish body after 3days, then examine the blood under microscope.3ppm concentration of blood was collected from the fish body after 4days, then examine the blood under microscope. 4ppm concentration of blood was collected from the fish body after 5 days, then examine the blood under microscope and observed the deformation and increase in the cellular size of the red blood cells, cytoplasmic degeneration and nuclear degeneracy.

Keywords: Amurcarp, Bavistin, Haematological parameters, Morphological examination.

INTRODUCTION

Fungicides is the biocidal chemical compounds helps to control the pest of agricultural products and then mixes with water then it affects the river bodies as well as the total ecosystem. This changes affects the physiological

behavior, and biochemical properties of aquatic organisms. These fishes are aquatic and cold blooded animals. Their existence and performance depends upon the environmental condition. All the species of fish are kept under optimum temperature. The existence of fish face environmental stress that depend on the parameter like physiological process to maintain constant internal body chemistry. Haematological indices used to analize the general physiological status of fish and can be used as stress indicator and response reaction of fish with varying environmental condition. The haematological test can be used to provide erythropoietic condition. Fungicides are the biocidal chemical compound that are used to kill parasitic fungi. These fungi can cause serious damage in agriculture so there is the loss of yield. These fungicides are used in agriculture and fight against the fungal infection. The fungicides are bought retail are sold in liquid form . Fungicides in powered form usually around 90%sulfur and other harmful chemical.

Bavistin is a fungicide which controls disease at every growing point plant. It works as preventive as well as curative, gives longer duration of control. Bavistin is used with other insecticides and fungicides. Bavistin has broader diseases control in field and horticultural crops. Bavistin contains 50% carbendazim WP . It is a broad spectrum systemic fungicides effective against a wide range of pathogenic fungi and is highly specific in its control of important plant pathogens on variety of crops. Bavistin is absorbed by plant and acts on fungal pathogen. Bavistin is a harmful chemical that has an adverse effect on the aquatic animal like fish. After adding the chemical bavistin in water then we observe that the movement of the fish slows down and its food intake capacity decreases . After that fish comes to stress. Then the fish face vey difficulty in respiration. These chemical bavistin affect the fish heart and damage worst way. The swimming ability decreases and its functioning stop and at last it dies. Haematological parameter blood is the indicator of pathogical change induce by the pollutants in fishes .The fish blood shows remarkable pathological change. Haematogical parameter are important for toxicological research and indicator of environmental stress and diseases in fish.

The optimal concentration of Bavistin will protect them from fungal diseases and will maintain their diversity and population. This fungicide can also be used significantly for other lives under water after proper investigation.

MATERIALS AND METHODS

Live and healthy *Cyprinus carpio* (Amurcarp) of same size and same range were collected from the local aquarium and acclimatized for one month under normal laboratory condition. This experiment is done for 30 days by taking six number of Amur carp . Out of six fish 3 fish are maintained in normal condition and considered as control (C) and other 3 are subjected to different concentration of the fungicide Bavistin in different containers labeled as C1 , C2 and C3 . The chemical amount taken in C1 was 2ppm, in C2 was 3ppm and C3 was 4ppm. The fish maintained under control were fed with normal diet and also normal water quality parameters (pH, temperature, dissolved oxygen) were maintained and water was changed once in 7 days of interval. The fishes are feed with proper diet at appropriate time interval, whereas the fishes exposed to Bavistin are also subjected to proper diet and the waste material eliminated from its body are removed regularly from the container. Blood sample were collected separately from the tail vein of fish. A thin blood flim is prepared by spreading a small drop of blood uniformly. After staining with Giemsa's stain the blood film is used to determine the morphology of blood (Fig.1).

RESULTS

The fishes kept at different concentration shows much difference in RBC count (Fig.2). Activities like movement , feeding habit ,swimming capacity which were observed to decrease, as they underwent stress. After the exposure to different concentration of biocidal, different morphological changes are observed like in case of 2ppm concentration few portion of erythrocytes are damaged and about 168 hours the movement of fish slows down and swimming capacity decreases. Then in case of 3ppm, 4ppm concentration damaged the red blood cells and karyohexesis and cytoplasmic degeneracy occurs, After 168 hours the fish dies .Similar changes were observed for 3ppm and 4ppm

concentration. Finally we observed that the colour of the fish changes after their death. Therefore we conclude from the total experiment that the bavistin is very harmful to the aquatic organisms .

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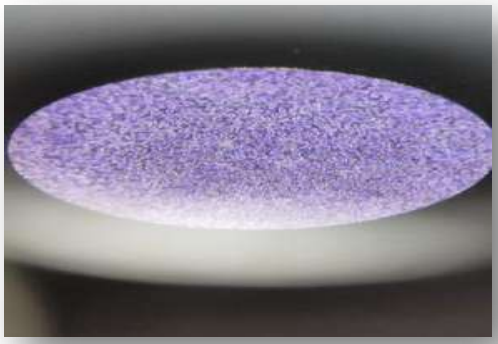

Fig.1- Blood smear under control condition

Fig.2- Blood smear under stressed condition

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RESEARCH ARTICLE

Insight into Peptic Ulcer Disease: It's Pathogenesis and Recent Development in Herbal Medicine for the Treatment of Peptic Ulcer

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ABSTRACT

Peptic ulcer disease continues to be a source of significant mortality and morbidity worldwide. It is a chronic disease affecting 10% of nationwide population. It is a collective term used for a group of chronic manifestations that affect mucosal integrity of stomach and/or duodenum. It is characterized by epigastric pain, perforations ,bloating, blood in stool or vomit, loss of appetite followed by weight loss. The formation of peptic ulcers depends on the presence of gastric juice pH and reduction in mucosal defences .Most cases of peptic ulcer disease are associated with Helicobacter pylori infection or the use of nonsteroidal anti-inflammatory drugs (NSAIDs), or both relating to mucosal damage. Around 2/3rd of patients found to have peptic ulcer asymptomatic and in symptomatic patients the most common symptoms is epigastric pain followed by dyspepsia, bloating, abdominal fullness, nausea etc, satiety. Conventional treatments of peptic ulcers, such as proton pump inhibitors (PPIs) like pantoprazole, rabeprazole, histamine-2 (H2) receptor antagonists like cimetidine, ranidine, ulcer healing agent like Sucral fate and for H. pylori eradication antibiotics are also used. however, the conventional treatment of peptic ulcer has some limiting factors, such as side effects, especially in patient with prolonged therapy and also the increases resistance of H. Pylori to antibiotics. however, the conventional treatment of peptic ulcer has some limiting factors, such as side effects, especially in patient with prolonged therapy and also the increases resistance of H. Pylori to antibiotics. On the other hand, medicinal plants and their chemical compounds are useful in the prevention and treatment of numerous diseases. A number of natural products are reported to exhibit antiulcer property in various animal studies and some of them are currently being used in various herbal formulations. Hence, in this present review we have discussed the aetiology, pathogenesis of peptic ulcer and herbal approaches treatment or prevention of peptic ulcers.

Keywords: Peptic ulcer, NSAIDs, H. Pylori,gastroprotective activity,herbal remedy

INTRODUCTION

chronic disease affecting 10% of nationwide population. Peptic ulcers are deep mucosal lesions extending beyond the muscular is mucosa coat of the gastrointestinal tract that are exposed to hydrochloric acid and pepsin.[1] Gastritis describes any inflammation of the gastric mucosa. The imbalance between mucosal defence and aggressive factors results in varying degrees of gastritis and/or frank ulceration. The commonest cause of primary peptic ulcers is Helicobacter pylori infection.[2] Improved socio-economic conditions, effective medical treatments and pervasive use of antibiotics for unrelated conditions have led to a steady decline in the rates of H. pylori infections, particularly in the developed world, and an increasing proportion of cases are H. pylori negative. [3] Primary peptic ulcers tend to be chronic, are often duodenal. Secondary peptic ulcers are usually acute, can occur at any age and are associated with a higher mortality in young children. [4]

Epidemiology

Peptic ulcers were rare before the 20th century. Gastric ulcers and, later, duodenal ulcers were increasingly described in the late 19th century, the incidence of duodenal ulcers increasing progressively and reaching a peak in the 1950s.The cause of this is unclear, because H. pylori is thought to have been ubiquitous in the human population for thousands of years. [5] H. pylori infection is still much higher, and migrants from developing to developed countries exhibit a high prevalence [6]. Helicobacter pylori is acquired by human contact, usually oro-oral rather than faecal-oral transmission. In developed countries, it is usually acquired by intrafamilial transmission; in developing countries, it is more often acquired from other children outside the family group. [7]

Pathophysiology

Traditionally, mucosal disruption in patients with the acid peptic disease is considered to be a result of a hypersecretory acidic environment together with dietary factors or stress. Risk factors for developing peptic ulcer include H. pylori infection, alcohol and tobacco consumption, non-steroidal anti-inflammatory drugs (NSAIDs) use, and Zollinger–Ellison syndrome. The main risk factors for both gastric and duodenal ulcers are H. pylori infection and NSAID use.[7] However, only a small proportion of people affected with H. pylori or using NSAIDs develop peptic ulcer disease, meaning that individual susceptibility is important in the beginning of mucosal damage. For example, polymorphisms of interleukin 1 beta (IL1B) affect mucosal interleukin 1β production, causing H. pylori-associated gastroduodenal diseases. On the other hand, the risk of complications of peptic ulcer is increased four times in NSAID users, and two times in aspirin users [8]. The concomitant use of NSAIDs or aspirin with anticoagulants, corticosteroids, and selective serotonin reuptake inhibitors increase the risk of upper gastrointestinal bleeding [9]. Although many people who use NSAIDs or aspirin have concurrent H. pylori infection, their interaction in the pathogenesis of peptic ulcer disease remains controversial. H. pylori-negative, NSAID-negative, and aspirin-negative peptic ulcer disease, which is classified as an idiopathic ulcer, can be diagnosed in about one-fifth of cases [10]. It is caused by the imbalance between factors that contribute to mucosal integrity and aggressive insults, but the pathogenic mechanisms behind the development of idiopathic peptic ulcer are still unknown A Danish study showed that psychological stress could increase the incidence of peptic ulcer [11]. Other aetiologies include ischemia, drugs (steroids, chemotherapeutic agents) and radiotherapy, viruses, histamine, eosinophilic infiltration, gastric bypass surgery, and metabolic disturbances [12]

Etiology and Pathogenesis of Ulcer

H. pylori Infection

H. pylori one of the main causes of stomach ulcer identified by the scientist 1982. H. pylori is a gram negative bacillus, microaerophilic flagellated spiral shaped bacteria. The type I strains of H. pylori possess a pathogenic activity, it encodes the effector protein cytotoxin associated gene (AcagA). After translocation into the host cell shape, increases motility of cell, followed by disturbs junctional activity of cell and caused gastric carcinoma and gastric ulcer**.** H. pylori increases expression of cytokines TNF ALPHA in gastritis. H. pylori infected gastric mucosa show infiltration of polymorphonuclear leukocytes, lymphocytes, monocytes and plasma cells in lamina propria.

Gastric Acid Secretion

Major ulcerogenic factor for induction of gastric ulcer disease acid. It has been recited that near about 50% ulcer patients are pepsin and acid hyper secretors.Secretion of acid is stimulated by three principle; gastrin, acetylcholine and histamine. The receptors on the surface of parietal cell include H2 receptors responding to histamine released from specialized mast cells. Receptors that are sensitive to the muscarinic effects of acetylcholine released from the vagus nerve and probably receptors responsive to endogenous circulating gastrin. Gastrin stimulates acid secretion either by direct stimulation of parietal cells or by the release of histamine from ECL cells. histamine stimulated acid secretion through a novel histamine receptor, the H2 receptor [15].

NSAIDS Drugs

NSAIDS also acts as antipyretic and analgesic property. It also used to treat arthritis muco-skeletal disorder. For about 25% of chronic users of these drugs developed gastric ulcer disease [16]. Various studies have been shown that NSAIDS aids progression of ulceration by overcoming the expression of enzyme cyclo-oxygenase (COX) which inhibit conversion of AA to PGs which imparts corrosive action with pepsin and progression pf peptic ulcer.NSAIDS inhibit COX-I which leads to endothelin-1(ET-1) a potent vasoconstriction which has been shown to induce mucosal injury.NSAIDS causes marked reduction in mucosal blood flowimparted platelet aggregation, mucous bicarbonate secretion, reduced epithelial cell renewal and are responsible for pathogenesis of ulceration.[17]

Aggressive And Defensive Factors Of Gastric Mucosa

Several cells of gastric mucosa contribute to gastric acid production. The G cells at the antrum of stomach release gastrin hormone. The hormone acts in enterochromaffin-like cells at the corpus of stomach, commanding it to release histamine. Histamine consequently will stimulate parietal cells to secrete acid. [18] Gastrin hormone also directly stimulates parietal cells and increases the performance of enterochromaffin-like cells and parietal cells. G cells, enterochromaffin-like cells and parietal cells are regulated through release of somatostatin peptide inhibitor from somatostatin cells, which reside in the entire gastric area.3 As it has been mentioned previously, prostaglandin is one of important defensive factors for protecting gastric mucosa [19] Synthesis of prostaglandin depends on activity of cyclooxygenase (COX) enzyme. Two forms of COX can be identified in various cells, i.e., COX-1 and COX-2. COX-1 is responsible for producing prostaglandin, which physiologically has important role to maintain homeostasis functions, such as preserving the integrity of mucosa and mucosal blood flow. NSAID suppresses COX-1 activity, thus forming lesions in gastric mucosa.4, 5 Aspirin, one of NSAID that has been widely used for several clinical indications, causes damage of gastrointestinal mucosa, induces stress ulcer and exacerbates the previous gastric ulcer. [20]

Clinical Manifestation And Diagnosis

The most common symptom with peptic ulcer disease is epigastric pain which may be associated with dyspepsia, abdominal fullness,nausea, bloating, and early satiety [21] Upper endoscopy can be used to diagnose peptic ulcer disease and is of particular urgency in those with dyspepsia. Endoscopy with Biopsy of peptic ulcers allows for characterization of a malignant vs benign. For diagnostic testing of H. pylori infection includes urea breath testing, stool antigen testing, rapid urease testing or histology of gastric biopsies taken at the time of upper endoscopy and serologic testing. The test for active infection are most preferable compared with serologic antibody testing due to low protest probability of infection. [22] Due to the possibility of false negative testing, testing confirm to eradication of H. pylori infection should be preformed no sooner than one month after completion of treatment of antibiotics [23].

Management of Peptic ulcer

For the prevention of recurrence of ulcer is important long-term goal to reduce mortality & morbidity.The objective of currently used antiulcer drugs is not only limited to control the progression of the disease but also to induce remission as quickly as possible and to maintain it for long time. For the management of peptic ulcer, it involves the use of proton pump inhibitors (omeprazole, pantoprazole, rabeprazole) H2 receptor antagonists (Ranitidine,

Cimeditine, famotidine), antacids (sodium bicarbonate,magnesium trisilicate, ulcer healing agent (sucralfate) and antibiotics like (metronidazole, tetracycline, amoxicillin, clarithromycin) [24].

Role of Proton Pump Inhibitors in the Treatment of Peptic Ulcer Disease

PPIs were introduced in the late 1980s.PPIs have substantially changed the approach to peptic ulcer disease and its management. PPIs remain the mainstay of medical therapy for peptic ulcer related gastrointestinal bleeding [24].Well performed systematic reviews support the initiation of PPLs prior to endoscopic evaluation for acute upper gastrointestinal bleeding, although a clear mortality benefit has not been demonstrated[25].The length of PPIs administration following the diagnosis of a peptic ulcer depends on the underlying ulcer etiology and it's associate complications. The main goal of use of PPIs therapy is to promote ulcer healing through suppression of acid [26]. Patient found with H. pylori positive on testing prompts treatment of the infection, at the other end patient with NSAIDs induced ulcers are counselled to avoid the aggravating agents. Also, patients with peptic ulcer disease who are on ongoing NSAIDs therapy, they also recommended to remain on PPIs co therapy [27]. PPIs are the most popular and effective prophylactic agents. The mechanism of action is reducing the production of gastric acid through irreversible binding to the hydrogen/potassium ATPase enzyme on gastric parietal cells.[28] Ulcers heal in more than 85% of cases with six to eight weeks of PPI therapy if the offending agent is discontinued. All of the gastric ulcers require repeat endoscopy to evaluate the success of healing. If ulcers fail to heal, drug compliance should be checked. For refractory ulcers, the doubling of PPI dose for another six to eight weeks is often recommended, although the evidence supporting this is weak. After the exclusion of false-negative H. pylori status, unusual causes of peptic ulcer should be explored, such as malignancies, infections, Crohn's disease, vasculitis, upper abdominal radiotherapy, cocaine use, and Zollinger–Ellison syndrome. PPIs are among the most commonly used and overprescribed medications in the world [29]. The side effects of the PPIs, such as a headache, diarrhoea, constipation, and abdominal discomfort, are minor and easily managed. However, recent studies have suggested an association between PPI use and several serious adverse effects, which has been a source of major concern to patients and physicians. [30] Some of the adverse effects of PPIs are related to their suppression of gastric acid secretion, allowing ingested microbial pathogens that would have been destroyed by gastric acid to colonize the upper gastrointestinal tract and cause infections. Reports are suggesting that the use of PPIs might increase the risk of enteric infections such as Salmonella and Campylobacter, community-acquired pneumonia, Clostridium difficile infections, and spontaneous bacterial peritonitis [31]. With gastric acid suppression, there is no stimulation of endocrine D cells to produce somatostatin, and thereby no inhibition of G cells for gastrin release, resulting in hypergastrinemia. Gastrin is a growth factor that can increase proliferation in Barrett metaplasia and the colon [32]. Nonetheless, PPI-induced hypergastrinemia in humans generally is mild, and rarely causes carcinoid tumours in human patients unless they have a genetic abnormality. Furthermore, PPI usage might protect against cancer in Barrett's oesophagus, since PPIs heal the chronic oesophageal inflammation of reflux esophagitis, which is a risk factor for the development of malignancy. Gastric acid inhibition by PPIs also can affect the uptake of certain vitamins, minerals, and medications. There are reports of patients on PPIs developing vitamin B12 deficiency and iron deficiency anaemia [33]. Additionally, PPIs might increase the risk for osteoporosis and bone fractures by interfering with the ionization and solubilization of the calcium salts that are required for their absorption.[34] The underlying mechanism for hypomagnesemia is still not clear. PPI-induced gastric acid suppression decreases ketoconazole absorption and facilitates the absorption of digoxin.[35] Furthermore, PPIs can affect the metabolism of other drugs metabolized by the cytochrome (CYP) P450 system; for instance, they can delay the clearance of warfarin, diazepam, and phenytoin. Considerable attention has been given to the potential of PPIs to reduce the antiplatelet action of clopidogrel, since both are metabolized by the CYP2C19 enzyme. The clinical importance of the interaction remains disputed, but the Food and Drug Administration (FDA) has issued warnings to avoid using omeprazole or esomeprazole with clopidogrel [36].

Role of H2 Receptor Antagonists in Peptic Ulcer Disease

In the era of PPI therapy, there is only a limited role for H2RAs in the treatment of peptic ulcer disease. As early as the 1980s, as compared with H2RAs, PPIs were demonstrated to improve rates of peptic ulcer healing[37]. A recent

randomized controlled trial showed that famotidine failed to significantly reduce the incidence of peptic ulcers or bleeding from peptic ulcers in patients with a history of both atherosclerotic and peptic ulcer disease and who take a thienopyridine. When patients who are found to have an H. pylorirelated ulcer undergo testing after antibiotic treatment to confirm H. pylori eradication, PPI use can lead to false negative test results. Therefore, it is recommended that patients switch to treatment with an H2RA rather than a PPI for the 2 weeks prior to H. pylori eradication testing [38].

Sucralfate

Sucralfate1 is a sulphated sucrose salt with a basic aluminium salt that is recommended for the treatment of peptic ulcer disease. It is believed to act primarily at the ulcer site by protecting the ulcer from the effects of pepsin, acid, and possibly bile salts after oral administration.Sucralfate has been compared with placebo and with cimetidine in patients with duodenal or gastric ulcer.[39]Sucralfate decreases the frequency of ulcerous lesions in animals, caused by a variety of ulcerogenic substances and experimental techniques. In healthy subjects, aspirin-induced gastric mucosal damage was completely prevented in 8 of 12 subjects by prior administration of sucralfate 1g. The ability of sucralfate to limit gastric mucosal damage is also suggested by a rise in transmucosal electric potential difference following its administration in patients with gastric ulcer.[40]

H. pylori Eradication Therapy

Treatment of Helicobacter pylori is necessary for the management of peptic ulcer disease and other gastrointestinal disorder [42].Due to the rising frequency of H. pylori antibiotic resistance, triple therapy with clarithromycin is no longer the optimal treatment for H. pylori, particularly in locations where local resistance to this antibiotic is greater than 20%.Alternative treatments for H. pylori eradication have been proposed [43]. Alternative treatments for H. pylori eradication have been presented, and these treatments are already being employed as novel and more successful treatments in normal clinical practise [44].The most common drugs used to treat this infection include amoxicillin, clarithromycin, tetracycline, bismuth, and omeprazole and lansoprazole and combination of these are used for the treatment and eradication [45].

Alternative Therapy for Peptic Ulcer

The main aim of peptic ulcer therapy is to heal ulceration, relieve pain & prevention recurrence and complication. The current treatment regimen available for the same consists of anti-secretory like H2 receptor antagonist, PPIs, different cytoprotective agents like sucralfate and in case of H. pylori eradication and treatment antibiotics are also used. [46] However, the conventional treatment of peptic ulcer has some limiting factors, such as side effects, especially in patient with prolonged therapy and also the increases resistance of H. Pylori to antibiotics.On the other hand, medicinal plants and their chemical compounds are useful in the prevention and treatment of numerous diseases.[47] As per WHO more than 80% of global population relies on traditional system of medicines for their health problems. Herbal product serves as lead compound for identifications of a number of bio-active molecules. These are widely used in traditional system of medicines for the treatment of various diseases as well as for health benefits and these are safer than synthetic molecules.[48]

CONCLUSION

As peptic ulcer is chronic disease and also it continues to be a source of significant mortality and morbidity worldwide. Conventional treatmentisavailable for the treatment peptic ulcer an eradication of H. Pylori but still there is reoccurrence and resistance antimicrobials so switching towards herbal therapy and nutraceuticalsare the new approach for the treatment of peptic ulcer disease in currentscenario. Herbal medicine has been traditionally uses by people for their good health and wellbeing. There are different phytoconstituents were able to protect the gastric and duodenal ulcer against different induction models that mimic the ulcer in men through multiple mechanism of action such as cryoprotections (increased mucus), antioxidants (increased activity of SOD and CAT enzymes and GSH level), immunoregulatory,antisecretory and anti-H. pylori. Thus, they can potentially be used as preventive and

complementary drugs or as dietary supplements to prevent the development of peptic ulcer and its episodes of recurrence and/or assist in the traditional treatment of ulcerative lesions. Many products of natural origin, especially composed of plant foods and plants, often referred to as complementary and alternative medicines, such as nutraceuticals and herbal medicines, respectively, have stood out for their therapeutic properties, which can assist in the management of many diseases.

Abbreviation

COX Cyclooxygenase
Cit C Cytochrome C
eNOS Endothelial nitric oxide synthase
FGF Fibroblast growth factor
GCs Soluble guanylyl cyclase
GPx Glutathione peroxidase
GR Glutathione reductase
GSH Glutathione
GST Glutathione transferase
NSAIDs Non-steroidal anti-inflammatory
nNOS Neuronal nitric oxide synthase
PP Peptic Ulcer
PGs Prostaglandin
PGE2 Prostaglandin E2
PPIs Proton pump inhibitors
ROS Reactive oxygen species
SH Sulfhydryl compounds
SOD Superoxide dismutase
TAC Total antioxidant capacity
HCl Hydrochloric acid

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Table No.1 Herbal Plant Having Antiulcer And Gastroprotective Activity

SL no.	Compound	Natural and/or Food	Route Administration/ Organism Test	Experimental Protocol/Dose	Effect or Mechanism	Reference
1.	Isoorientin	Gentiana triflora and Eremurus spectabilis	(p.o)/Rat	in vivo NSAIDs (indomethacin)—25, 50, 100 mg/kg	↓ MDA ↑ GSH, SOD	49
2.	Chrysin	Passiflora incarnate,	(p.o)/Rat	in vivo NSAIDs	↑ Mucus,	50

		Oroxylum indicum, Matricaria chamomilla, propolis		(indomethacin)—50 and 100 mg/kg	GSH, CAT, VEGF ↓ MDA	
3.	Quercetin	Food source: onions, broccoli, apple, cherry and grape	(p.o.)/Rat	in vivo NSAIDs (indomethacin)—50 and 100 mg/kg	↑ Nrf2, SOD, GPx ↓ ICAM-1, MPO, P-selectin	51
4.	Kaempferol	Food source: broccoli, cabbage, beans, leeks, tomatoes, strawberries, grapes and propolis	(p.o.)/Mic	in vivo Ethanol—40, 80 and 160 mg/kg	↓ MPO, TNF-α, IL-1β, IL-6 ↑ NO	52
5.	Kaempferide	Propolis	(i.p)/Mice	in vivo HCl/Ethanol—3 mg/k	↑ SOD, CAT, GST, mucus ↓ MPO	53
6.	Morin	Species of Moraceae family	(p.o.)/Rat	in vivo NSAIDs (indomethacin)—50 mg/kg	↓ MPO, NF-κB, TNF-α, iNOS, ICAM-1, IL-6, caspase-3 ↑ PGE2 , SOD	54
7.	Rutin	Food source: tomatoes, orange, carrots, sweet potatoes, black tea, and apple peels	(p.o)/Rat	in vivo Acetic Acid—20, 40 and 80 mg/kg	↓ MDA ↑ GPx	55
8.	Rutin	Food source: tomatoes, orange, carrots, sweet potatoes, black tea, and apple peels	Cell culture	in vitro Proton pump activity—IC50 of 0.0590 mMol/L	Inhibition	56
9.	Catechin	Green tea	(p.o)/Rat	in vivo NSAIDs (ketoprofen)—25 mg/kg	↑ GPx, GR, Nrf2	57
10.	Epicatechin	Green tea	(p.o)/Rat	in vivo Pylorus ligature—25 and 50 mg/kg	↓ H+ secretion	58
11.	Baicalin	Scutellariabaicalensis	(p.o)/Rat	in vivo Acetic Acid—6.5 and 13 mg/kg	↑ SOD, GSH, GPx ↓ MDA, IL-8, TNF-α	59
12.	Baicalin	Scutellariabaicalensis	GES-1 cells	in vitro anti-H. pylori—IC50 0.431 mMol/L	↓ IL-8, IL-1β, Vac A, urease, adhesion, hef	60

13.	Baicalein	Scutellariabaicalensis	Culture cell	in vitro Proton pump activity—0.0370 and 0.111 mMol/L	Inhibition	61
14.	Nobiletin	Citrus fruits	(p.o)/Mice	in vivo Ethanol—5, 10 or 20 mg/kg	↑ PGE2 , SOD ↓ TNF-α, IL-6	62
15.	Genistein	Soy-based foods (Glycine max or Soy hispida)	(p.o)/Rat	in vivo NSAIDs (indomethacin)—10 mg/kg	↓ TNF-α, MDA, iNOS	63
16.	Hesperidin	Citrus fruits (orange, lemon)	(p.o)/Rat	in vivo Stress—100 mg/kg	↑ GSH, SOD, CAT, mucin ↓ MDA	64
17.	Neohesperidine	Citrus fruits (orange, lemon)	(p.o)/Rat	in vivo NSAIDs (indomethacin)—100 mg/kg	↓ COX-2, TNF-α, MDA ↑ GS	65
18.	Biochanin A	Soy-based foods	p.o)/Rat	in vivo Ethanol—25 and 50 mg/kg	↑ NO, SOD ↓ MD	66
19.	Silymarin	Silybum marianum	(p.o)/Rat	in vivo Ethanol—50 mg/kg	↓ MPO, TNF-α, IL-6, NF-kB ↑ GPx, SOD, Nfr2	67
20.	Karanjin	Pongamia pinnata	Culture cell	in vitro Proton pump activity-0.0273–0.192 mMol/L	Inhibition	68

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RESEARCH ARTICLE

Quantification of Exopolysaccharide (EPS) Production by Pseudomonads under Salt Stress

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ABSTRACT

Bacterial exopolysaccharide (EPS) are mixture of polysaccharides, proteins and nucleic acids. Increasing attention is being paid to these molecules because of their bioactive role and their extensive range of potential applications in different industries. This study aims to obtain the information about the ability to produce EPS by Pseudomonads under different salt concentrations. First, attempt has been made to isolate the exopolysaccharide (EPS) producing bacteria, then production of EPS was recovered. All the isolated 10 Pseudomonads were found to be gram negative and reflected a positive KOH solubility test. Among 10 isolates, CP-3, CP-6 and CP-7 were found to be potential isolates for EPS production. These isolates were grown in different salt concentration from 1 to 5% w/v (NaCl). The carbohydrate and protein content of EPS was also determined.

Keywords: Exopolysaccharide (EPS), Pseudomonads, Salinity stress, Industry Innovation

INTRODUCTION

Exopolysaccharides (EPS) are bacterial polysaccharides that are produced extracellularly by cell wall-anchored enzymes and then released into the environment. Exopolysaccharides are sugar repeat units that can be linked to proteins, lipids, chemical and inorganic substances, metal ions and other molecules. EPS diversity is high among microbes due to a variety of accessible monosaccharides, non-carbohydrate substituents, and linking types. A lot of work has gone into figuring out how harmful bacteria and enteric organisms work (Whitfield, 1988). The function of EPS is determined by structural units and the microorganism's environment. EPS can protect bacteria from adverse environmental conditions by solidifying their structure and it can also contribute to their pathogenicity (Mishra and Jha, 2013). EPS has a variety of activities in bacteria, including allowing nitrogen-fixing bacteria to adhere to plant roots, contributing to soil aggregation and heavy metal binding, and serving as a carbon and energy source (Krithiga

et al., 2014). Microbial exopolysaccharides are used as immunomodulators and healing agents in the pharmaceutical industry, as well as gelling agents, lubricants, coagulants and protective colloids in the food and other sectors. Some EPSs are utilised as biosurfactants in the decontamination of areas polluted by petrochemical oil (Mishra and Jha, 2013), which can be efficiently used in various industries in an innovative approach.

Salt oceans, hypersaline lakes, salt marshes, salt springs, coastal dunes and salt deserts all have halotolerent microorganisms (Margesin and Schinner, 2001). Halophile exist in high salinity environments and require a high salt concentration to survive, whereas halotolerent microorganisms live in high salinity environments but do not require a high salt concentration to survive. Non-halotolerent bacteria can grow at a concentration of 1-2 percent w/v salt, while mildly tolerent bacteria can thrive at a concentration of 2-8 percent w/v salt. Bacteria that are moderately tolerent can grow up to 18-20 percent w/v salt concentration, whereas bacteria that are extremely tolerent can grow over a range of salt concentrations from zero to saturation (Rahman *et al*., 2017). To balance out the osmotic level inside the cytoplasm, the halotolerent bacterium maintains a low ionic concentration by synthesising suitable solutes. This internal environment maintenance system, as well as the features of the cytoplasm, assist them in adapting to changes in the saline environment (Roberts, 2005). The ability to create EPS under salt stress could assist the plants gradually capture the salt Molecule and reducing stress. In the presence of salt, several halotolerent strains alter the synthesis of extracellular polysaccharide. As a result, the greater the potential to manufacture large amounts of EPS, the better the possibilities of boosting plant development. Bacterial EPS reduce the amount of Na^+ available for plant uptake, reducing salinity stress (Upadhyay *et al*., 2011). In the light of all these information, present dissertation of work was framed to estimate the EPS producing ability of native Pseudomonad isolates.

MATERIALS AND METHODS

The isolation of rhizobacteria in the present study was done during 2021. Rhizospheric soil were collected from different crops and land used system. Soil of nearly 15 cm depth having root zone were collected and kept in zip lock bags with proper tagging inside ice cooled boxes and taken to laboratory, kept at 4°C and the isolation was done within 48 h. Along with the soil sample, GPS coordinates like latitudes, longitudes were also taken under the observation. The isolation of Pseudomonads was done on an improved Pseudomonas Selective Media (PSM) (Hi Media) by serial dilution method (Jhonson and Curl, 1972) from soil samples, for that, 10g air dried soil was added to 90 ml of sterilized distilled water and was serially diluted upto 10^{-8}. The plates were incubated at 28 ± 1 °C with PSM for 24-48 h. On the basis of colony morphology, the colonies appearing on the medium were counted and were transferred to Potato Dextrose Agar (PDA) medium. The cultures were maintained on PDA slants at 4°C for further study. The isolates were assessed for their potentiality to grow on high salt, for that they were inoculated into 20 ml of various level of salt augmented Nutrient Broth (NB) media of 1%, 2%, 3%, 4% and 5% salt concentration and their OD at 600 nm were observed after incubation of 48 h of inoculation at 28±2°C. The Biochemical profiling of the isolates were studied for their gram reaction test and KOH solubility test. Isolates which were able to produce Exopolysacharide (EPS) produces a biofilm on the surface of the liquid medium (Muminah and Hazarin, 2015). EPS was extracted by adding 500µl 1mM EDTA in 50ml liquid medium and shaken untill homogenous mixture was form.The mixture was centrifuged at 9000 rpm for 10 min, supernatant was taken and coupled with cold acetone solution with a ratio of 1:3. Then again centrifuged at 15000 rpm for 30 minutes and pellet was taken. EPS was then washed with distilled water and dried at 60°c for 24 h and stored in eppendorf. Determination of carbohydratde and protein of EPS is carried out by phenol sulfuric acid method and folin-lowry method respectively (Patil and Shirsath, 2015).

The data recorded in the present work was analyzed by one-way analysis of variation (one-way ANOVA). Statistical analysis was performed using SPSS 12.0 for Windows (SPSS Inc., USA). The variance and means of separation were performed using Duncan's new multiple range test (DMRT) at $p \leq 0.05$.

RESULT AND DISCUSSION

Isolation of rhizobacteria from rhizospheric soils

The rhizospheric soil samples (adhering soil with root) were collected, air- dried under shade, properly ground, sieved and stored at 4°C up to 48 h before used for isolation and enumeration of Pseudomonads from the root zone of different hosts by the serial dilution technique in specific media as mentioned in material and methods. Rhizobacterial colonies were selected after observing their morphology and pigmentation on medium after 24-48 h of incubation at 28±2°C temperature. Colony sizes varied greatly from 4-10 micrometers (µm) long and 0.25-1.0 micrometers (μm) in diameter.

Salt tolerance activity

All the isolates were observed for their growth (OD_{600nm}). The isolates possess a decreasing growth pattern from 1% to 5% NaCl concentration (Table 1). Among the ten rhizobacterial isolates, CP-3, CP-6 and CP-7 have maximum salt tolerance (according to Duncan's multiple range test) upto 5% NaCl concentration and the maximum growth at 5% NaCl concentration was observed in CP-6 (0.0260) followed by CP-7 (0.0255) and CP-3 (0.0190). All the isolates were shown to reflect a negative gram reaction and positive KOH solubility test. The evaluation of salt tolerance, along with other factors, is an important aspect in the selection of effective microorganisms. Higher NaCl concentrations have a negative influence on the ability of salt tolerant Azotobacter isolates from different parts of India to fix nitrogen, according to Iswaran and Sen (1958). According to Ramadoss and Kim (2013), 92.8%, 70%, 32%, and 25% of the total 84 bacterial strains isolated from soils and water samples taken from salt-dominated areas of the Jaisalmer region could grow well in 5, 10, 15, and 20 percent NaCl, respectively.

EPS production under various salt (NaCl) concentration

Production of EPS was performed by batch culture with incubation period of 72h. Viscous growth was observed in the broth. Extraction of EPS was carried by centrifugation of the liquid medium, followed by ice cold acetone precipitation, which is recovered by again centrifugation and pellet was taken and dried and EPS powder was stored in 5 ml centrifuge tubes.

At different salt stress (5%, 4%, 3%, 2% and 1%) level, CP-7 produced highest amount of EPS (0.16, 0.38, 0.64, 1.00 and 1.7 g dry weight/l respectively) followed by CP-6 (0.14, 0.37, 0.71, 0.90 and 1.55 g dry weight/l respectively) and CP-3 (0.12, 0.28, 0.60, 0.88 and 1.4 g dry weight/l respectively) (Fig 1). Some halotolerent strains modifies the production of extracellular polysaccharide in presence of salt. For eg.*Rhizobium meliloti* strain EFB1 colonies when grown in presence of 0.3 M NaCl show a decrease in mucoidy, and in salt supplemented liquid medium this organism synthesizes 40% less exopolysaccharide (Lloret *et al*., 1998). Bacterial exopolysaccharide (EPS) help to mitigate salinity stress by reducing the content of Na+ available for plant to uptake (Upadhyay *et al*., 2011).

Enumeration of the total carbohydrate and protein content of EPS in soluble form

Carbohydrate and protein ration determines the purity of extracted EPS and high C/P ratio denotes the highly pure EPS and less contaminated. CP-6 isolates showed the highest C/P ratio (3.70) followed by CP-3 (3.32) and CP-7 (2.37) (Table 2). When whey was used, the total carbohydrate content reduced from 380 to 150 mg/g, however when glucose was used, the total carbohydrate content increased to 464 mg/g for dissolved EPS of *Bacillus pseudomycoides* U10 (Solmaz *et al*., 2018).

Conclusion and future scope

Bacterial exopolysaccharide (EPS) help to mitigate salinity stress by reducing the content of Na^+ available for plant to uptake (Upadhyay *et al.,* 2011). EPS producing bacteria enhance the volume of soil macropores and soil aggregation resulting in water and fertilizer availability for inoculated plants (Alami *et al.,* 2000).In this concern our aim to isolate potent microbes which should be high EPS producer under saline stress condition. Among the 10 rhizobacterial isolates, we observed only 3 isolates can produce EPS in a significant amount as compared to the rest 7. Being

halotolerant, all the three (CP-3, Cp-6 and CP-7) bacterial isolates have maximum growth at salinity stress. Molecular identification, plant growth promotion activity, EPS structural composition, EPS chemical properties and the EPS functional properties may be determined from the respective isolates, which can be prove as a better option to combat the problem of salinity stress in crop production under saline soil. These type of innovative approaches in the field of biocontrol agents may serve as a boon for population in combating with the problem of crop production. It satisfies the requirement of ninth sustainability development goals (SDG 9).

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Table 1: Growth of Pseudomonad isolates under different salt concentration

Isolates	OD @ 600nm of different salt(NaCl) concentration				
	1%	2%	3%	4%	5%
CP1	0.0250[b]	0.0160[b]	0.0080[b]	0.0050[b]	0.0020[b]
CP2	0.0320[b]	0.0235[b]	0.0100[b]	0.0075[b]	0.0065[b]
CP3	0.2110[a]	0.1015[a]	0.0600[a]	0.0365[a]	0.0190[a]
CP4	0.0227[b]	0.0110[b]	0.0075[b]	0.0060[b]	0.0045[b]
CP5	0.0176[b]	0.0093[b]	0.0060[b]	0.0035[b]	0.0015[b]
CP6	0.2285[a]	0.1045[a]	0.0715[a]	0.0550[a]	0.0260[a]
CP7	0.2145[a]	0.1070[a]	0.0610[a]	0.0385[a]	0.0255[a]
CP8	0.0225[b]	0.0097[b]	0.0085[b]	0.0065[b]	0.0050[b]
CP9	0.0305[b]	0.0116[b]	0.0080[b]	0.0055[b]	0.0040[b]
CP10	0.0320[b]	0.0195[b]	0.0155[b]	0.0075[b]	0.0055[b]
SE(m)	0.01	0.005	0.007	0.005	0.002
CD	0.032	0.015	0.021	0.014	0.007

Values are means over two replications. Means followed by common letter in a column is not differ significantly ($p \geq 0.005$) according to Duncan's multiple range test.

Table 2: Chemical characterization (carbohydrate and protein content) of EPS

Isolate	EPS production (g/l)	Carbohydrate(C) mg.g^{-1}	Protein(P) mg.g^{-1}	C/P Ratio
CP-3	1.4	265.95	80.05	3.3223
CP-6	1.55	199.2	53.8	3.7026
CP-7	1.7	136.575	57.55	2.3732

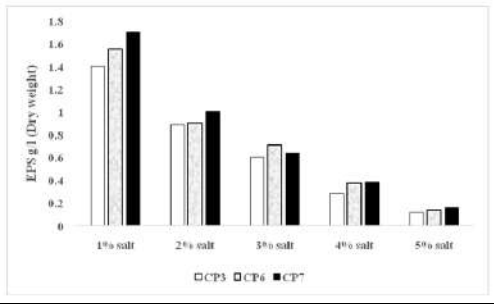

Fig. 1: Exopolysachardide production of three Pseudomonad isolates under different salt stress condition

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RESEARCH ARTICLE

Dead-Box RNA Helicases In Cell Cycle Control And Clinical Therapy

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ABSTRACT

The cell cycle is controlled by a variety of signalling track that govern whether cells will accelerate, remain dormant, capture, or die. Many diseases have been linked to abnormal cell cycle regulation. As a result, there is a pressing need to comprehend the various chemical pathways that control the cell cycle. RNA helicases are a diverse group of enzymes. Proteins involved in all phases of RNA metabolism, such as RNA unwinding and annealing molecules that clamp protein complexes on pre-mRNA, rRNA, and miRNA processing to regulate gene expression, RNA or remodelling ribonucleo protein complexes are used. Helixes of RNA are also known as RNA helicases. Direct connection to regulate the activity of particular proteins. The control of a wide range of genes by RNA helicases has been linked to a variety of cancer, neurological disarray, ageing, and polycystic kidney disease with autosomal dominant inheritance, to name a few (ADPKD). Cell proliferation, cell cycle arrest, and apoptosis are examples of cellular processes. Recent research has revealed. Since RNA helicases are involved in the regulation of cell cycle progression during each phase of the cycle,G1-S transition, S phase, G2-M transition, mitosis, and cytokinesis are all examples. In this review, we'll look at discuss the critical functions and mechanisms of RNA helicases in cell cycle regulation. RNA helicases offer a diverse set of targets for the development of novel therapeutics. Drugs those are either therapeutic or prophylactic. We also go over the various RNA helicase targeting tactics, the many different types of chemicals investigated, the predicted substances' inhibitory mechanisms on certain the therapeutic potential of RNA helicases possibilities with the presence of these chemicals future therapy for a variety of ailments.

Keywords: Helicases, therapeutics, drugs, cell cycle, RNA.

INTRODUCTION

Cell Cycle

The cell cycle is a set of activities that take place throughout the interphase and mitotic phase (M-phase) of a cell's life cycle. The longest phase of the cell cycle, the interphase, is when thecell prepares itself by duplicating genetic material to divide. Three phases make up the interphase. The first-gap phase, or G1, is one of the sub-phases. During the G1 phase, cells expand in size and produce new proteins. Cell organelles and other proteins, as well as accumulatinga sufficient amount of energy required to get ready cells for division, synthesis, and replication of DNA are referred to as S-phase.DNA and the centrosome during this phase, cells are replicated and the mitotic spindle is formed. The second gap phase is known as the G2-phase. During the G2 phase, cells store energy and expand in size. A period known as the mitotic phase follows the interphase (M-phase) [1-10]. The M-phase is the final stage of the process. Mitosis and cytokinesis are two important processes in the cell. There are four stages to mitosis. Prophase, metaphase, anaphase, and telophase are the four stages of the cell cycle. Are the four sub-phases of the cell cycle. The nucleus of the cell is divided. During mitosis, a full pair of chromosomes is transferred to two daughter cells. The cytoplasm is the liquid part of the cell. In the process of cytokinesis, a cell splits into two independent cells. The cell cycle is controlled by a group of proteins known asproteins that control the cell cycle. The cyclin and cyclin-dependent kinase (CDK) families are criticalcell cycle regulators are proteins that control the progression of a cell's life cycle. In animal cells, at least nine CDKs have been discovered, with CDK1, CDK2, CDK3, and CDK4 are all transcription factors which are playing key roles. The control of the cell cycle directly. The active CDKs at every stage collaborate cyclins are proteins that govern cell cycle progression in general. With its companions, cyclin A2 and cyclin B1, CDK1 controls the G2 and M phases of the cell cycle. CDK2 controls the G1, S, and M phases of the cell cycle.G2 interacts with the phases are formed by cyclin A, cyclin D, and cyclin E. The protein CDK3 regulates the cell cycle. CDK4 and CDK6 drive the G1 phase of the cell cycle, which is accompanied by cyclin C. Cyclin D (D1, D2, and D3) and cyclin E are its companions [11-20].

There are three checkpoints in the cell cycle: in metaphase, as well as near the end of G1 and the start of G2 to G2/M.If a cell does not meet all of the conditions, the G1 checkpoint prevents the cell cycle from entering the S phase, allowing the cell to either try to meet the conditions or enter the G0 phase. The G2 checkpoint prevents the arrival if certain conditions are not met, the cell cycle enters the mitotic phase, ensuring that all of the cells are replicated. The genetic material has been successfully duplicated and is in great working order [21-34]. The cell cycle will be halted if the DNA is damaged, allowing the broken DNA to be repaired. The M checkpoint, also known as the spindle checkpoint, occurs at the end of metaphase to ensure that the cycle will be terminated if each pair of sister chromatids is not adequately tethered to the two spindle microtubules. RNA helicases are thought to be involved in these processes, according to recent research [35-48]. The current study emphasizes the importance of critical proteins in maintaining human cell physiology and thus aligns with the objectives of one of the United Nations formulated Sustainable Development Goals (SDGs); SDG3 which ensures healthy lives and promotes well-being for all at all stages.

RNA Helicases

RNA helicases are highly conserved enzymes that play a role in almost every phase of RNA metabolism. RNA helicases employ ATP to bind and restructure RNA, RNA secondary structure, and RNA-associated rib nucleoprotein (RNP) complexes. Transcription, degradation, translation initiation, mRNA splicing, and ribosome biogenesis are all examples of biological processes.RNA helicases are proteins that bind to RNA which divided into numerous super families based on the motifs that have been conserved in their contents. Because they share a conserved structure, the majority of RNA helicases belong to super family 2 (SF2), which consists of eleven subfamilies, five of which are known as DExH/D helicases (DEAD-box, RIG-I-like DExH, SKI2-like DExH, viral

DExH, and DEAH/RHA) [49-60]. (Asp-Glu-Ala-Asp/His). DExH and DEAD-box (DDX) proteins have a three-dimensional core structure with at least 12 conserved proteins in common. RecA-like domains are two tandemly repeated amino acid motifs. The ATP binding motifs (Q motif, I motif, and II motif), the ATP hydrolysis motif III, and the RNA-binding motifs (Ia motif and Ib motif) (Ia motif and Ib motif) are all found in RecA domain The RNA-binding motifs IV and V, as well as motif VI, make up RecA domain 2. ATPase and unwinding activities are regulated. According to previous research, motif IaIb and IV are structurally comparable to motifs IV and V, therefore they should work together. Functions Most RNA helicases have N- and/or C-terminal extensions can bind to RNA to link with certain cofactors of RNA or proteins RNA helicases with a DEAD-box are a type of RNA helicase that may unwind and rearrange RNA molecules with the help of an ATPase [61-66].

RNA helicases play a role in a variety of biochemical processes Gene expression is controlled by RNA helicases. By catalysing rearrangements of RNP complexes at the start of gene transcription, and later by regulating ribosome synthesis, At the end of gene transcription, RNA export, commencement and termination of translation, and mRNA decay occur. The majority of RNA helicases are RNA helicases that travel through a isolated strand of RNA, unwinding subordinate structures and dislodging other attached RNAs or proteins in the process. Several RNA helicases with the DEAD box, like eIF4aA (eukaryotic initiation factor 4A is a protein that has a role in the initiation of eukaryotic), can directly bind to the RNA duplicate standard and it will melt Second, RNA helicases have the ability to control the cap-dependent beginning of translation of mRNAs with a complicated 5'UTR structure. For instance, eIF4A is a translation requirement. Unwinding oncogene 50UTRs with secondary structures that are complex in the MYC, NOTCH1, MYB, CDK6, MDM2 are examples of 50 untranslated regions. The eIF4F translation initiation complex, which recruits the 40S ribosomal unit to the 5' m7G-cap structure of the mRNA in eukaryotes, is made up of three subunits: eIF4E, eIF4A, and eIF4G.The DEAD-box, which contains RNA helicases such as DDX1, DDX5, DDX17, and DDX20, is the third component through interactions with spliceosome components, DDX21 and RHA can operate as transcriptional co-executer or co-reducer [67-74]. The viral infection patho-physiology, ageing, ADPKD (autosomal dominant polycystic kidney disease) is a neurological condition illnesses, and cancer are all examples of autosomal dominant diseases, all include DEAD-box containing RNA helicases. First, a decrease in DDX3 is connected to hepatitis virus infection, particularly HBV. During influenza dsRNA is prevented by UAP56 or its paralog URH49 viral infection from accumulating due to RNA unwinding. Second, in the aged mouse brain, the DDX5 (also known as p68) is an RNA helicase frequently down regulated, implying that p68 function is linked to ageing. Third, as we previously shown that p68 regulates cystic fibrosis in Pkd1 mutant renal epithelial cells and tissues. Through activation of the PKD-associated protein kinase, renal epithelial cell proliferation and renal fibrosis are promoted.ERK, mTOR, Rb, and TGF-1 are just a few of the pathways involved. Finally, research have shown that indicates DDX3 mutations are a major source of neurodevelopment problems for example Intellectual difficulties, autism spectrum disorder (ASD), hypotonia, and corpus callosum abnormalities, microcephaly, and seizures are only few of the conditions that can affect people are some of the conditions that can affect people. Furthermore, the RNA helicase DDX6 promotes. Increased Let-7a is a microRNA with a lot of activity promotes neuronal differentiation [75-90]. Finally, DDX5 has been linked to oncogenesis in a variety of cancers (e.g.,NSCLC, breast cancer, gastric cancer, multiple myeloma, and glioma are some of the most common cancers.) through abnormal expression or the control routes of proliferation, metastasis, and invasion. The specifics the transition between stages of the cell cycle is critical for growth, and poorly regulated of this transition is problematic. The disruption of the cell cycle causes a variety of human illnesses, including the promotion of oncogenesis. This review will focus on the primary functions of RNA helicases in cell regulation. Cycle, and discuss RNA helicase inhibitors such as eIF4A, DDX3, and DDX5, as well ascell cycle modulation is a viable therapeutic method [91-96].

The Role of RNA Helicases in Cell Cycle Progression Regulation

RNA Helicases Control the G1-S Transition

The G1 phase of the cell cycle is the first time the cell prepares for DNA replication. CDK activity stimulates replication of DNA and begins the transition from G1 to S phase in the G1 phase. Cyclin D/CDK4/6 complexes play a key function in cell proliferation in general. Growth factor signalling stimulates the synthesis of cyclin D in the early

G1 phase, then causes the creation of cyclin D/CDK4/6 complexes, which activates cyclin D.CDKs are a type of protein kinase. The complexes of cyclin D/CDK4 and cyclin E/CDK2 phosphorylate each other in order. The inactive form of retinoblastoma protein (RB) causes E2F to be released from the Rb-E2F complex as well as E2F activation. To enhance G1/S transition, the active E2Fcontrols the transcription of genes involved in the course of the cell cycle, such as CDK2, cyclins A and E, and DNA synthesis are all involved in DNA synthesis.p53 works as a transcription factor when DNA is damaged. To increase the expression of the p21 gene, resulting in interruption of the G1/S cell cycle RNA helicases play a role in transcription, translation, and post-translational processes. Cell cycle regulators are expressed in a variety of ways is controlled [97-100]. DDX3/Ded1 is one of the most widely used which is well-studied DEAD-box RNA helicases. RNA metabolism, which encompasses Pre-mRNA splicing, RNA export, and translation are all steps in the transcription process, which is controlled by DDX3, and is important in a variety of biological activities. DDX3 when it interacts with ATP, it also causes phase separation.DDX3 is also involved in the regulation of during mammalian embryonic development, cell apoptosis is mediated by the p53 signalling system. Models DDX3 dysregulation is linked to a number of illnesses, including cancer. Inflammation, viral infection, neurological diseases, and cancer are all common causes of death [101-110]. The involvement of DDX3 in oncogenesis is linked to cell proliferation, cell division, and cell survival regulation.

In medulloblastoma, colorectal cancer, and other cancers, increased DDX3 expression stimulates cancer cell proliferation. Depletion of DDX3 promotes cell cycle arrest in breast, prostate, and lung cancer. In cancer cells from those tumours, arrest in the G1 phase. Taking down ofDDX3 also prevents cells from progressing through the cell cycle by preventing them from entering the S phase. Mechanically, the cell cycle regulator cyclin E1 mRNA is5□ UTR translated more quickly when DDX3 is present. Furthermore, DDX3 inhibits Krüppel-like factor 4 (Klf4) expression by modifying its mRNA splicing, leading in an increase of CCNA2 and CDK2 expression. In conclusion, DDX3 enhances the G1/S transition via boosting the translation of cyclin E1.KLF4 expression is suppressed, while CDK2 expression is promoted. DHX33 is involved in the synthesis of ribosomal RNA and the translation of mRNA. By boosting the Bcl2, MMP9, MMP14, and plasminogen activator of the urokinase type are among the genes transcribed by DHX33. promotes a variety of cellular functions, including cell cycle progression, apoptosis, and migration. DHX33, which is over expressed in a number of ways forms of human malignancies, including lung cancer and glioblastoma, is necessary for the transition from G1 to S phase of the cell cycle.In distinct cancer cells, DHX33 loss resulted in a large rise in G1-phase cells and a significant decrease in S-phase cells. DHX33 links Pol II binds to the promoters of cyclin E2, cyclin D1, E2F1, MMP9, MCMs CDC6, and CDC20 and begins transcription [111-118]. DHX9 affects transcription, translation, miRNA processing, RNA transport, and genome maintenance are all steps in the transcription and translation process. are all activities that take place in the human body as a multifunctional protein. Cervical cancer, breast cancer, prostate cancer, colorectal cancer, hepatocellular carcinoma, and Ewing sarcoma are all cancers that affect the female reproductive system are all cancers that affect the female reproductive system are all malignancies in which DHX9 is overexpressed.DHX9 knockdown causes cell cycle arrest in the G0/G1 phase. CDK6, aG1/S phase and cell division require this protein, is adversely regulated by DHX9binding to the 3'-untranslated region (3'UTR) of CDK6 mRNA to reduce its stability and polyribosome integration, leading in a reduction in G1/S transition.Furthermore,CIZ1 translocation to the nucleus is caused by DHX9's interaction with CIP1-interacting zinc finger protein 1 (CIZ1), which is required for cell cycle advancement. DHX9 is also involved in cell regulation. cAMP-response element-binding, proliferation via interaction with EGF receptorBRCA1, protein, and RNA polymerase II [119-126].

As a key nucleolar protein, DDX21 is involved in ribosomal RNA synthesis and transcriptional control. DDX21 is a c-Jun transcriptional catalyst that regulates downstream target gene mRNA expression through their direct contact. EGFR and cyclin D1 are two examples. In colon cancer, lymphomas, and other cancers, DDX21 is dysregulated other malignancies. Neuroblastoma and a certain types of breast cancer. DDX21 up regulation activates the transcription factor AP-1, which increases breast cancer cell growth. Influence as a result of cyclin D1 transcription and rRNA processing, in an expansion in the number of cells in the S phase. In Hela cells, expunction of DDX21 stops the cell cycle during the G1/S transition. Furthermore, DDX21 interacts with PARP-1, causing PARP-1 to ADPRylate it. The activity of DDX21 is reduced when PARP is inhibited. And in breast cancer cells, it inhibits cell proliferation [127-

130]. Transcription, translation, and mRNA decay are all aspects of RNA biology, is regulated by the eIF4A family of proteins. Through translational regulation, eIF4A plays a role in gene expression as well. eIF4A regulated ribosomes were discovered using ribosome profiling. The genes Cyclin D1, Cyclin D2, and CDK6 are involved in the G1/S phase transition. eIF4A has three paralogous genes: eIF4A1, eIF4A2, and eIF4A3.eIF4A3 is an exon-binding protein

(RBP) that works as a protein that binds to RNA (RBP).The EJC is a nu cleoplasmic junction complex that is mostly found in the nucleus. In colorectal cancer, eIF4A3 is substantially expressed.The binding of eIF4A3 to LncRNA H19 inhibits eIF4A3 from being activated from being recruited to cell cycle regulators' mRNAs such as for post-transcriptional modification, cyclin D1 and cyclin E1 are used accelerated colon cancer progression [131-140].

Through the hydrolysis of ATP to reorganise local RNA–RNA or protein–RNA interactions, DDX46, also known as Prp5,has a number of roles in nuclear pre-mRNA splicing.DDX46 expression is enhanced esophageal squamous cell carcinoma is a kind of colorectal cancer, osteosarcoma cells, and stomach cancer DDX46 knockdown is effective. Cancer cell growth, conquering, and programmed cell death are all inhibited. Stillness of DDX46 stopsat esophageal squamous cell carcinoma cell lines, the cell cycle is in the G1 phase. Furthermore, knocking down DDX46 dramatically lowered Akt and IB phosphorylation. Further research is needed to see if DDX46 affects the transition from G1 to S phase is mediated by Akt and IB.

S Phase Progression is Regulated by RNA Helicases

Genetic resources such as DNA are synthesised during the S phase of the cell cycle produced genetic resources such as DNA are synthesised during the S phase of the cell cycle full genome, which is required for the division of cells. When cells enter the S phase, the cyclin E/CDK2 complex is activated. To prevent DNA re-replication, it must be silenced. CDK2 dissociation from. The cyclin E/CDK2 complex binds to the freshly produced cyclin A to form a complex. CDK2/cyclin-dependent kinase 2 (CDK2/cyclin A complex that has the ability to proteins that are requisite for survival are phosphorylated. The S phase has come to an end. The gene is transactivated by thep53 isoform that has been spliced (Delta-p53). Endogenous p21 declaration, which inhibits CDK2/cyclin, should be suppressed, and S phase advancement should be retarded.

So far, only DDX51, an RNA helicase, has been associated to S phase progression. Down regulation of DDX51 has been shown to cause cell cycle arrest in the S phase, most likely due to rRNA processing and other signalling pathways regulated by DDX51. Throughout theDDX51 interacts with pre-60S complexes throughout the rRNA process, promoting U8 snoRNA is removed from pre-rRNA, which is essential for ribosomal development. DDX51 also acts as a p53 negative regulator, promoting cell growth aggressively. Furthermore, through enhancing the the Wnt/-catenin activity signalling path, DDX51 has been shown to increase the growth of breast cancer cells. Furthermore, DDX5 has the ability to enhance cell proliferation carcinoma of the lungs by increasing cyclin D1 transcription in non-small cells [141-146].

Compounds against RNA Helicases Are Developed Using A Variety Of Targeting Strategies.

Because of their vital involvement in the cell cycle, cell proliferation, cellular transformation, apoptosis, cell adhesion and motility, and medication development for viral infections, neurodegenerative disorders, and malignancies, RNA helicases are active targets for drug research. Specific and selective inhibitors for on the basis of the crystal structures, as well as the mechanism(s) by which they work of the enzymes, RNA helicases have been developed. In general, inhibitors are substances that block the action of other substances. of RNA helicase activity may function through one or more of the following mechanisms: By interfering with ATP binding, RNA helicases' ATPase activity is inhibited, decreasing the energy required for unwinding and repositioning; inhibiting helicase action by taking up residence in the site for RNA binding competitively RNA helicases onto RNA; and stability of RNA helicases on RNA, resulting in translation initiation reserve.

CONCLUSIONS

RNA helicases are highly conserved enzymes that are engaged in a variety of cell cycle regulatory processes and are important for RNA metabolism. At each phase of the cell cycle, RNA helicases play a role in cell cycle regulation through a variety of mechanisms, includes (1) translation of cell cycle stage associated cyclins and CDKs, (2) transcriptional and translational regulation of some cell cycle regulators, and (3) transcriptional and translational regulation of some cell cycle regulators. regulation of cell cycle stage associated cyclins and CDKs effectors involved in the cell cycle, such as p21, undergo post-translational alteration. Progression.DDX3 controls the cyclin A1, cyclin E1, and cyclin F1 expressioncyclin F1, and cyclin F1. DHX33 controls the transcription of a number of cyclins and CDKs. DDX21 is a transcription factor that controls gene expression. The expression of cyclin D1 is governed byDDX56, a G2–M cell cycle regulator. gene that acts as a roadblock.DDX5 (p68) regulates the production of cyclin D1, which is required for p53 activation. The development of the cyclin D–CDK complex is regulated by DHX9.G1/S cell cycle detain is regulated by DDX46. CDK inhibitors, such as DDX41, are repressed by DDX41. As in p21 the impact of RNA helicases on cell cycle progression differs depending on the cell type, and inhibitors that target RNA helicases should have a major impact on cell control. Cycle and the proliferation of cells RNA helicase inhibitors have already been discovered in small molecules. These enzymes' action implement(s) and crystal structure(s)were used to design them. These inhibitors have been discovered in vitro and in vivo and may be explored stimulate in the future. As a potential therapeutic option for a variety of illnesses, including cancer and ADPKD.

Statements and Declarations

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval and Consent To Participate

It is a review article. No ethics approval is required.

Consent to Publish

Not applicable.

Human and Animal Rights

It is a review article. No animals were used in the study.

Availability of Data and Materials

Not applicable.

Credit Authorship Contribution Statement

All the authors have substantial contribution for the preparation of the manuscript. Gagan Kumar Panigrahi, Adyasha Pradhan and Aseema Rath conceived the idea. Data curation and writing: Adyasha Pradhan, Aseema Rath, Annapurna Sahoo, Ved Prakash Prusty, Rahul Mohanty, Shraban Kumar Sahoo, and Gagan Kumar Panigrahi. All the authors have read and approved the final manuscript before submission.

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RESEARCH ARTICLE

Emerging Issues and Challenges of Women Entrepreneurs

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ABSTRACT

Women entrepreneurs start their own business for their development and empowerment. But they have to face lot of issues and challenges to achieve their goal. Entrepreneurs generally try to do innovation for the business to get profit. Government of India is doing a lot of work for innovation and entrepreneurship. Still there is a lot of gap. Many policies and schemes are there for entrepreneurs and startups specifically for women entrepreneurs. Government is giving support to both urban and rural entrepreneurs. Women entrepreneurs are trying hard to sustain in the business to empower themselves. This paper is trying to analyse the problems and issues of women entrepreneurs and also suggestions given to overcome the problems.

Keywords: Women entrepreneurs, Startups, Women empowerment, Government schemes, Emerging issues

INTRODUCTION

Now a day women are not only doing household work, they also do their own business and startups. They are in the news in every aspect of life. They are no more behind men. Many Indian women entrepreneurs are renowned not only in India but also they are famous in all over the world. Women are not only giving support in their home but also supporting the Indian economy. No doubt they are facing a lot of problem in balancing their family and business. In India women entrepreneurs' means where she has minimum 51% financial interest and minimum 51% of the employees are women. They have to do all the work as the men do as entrepreneur like innovation, administration, coordination, leadership, risk taking etc. They have to do all the things effectively. For this they have to face a lot of challenges and issues in their way. They have to work hard to prove them. It is not easy for them. Government, society and family should support them to achieve their objective. They have to always face discrimination with men. Many positive changes are happening in the society as women are entering to the field of

entrepreneurship. It is expected that more and more women will become entrepreneurs with the government support and self-motivation. It will increase the women empowerment in our country. Ultimately it will increase the economic development of our country. Sustainable Development Goals (SDGs), is one of the important aspects for economic development. SDG 9 is for industry, innovation and infrastructure. If more women entrepreneurs will come it will definitely fulfill the objective of SDG 9. This paper is focusing on the different emerging issues and challenges faced by the women and also suggestions to overcome the problems in entrepreneurship.

LITERATURE REVIEW

Wadhawan. N (2017) found in her study that Government of India is taking a lot of initiatives for the women entrepreneurs through different policies, programs and schemes. But there a requirement of more support by the government for the development of women entrepreneurs. Rural women don't have any knowledge or awareness about the legal procedures to get funding or how to start a business. These women need proper training about entrepreneurship. Government and the society have a major role to create a favourable environment for the women to start a business without thinking about gender inequality. Mishra & Kiran (2014), discussed regarding the entrepreneurial activities of rural women in India. They found that women are getting more social and financial independence by starting their own business. Development in the women entrepreneurship is also required for the development of the economy. They have also discussed on some factors which can increase the skill of women entrepreneurs. (Dangi& Ritika, 2014)analysed on the role of Micro, Small and Medium Enterprise (MSMEs) for the development of entrepreneurship in India. Importance of MSMEs and the problems of women entrepreneurs is also discussed in the research paper. Swetha & Rao (2013) found in their study that; entrepreneur can change the society through innovation. Many of the Indian entrepreneurs are inspirations to the young entrepreneurs. They have achieved success by overcoming many problems in their journey. Life of the entrepreneur is not smooth. Women has a major role for the development oftheir family and so also the nation. Shah H., (2013)identified some strategies and plans which will be helpful for the women entrepreneurs of India. The policies and practices can develop the women entrepreneurship in India. They mainly focused on that till now, women entrepreneurship is not given that much of importance for the development of the nation. They have given many cases, which will be helpful for the development of women entrepreneurs. Vijaya kumar and Jaya chitra, (2013) discussed about the challenges, which are creating problems for women entrepreneurs. They have also given some suggestions to overcome the problems. They analysed some of the government policies and plans for the development of the women entrepreneurs. Mahajan S., (2013) found that women entrepreneurs are the most developed human resources in the present era. He has taken a case of Hina Shah as a successful women entrepreneur. He has also given some suggestions for the development of women entrepreneurs based on the Hina Shah case. Pharm & Sritharan (2013) identified that rural entrepreneurs are facing a lot of problem on financing, leadership skills, marketing because of lack of awareness. Rajasekaran& Sindhu(2013)analysed on how the self-help groups are helping rural women to start their entrepreneurship. They found that because of the help of self-help groups, the number of women entrepreneurs is increased. Mehta & Mehta (2011) explained that the entrepreneurs are the innovators. Through innovation they can earn huge amount of profit. Major part of the population is women. If favourable environment can be created for women entrepreneurs, it will make a big change in our economy. Rashmi Gopinathan (2010) found that the women entrepreneurs have a great impact on their family. Assets gives the pictures of the financial condition of the company.

Objectives of the Study

- To find the status of women entrepreneurs in India and also the issues and challenges faced by them.
- Suggestions to overcome the problems and growth of women entrepreneurs.

Research Methodology

The research is mostly descriptive and supported by different theoretical findings and analysis. This study is done by using secondary data from different government resources, newspaper, journal and articles.

Characteristics of Women Entrepreneurs

Women entrepreneurs have many characteristics. Some of them are

- They have a capacity to take risk.
- They are self-motivated
- They can easily coordinate the system
- Leadership quality is high
- Their goal is clear
- Confidence is also very high
- They are good in relationship building
- They can handle multiple task at a time easily
- They work for accomplishment and achievement keeping money as secondary motivation
- They are self-starter.

Motives of Women Becoming Entrepreneurs

A lot of studies say that the reason of women starting a business is different from men. Men mostly start business for profit where as women start business to get a feeling of accomplishment. Women generally give more importance to self-satisfaction than money. Also many women are there who gives priority to money. Research says on an average women enter to the entrepreneurship after 10 years than men. Due to lack of experience, motherhood, family problems they enter to the business late. Many of the women entrepreneurs started their business due to problems in life like divorce, problem in job, pregnancy, health issues and family problems etc. But now a day's many women are choosing entrepreneurship from the beginning rather than doing a job. They are doing well in finance, manufacturing which are known as nontraditional business. So the presence of women in traditional business like food, fashion, cosmetics, is changing.

The Importance of Women Entrepreneurs

Only one third is the women entrepreneur out of total entrepreneur. But half of the population is women in the world. So there is a big gender gap in entrepreneurship. There is a lot of scope for the women in the entrepreneurship. Government is giving more focus on innovation in entrepreneurship. As women are using different products than men they can think and innovate in a different way than men. But due to many problems and challenges women prefer to do job or to be at home. Also by entrepreneurship women can empower themselves which will increase the economic development of our country. Women always have a hidden strong desire to achieve in their life. Women entrepreneurs are increasing in India. The hidden talent of entrepreneurship is coming out in the women. Women have the potential to grow in entrepreneurship. By growing they can add value to the society and economy. Women entrepreneurs are involved in all types of industries. Digitalisation is giving more scope to the women for job creators rather than job seekers.

Challenges for women entrepreneurs

a. **Low educational qualification**: Women entrepreneurs have low educational qualification and less experience than men. Their productivity is less due to low skills and expertise in work.
b. **Work life balance:** Women are always facing problem in managing business and family. Women are generally considered as to take responsibility of family, caring children doing household work than doing business. Most of the time they don't get family support to achieve their goal.
c. **Financial problems**: Women entrepreneurs generally face lot of problems in getting loan from banks and financial institutions. Even the banks and financial institutions need the guarantee from some male from the family. For the documentation also they need the signature of male member.
d. **More responsibilities**: Women may be rural or urban have a lot of household work getting very less time for themselves or to do any kind of business.
e. **Lack of support from family**: Most of the time women don't get family support to do business like men. Generally they are expected to do household work and caring family. It reduces the motivation of women to be an entrepreneur.

f. Low self-confidence: Many of the women have low self-confidence to start business. They need some motivation by others. If they will not get that then it is very difficult for them to enter to the business world.

g. Low risk taking capacity: Women are always dependent on male from childhood for doing any work outside home. So they have low confidence for taking any initiative to do business.

h. Increasing corruption: Women are facing problems due to corruption. For getting any kind of loan also they are facing problem.

i. Obstacles by society: Sometimes the society itself creates problem for the women to become entrepreneurs. People don't believe from the beginning that women can be successful in doing business.

j. Low self-motivation: Motivation is very much required for doing any kind of business. But due to the problems in life women have low self-motivation.

Suggestion For The Development Of Woman Entrepreneurship

Scope of women entrepreneurship in India is very high. But women need continuous motivation, training program and support by the government.

Some of the suggestions for the development of women entrepreneur are:

a. Women should get proper awareness about entrepreneurship and startups through different programs.
b. Government should give more schemes for women entrepreneurship looking at the problems and challenges of women.
c. More and more training should be given to the women for entrepreneurship.
d. Counseling can be given to the women by successful women entrepreneurs.
e. There should be effective women entrepreneurship cell to handhold small women entrepreneurs.
f. They should able to get loan with low interest rate and less formal documentation.
g. They should get training to prepare a right business plan.

CONCLUSION

In India Government has taken many steps for the development of women entrepreneurs. Now a day many training programs, policies are done by the Government. But still there is a lot of gap. Women should be given more priorities while taking any decision regarding entrepreneurship. Women are not only doing the household work also doing remarkably good in entrepreneurship.Women entrepreneurs may be from urban or rural area facing challenges and problems every day. Government is in favour of women entrepreneurs but more initiatives can be taken. Rural women those particularly with low education are facing a lot of problem in getting loan, legal process and also to start the business. Women entrepreneurs need training in different functional activities of the business. Government, family and society should support women for the entrepreneurship which will make them self-employed and empowered. Without thinking about any gender inequalities, everyone should motivate women to start their own business. Government has given equal opportunities and equal rights to women and men. But unfortunately all the women are not able to get the benefits. Now the time has come that they have to fight for themselves. They have to be more innovative in entrepreneurship. They should take the benefits of the government programs and schemes.

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RESEARCH ARTICLE

Mathematical Modelling and Analysis of Blood Flow in Human Body

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ABSTRACT

The blood flow in human body has been analyzed through mathematical modeling considering all physical as well as Physiological parameters of blood. The process of oxygenation of blood in cardiovascular system has been considered and circulation of it through human body has been studied.

Keywords: blood flow, cardiovascular, Physiological, Non Newtonian fluids.

INTRODUCTION

The applications of mathematics are emerging in their scope, variety and depth. Besides the rapid growth of applied mathematics in the traditional fields of the physical sciences, the new fields of its application have emerged in biology, ecology, genetics, medical sciences and social sciences etc. Mathematics, a powerful tool to interact with almost all sciences has made tremendous contributions to physical sciences (Physics, Chemistry etc.), industrial sciences (Stock control, programming etc.), technological sciences (engineering, control systems, computers, space technology etc.), and life sciences (genetics, agriculture, medicine, cybernetics etc).

Mathematics has entered the field of life sciences through medium of mathematical modellings and statistics. In the beginning mathematics was used to study genetic characteristics in peas. Mathematics for life sciences is termed as Bio-mathematics synonymously known as mathematical bio-sciences. In mathematical bio-sciences, the application of mathematical modeling and mathematical technique are studied to get and insight into problems of bio-sciences. Besides the mathematicians, the physicists, statisticians, computer scientists, mechanical engineers, chemical engineers, botanists, zoologists, ecologists, agricultural scientists, demographers, physiologists, medical scientists and many other have made valuable contribution to this branch. It was observed that machines and organism have much similarity as regards structure and function. At the end seventh century, the control mechanism in physiology (the science of functions and phenomena of living beings) was considered for the first time. Mathematical bio-

sciences are mainly considered with mathematical modeling in biology and medicine, and deal with those areas of bio-sciences which have already been mathematicised.

MODELS AND ITS CLASSIFICATION

A model is defined as an idealized representation of real life system. There are several models in each area of business or industrial activity. Models may broadly classified as:

Physical Models

This mimics the systems as it is, by enlarging or deducing the size. In other words, it is an reflection.

The Physical models are easy to watch, construct and explain. Its purpose is descriptive rather than explanatory. This model is not much helpful for the purpose of predication.

Analogue Models

In this model, one set of vital characters should be chosen and used for representing another system. Then the result of new system is interpreted with the original problem or the original system.

For example, the graph is prepared to represent position of different city with the properties of distance or time of journey from one city to other represented by counter line.

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Mathematical (Symbolic) Models

This model employs a set of mathematical symbols (i.e., letters, numbers etc) to represent the decision variables (those unknown that are to be determined from the solution of the problem). These variables are related together by means of mathematical equations or set of equations to describe the behavior (or properties) of the system. The solution of the problem is obtained by applying mathematical techniques to the model. The mathematical model is usually easiest to manipulate experimentally and the most general and abstract. A large number of mathematical models have been developed to get and insight into complex biological, ecological and physiological situations. Before formulating a new mathematical model, and insight into the situation is essential because the situation in life sciences are not simple. With the help of mathematical techniques, the model is solved and results are compared with observations. The mathematical model needs improvements if there exists discrepancies between theoretical conclusion and observations. The process is repeated until a satisfactory model is obtained.

The neuro-physiological models of the brain are made and their adequacy is tested by mathematico-deductive methods. The mathematics is helping a biologist in the same way as it helped the electrical engineers to build the electronic computer. It is hoped that, in the 21st century, we shall have as much life sciences generated mathematics as we have physical sciences generated mathematics today. It is need of the hour to have mathematico-biologists and bio-mathematicians.

Mathematical bio-sciences is an inter-disciplinary subject. The mathematical modeling and mathematical techniques are applied to get an insight into complex biological, ecological and physiological situations. Mathematical biomechanics is one of the important discipline included in mathematical biosciences which deals with:

(a) Bio-solid mechanics which studies along with other things stress and strains in bones and muscles,

(b) Cochlear dynamics which is mainly concerned with flow of fluid in ear.

The term “Bio-fluid mechanics” refers to that study of biological systems where the concepts of fluid mechanics, relevant of study of the mechanics of flow of viscous fluid in different types of tubes.

Analysis and understanding of various aspects of blood flow is extremely important for getting an insight into the study of flow of blood on the entrance region of tube constitutes the problem of fundamental interest in bio-mechanics. For a fluid entering an annulus in laminar flow changes from an initial condition close to the fluid velocity profile at the inlet to a fully developed condition at a certain distance down-stream.

NEWTONIAN AND NON-NEWTONIAN FLUID

Newtonian fluids are characterized by the fact that in presence of pure shear the hydrostatic state of stress becomes supplemented merely by a shear stress whose magnitude increases with shear viscosity. Thus, for incompressible viscous fluids the relationship between the frictional stresses and the velocity gradient is expressed by a single material constant, known as shear viscosity, Fluids whose material behavior deviates from its ideal behavior are called non-Newtonian fluid.

Thus, a fluid satisfying Newtonian hypothesis

$\tau = \mu\frac{du}{dy}$

where τ the shearing-stress, μ the coefficient of viscosity and $\frac{du}{dy}$ strain rate, is called Newtonian fluid. Thus, stress on a fluid is linearly proportional to the strain rate of the fluid in Newtonian fluid.

The fluids which do not satisfy Newtonian hypothesis are called non-Newtonian fluids.
In recent years, especially with the emergence of polymers, it has been found that there are fluids which show a distinct deviation from Newtonian hypothesis. Such fluids are called non-Newtonian fluids. The non-Newtonian

fluids are broadly classified into the following categories:

i. Purely Viscous Fluids
ii. Visco-Plastic Fluids
iii. Visco-Elastic Fluids

PHYSICS OF BLOOD, BLOOD FLOW AND PRESSURE

Colemn and Nol [1] defined blood as non-Newtonian incompressible second order fluid. It is also known that blood exhibits a non-Newtonian (3) character at very low shear rate and so as visco-elastc non-Newtonian fluid may be modeled for blood. The blood is a complex mixture consisting of a fluid part, the plasma which contains many organic and inorganic substances in solution, and the erythrocytes or red cell, leukocytes or white cells and thermocytes which are suspended in the plasma.

The plasma contains water (90-92%), proteins nutrient materials, organic waste product, hormones, enzymes etc., of the particular matters, the red cells are dominant occupying a volume fraction of 35-50% of the blood and 97% of the total cell volume. Platelets are very minute and much smaller than all the remaining cells, in the blood. There are about 300000 platelets in a cubic millimeter of blood. The oxygenated blood is transported from lungs to different parts of the body. This transportation is carried out by the hemoglobin present inside the erythrocytes. Many nutrient materials such as glucose, vitamins etc., dissolved I plasma are carried by the blood to the blood cells for maintaining the constant functioning of blood cells.

The vascular system conveys the blood to various parts of the body. It consists of a branched system of arteries and arterioles a diffusing system of fine capillaries which are in contact with the cells of the body. The veinous system returns the blood vessels, can be represented as Newtonian fluids while in the microcirculation the blood clearly behaves like a non-Newtonian fluid, since the radii of the blood cells are larger than the radii of the blood vessels.
Mathematical models describing blood flows would be helpful in understanding various problems of physiological flows. Also by employing non-Newtonian constitutive equations, some typical problems of the flows of blood can be analyzed. The constitutive equations of second order fluid are very helpful for describing blood flow.

Circulation of Blood

The most important feature of the circulation is that, if a given amount of blood is pumped by the heart same amount must also flow through each sub-division of circulation. Blood flows with almost no resistance in all the large vessels

of the circulation, but this is not the case in all the large vessels of the circulation, but this not the case in arterioles and capillaries. To cause blood to flow through these "resistance vessels", the heart pumps blood into the arteries under high pressure normally at systolic pressure of 120mm Hg in the systematic system and 22mm Hg in the pulmonary system(2).

Cardiovascular System

The cardiovascular system consists of the following:

a. The heart (which acts as a pump), whose elastic muscular walls contract rhythmically making possible the pulsatile flow of blood through the vascular system.
b. The distributory system (comprising of arteries and arterials for sending blood to the various organs of the body).
c. The diffusing system (made up of capillaries which are in contact with the cells of the body).
d. The collecting system of veins (which collects blood depleted of oxygen and full of products of metabolic processes of the system).

The lungs which provides a region of inter phase transfer of O_2 to the blood and removal of CO_2 from it and the kidney lever and spleen, which help in maintaining the chemical equality of blood under normal conditions and conditions of extreme stress are the organs which supplemented the function of cardiovascular system.

Deoxygenated blood enters the right atrium (RA) from where it goes to the right ventricle (RV), when the heart contracts the tricuspid value between RA and RV closes and blood is pushed out to the lung through pulmonary artery (PA) (7) which branches to the right and left lungs where CO_2 is removed and blood is oxygenated(12). The blood returns from the lungs (8) through pulmonary vein (PV)(18) to the left atrium (LA) and then it goes to the left ventricles (LV) and from there, due to contraction of the heart it enters the aorta from which it travels to the other arteries and the rest of vascular system.

Factors Affecting the Blood Viscosity

The blood viscosity is affected by the following factors:

a. Fahraeus-Landquist effect which is visible when vessel diameter falls below approximately 1.5mm. The effect is due to the alignment of the red cells in a line instead of randomly when pass through the vessels as a single plug thus eliminating the viscous resistance.
b. The viscosity of blood rises enormously as its velocity of flow falls. As the speed of blood flow in small vessels is very low, blood viscosity can rise ten-fold from this factor. The effect partly caused by rouleaux formation.
c. Cells also often stack at constrictions in small blood vessels; this occurs especially in capillaries where nuclei of endothelial cells protrude in capillary lumen. As this occurs, blood flow becomes totally blocked for a fraction of second, up to for larger period of time. Thus giving an apparent effect of greatly increased viscosity.

As some of these effects tend to increase and some tend to decrease, it can be assumed that overall viscous effect in small vessels are approximately equivalent to that occur in large vessels.

Effect of Pressure of Vascular Resistance and Tissue Blood Flow

The rise in arterial pressure results a proportionate increase in arterial pressure which results a proportionate increase in blood flow through the various tissue of the body, this is because a rise in arterial pressure not only increases the force that tends to push blood through the vessels but also distends the vessel at the same time, which reduces the resistance. For the majority tissues, the blood flow at 100 mm Hg arterial pressure is usually about four times as great as the blood flow at 50mm Hg. The blood flow stops completely even when a small amount of pressure is still in the arteries due to two major reasons:

a. The arterial pressure falls to gradually lower levels, to the extent to which the pressure stretches the vessel wall diminishes finally reaching a point at which the pressure insists, the vessel is no longer capable of opposing the muscular tone in the vessel wall and keeping the vessel open.
b. The second reason for ceasation of blood flow at low arterial pressure is the symptoms for the blood cells to become jammed in the arteries and capillaries when the pressure becomes too little to compel the cells to pass obstruction points.

Vascular Dispensability

The blood vessels are distensible and so the diameter of blood vessels increases as the internal pressure increases, the vascular dispensability differ greatly in different segments of the circulation.

$$\text{Vascular distensibility} = \frac{\text{Increase in volume}}{\text{Increase in Pressure X Original Volume}}$$

PHYSIOLOGICAL FLUID DYANAMICS

Concept of fluid dynamics are used to study the physiological problems. The study of flow through cardiovascular system, stenosis development, peristalsis etc., are in the ambit of physiological fluid dynamics. Physiological fluid dynamics is an important inter-disciplinary area which requires close collaboration among medical, engineering and applied science research workers. In the past collaboration has resulted in development of several devices like cardick assist devices, haemodialysis devices, artificial organs which function almost like natural one. Encouraged by the development of several devices the Scientific Committee on Physiological Fluid Dynamics(6) had organized the First International Conference on this topic in 1983, the proceeding of this published in the form of a book entitled "Physiological Fluid Dynamics I" acquired acclamation of all Scientists working in this area.

The significant growth in this area of Biomedical (4) engineering through the development and incorporation of newer experimental and theoretical techniques have thrown more light on the salient aspects of the physiological processes and have improved our knowledge in understanding complicated cardio-vascular diseases. The clarification of problems in physiological mechanics requires detailed study of both mechanics and mechano-biological interactions. The prominent factors responsible for the complexity of the mechanics of the circulation are the complex shape of the structure through which the blood flows, their elasticity, the unsteadiness of blood flow and complex theological properties of blood.

Katherine & Graham(22) revealed that when blood flow occurs, that exert shear stress which provides endocardial cells a changes in proliferation, differentiation, cell shape, and permeability. Khalid A.K, et.al.(23) has stated that during development of blood flow models, some assumption like cross section area of blood vessel remain constant with time and distance. Also the pressure gradient remains constant over the distance. From ancient time to present time with increasing biological knowledge and mathematical techniques the mechanics of blood flow has been a subject of much relevance in physiological and medical sciences. These days, mathematicians interested in biological and medical problems, are engaged in evolving new mathematical methods to deal with complex situations in life sciences.

CONCLUSION

The modeling and analysis of blood flow problem is an important topic of fluid dynamics. The behavior of blood flow which is a non Newton I an fluid can be analyzed more accurately by using suitable mathematical model considering all the physical and physiological parameters. By this way, the Good health and wellbeing of human body can be achieved.

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RESEARCH ARTICLE

Graphene Oxide-MgO Nanocomposite for the Removal of Toxic Cr(VI) Ions

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ABSTRACT

In this present study, we have synthesized MgO, GO and GO-MgO nanomaterials by simple precipitation method by using magnesium nitrate as starting material and polyethylene glycol as stabling agent where sodium hydroxide is precipitating agent. Then obtained nanomaterials are calcined at 350^{0}C to form desire product. FESEMimages indicate the formation of fine nanoparticles on GO surface. The formation of the phase and crystal structure is determined by XRDstudy. Further confirmation of formation is done by FTIR and Raman using the different peaks. Then, the three prepared GO, MgO and GO-MgO nanomaterials were used as adsorbent for removal of carcinogenic Cr(VI) from aqueous solution. From the adsorption study, it is found that among the three prepared materials GO-MgO nanocomposite is the most effective adsorbent for the adsorption of Cr(VI) from aqueous solution due to synergetic effect of GO and MgO. From the experimental results concluded that Cr(VI) adsorption is mainly pH dependent and maximum adsorption occur at pH=4 for GO-MgO. Again the adsorption data was fitted with various kinetics models and shown that Cr(VI) adsorption on GO-MgO follows pseudo second order kinetic model

Keywords: Graphene oxide, Magnesium, Adsorption, Chromium, Nanomaterials

INTRODUCTION

In the modernized society, the water pollution is a major global problem intimidating the life system, which accounts for a large number of diseases and death by consuming contaminated water. There are various types of water contaminants such as inorganic pollutants like arsenic, cadmium, chromium, fluoride, lead, mercury etc. and organic contaminants like acrylamide, phenol, benzene hexachloride, carbon tetrachloride and different organic dyes like congo red, methyl blue, methyl orange etc[1–4]. Inorganic pollutants like heavy metal ions and fluoride are essential nutrients in certain concentration, but above that threats to environmental and human health at high concentrations. The maximum acceptable concentrations of these inorganic pollutants in drinking water have been set by World Health Organization (WHO) and many countries is shown in table-1.Toxic metal ions such as Hg(II), Pb(II), Cr(VI), Cd(II), and As(III)/(V) and fluoride(F^-) are non-biodegradable and can easily accumulate in the environment and living organisms due to their small size and their metabolites are toxic, carcinogenic, mutagenic, chromosomal fractures and responsible different respiratory disorders. From environmental safety point of view, the removal these inorganic contaminants from waste water effluent before discharging into natural water stream are extremely important [5–8]. Several processes like reverse osmosis, precipitation, activated carbon filter, membrane separation, ion exchange, photocatalysis, adsorption, solvent extraction, nanofiltration etc, have been used. Among them, adsorption is the most commonly used method, due to its low cost, simple operation and design requirements, low residual product generation, its lack of interaction with toxic substances and possibility to reuse the adsorbent[9–11]. The nano sized metal oxide adsorbents are known to be the promising candidates for removal of inorganic pollutants from aqueous media, due to their large surface areas and high reactive sites[12–14]. Due to environmental friendly and cost effective metal oxide (mainly Aluminium, Iron, Magnesium etc.) nanocomposites can be used in various field including catalyst industry, gas sensors, solar cells, adsorption and so on[15–19].They are classified as the promising ones for heavy metals and fluoride removal from aqueous systems. Many investigations have shown that metals oxide nanomaterials are good adsorbents. However, nano sized metal oxide adsorbents aggregate during adsorption process, and because of their small size,it is difficult to separate from waste water and it is also decrease the adsorption capacity.In order to decrease the aggregation behavior of nanomaterials, easy separation and improve the adsorption capacity resent research focused on development of engineered nanomaterials mounted onto high surface area Graphene oxide nanosheet substrate [20,21].

Graphene is one of the most fascinating advanced carbon-based nanomaterials having a two dimensional honeycomb sp^2 carbon lattice, large theoretical surface area (2630 m^2/g), excellent chemical inertness, high transparency, enormous electron mobility, good thermal conductivity and remarkable elasticity [22–24]. Therefore, graphene is considered a favorable material for various applications such as sensors, transistors, catalysis, and environmental pollution treatment. Graphene Oxide (GO) is an oxidized derivative of graphene which contains epoxide, hydroxyl, and carboxyl groups. These functional groups lead to the negative charge, hydrophilicity and easy dispersion of GO in aqueous solutions. These characteristics make GO a potential candidate for the removal of different pollutants by adsorption [25,26]. Due to its large surface area and presence of large number of functional groups, GO can be used as an excellent platform to grow various nanoparticles. In addition, GO also helps in preventing agglomeration of nanoparticles therefore it can be effectively used as template/precursor for the growth of different kinds of nanoparticles. In case of functionalization of graphene oxide with metal oxide nanomaterials, graphene not only serves as a highly conductive support material but also provides a large surface for the dispersion of metal oxide nanoparticles [6,27,28].Now-a-day, surface modified GO by using different organic, inorganic groups and polymer has also been used for removing environmental inorganic pollutants to achieve high adsorption efficiency because these functional group can form stable chelates with heavy metal ions. Metal oxide, based on functionalized graphene oxide nanocomposites has received more attention in the adsorption field due to achieve high capacity and electivity in the last few years [29–33].

The 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to

prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs. The beauty of this work is its full fill the SDGs number 3 (Good Health and well-being), 6 (Clean water and Sanitation), 11 (Sustainable cities and Communities) and 12 (Responsible consumption and Production) and 14 (Life below water).

MATERIALS AND METHODS

MATERIALS

All of the chemicals were of analytical grade and used without further purification. Graphite powder (300 mesh), Poly ethylene glycol (PEG; Mn=20,000), Magnesium nitrate hexahydrate($Mg(NO_3)_2.6H_2O$) were bought from Sigma Aldrich (USA). Ethanols (C_2H_5OH), Sodium Hydroxide (NaOH), Hydrochloric acid (HCl), potassium dichromate ($K_2Cr_2O_7$),1,5-diphenylcarbazide (DPC),potassium permanganate ($KMnO_4$), hydrogen peroxide (H_2O_2, 30%), sulfuric acid (H_2SO_4, 98%), Acetone (CH_3COCH_3)were purchased from Merck (INDIA). A standard 1000 mg/L concentration of Cr(VI) solution was prepared by adding 2.83g of $K_2Cr_2O_7$ in 1000 mL of double distilled water. The desired chromium solution was prepared by dilution of this stock solution.

Preparation of Adsorbent

Synthesis of GO

GO was prepared from graphite powder according to modified Hummer's method by oxidation treatment of GO[34]. Briefly, 3 g of graphite powder and 3g of sodium nitrate were dissolved in 75 mL of sulfuric acid (98%) and stirred for 2h in ice bath. After that 9g of $KMnO_4$ was added slowly under continuous stirring conditions for another 2h. The temperature of the reaction mixture was increased to 98 °C and continuously stirred for 12 h. Afterward, the suspension was cooled to room temperature and mixed with ~100 mL water followed by 30mL of 30% H_2O_2 and sonicated for half an hour to exfoliate GO into single layers. The diluted mixture was then centrifuged for 15min at 10,000 rpm. The solid residue was washed with 5% HCl and distilled water several time for complete neutralization followed by vacuum-dried at room temperature for 12 h, to obtain GO powder.

Synthesis of MgO nanomaterial

Co-precipitation method was used to synthesize MgO composite nanomaterials [35]. In this method, $Mg(NO_3)_2.6H_2O$ and polyethylene glycol (PEG; MW: 20,000) were dissolved in 70 mL of ethanol with 1:2 mol ratios of Mg and polymer respectively (where PEG was used for controlling the size of the nanocomposite). Then 2M NaOH was added drop wise to the mixture up to pH 11 under magnetic stirring. After 3h of vigorously stirring, the white precipitated reaction mixture was obtained. After that the prepared sample was washed several times with ethanol and distilled water and then dried at 60^0C for 4 hours. Then the dried sample was calcined at 350^0C for 3hours with heating rate 10^0C /min to form MgO nanomaterials.

Synthesis of GO-MgO nanocomposite

A simple one step co-precipitation method was used for the synthesis of GO-MgO nanocomposite in which $Mg(NO_3)_2.6H_2O$ and polyethylene glycol (PEG; MW: 20,000)acted as the MgO precursor where GO is the supporting material (shown in Figure-1). In this synthetic procedure, 0.5g of GO was spread uniformly into 30 mL of ethanol by ultrasonication for 1 h. In another beaker, 30 mL of ethanolic solution of $Mg(NO_3)_2.6H_2O$and PEG with 1:1:2 mol ratios of Mg and PEG was taken and stirred vigorously for 60 min. After that, the GO suspension was added to the above solution with stirring. Then the pH of the reaction mixture was adjusted up to 11 by drop wise adding of 2M NaOH solution under stirring. Then black colored composite was obtained and It was separated by centrifugation and then continually washed with distilled water and ethanol, and then dried at 60^0C for 4 hours. Then the prepared sample was calcined at 350^0C for 3hours with heating rate 10^0C /min to form GO-MgO nanocomposite.

Characterization

The crystalline structure of the prepared GO based composite nanoadsorbents was studied by using a PAN analytical powder X-ray diffractometer (XRD) with Cu Kα radiation (l) 1.54156 A^0. The X-ray scanning rate was 10^0/min with a step size of 0.05^0. The functional groups of the prepared composites were characterized by Fourier transform infrared spectrometry (FT-IR) on a Nicolet IR100 Spectrometer in the range of wave number from 4000–400 cm^{-1}.Nova Nano SEM 450 Field emission scanning electron microscopy (FE-SEM) was used to understand the morphology of prepared nanocomposites and It is worked at an acceleration voltage of 15-20 kV.

Adsorption experiments

In order to investigate the removal of Cr(VI) a number of adsorption experiments were performed by changing pH and contact time. All the adsorption studies 0.05g of adsorbent was used in 100mL of 50mg/L Cr(VI) solution in 100 mL of blue capped glass bottles at pH 4 with a fixed time of continuous shaking using a thermostatic orbital shaker at 200rpm. After adsorption experiment, the composite nanoadsorbents were detached out using a centrifuge with 8000 rpm for 15 min, after that the adsorbent free solution was collected for analysis. The Cr(VI) concentration after adsorption were determined by a UV-visible spectrophotometer (UV-Shimadzu 2450) following the 1,5-diphenylcarbazide (DPC) method[36].The effect of pH for Cr(VI) adsorption on adsorbent surface was investigated by changing the pH of the solution from 2 to 9 using HCl (0.1M)or NaOH (0.1M)solutions. Kinetics study of Cr(VI) removal was examined by varying the contact time from 10 to 60 min while other effective adsorption parameters were constant (concentration of solution ;50mg/L at pH; 4).All the above experiments for Cr(VI) removal were carried out at room temperature. The equilibrium adsorption capacity (q_e in mg/g) and percentage of removal efficiency (%R) were obtained using equations 1 and 2 respectively [37].

$$q_e = \frac{(C_0 - C_e)V}{m} \quad (1)$$

$$\%R = \frac{(C_0 - C_t)}{C_0} \times 100 \quad (2)$$

Where C_0 (mg/L) and C_t (mg/L) are the concentration of Cr(VI)initially and at time t respectively. C_e (mg/L) is the equilibrium concentration of Cr(VI) in aqueous solution. V (L) and m (g) are the volume of solution and mass of the adsorbent respectively.

RESULTS AND DISCUSSION

Characterization of nanocomposites

Fig. 2 reveals the XRD patterns of GO, MgO and GO-MgO nanocomposites. The peak at 2θ=10.85° was confirmed the formation of GO from grahite powder. The XRD pattern of MgO contains characteristics peaks at at 2θ=37.05°, 43.42° and 62.1° belong to the plane (111), (200), and (220) respectively are index to cubic structure of MgO according to JCPDS no. 45-0946 [38]. For GO-MgO all the above peaks are found but the peaks intensity decreases due to the polycrystalline nature of composite [39].

The FESEM image of the GO (Fig. 3a) showed the characteristic wrinkled and sheet-like structure with smooth surface. The FESEM image of the GO-MgO nanocomposite is shown in Fig. 3b, which clearly indicates that nanoparticle was formed onto the GO layers with different morphology compare to GO.Fig.3c shows the SEM-EDX spectra of GO-MgO, from this figure we have confirmed that the prepared composite contains Mg, C and O with 16.24, 25.34 and 58.42 weight percentages respectively.

Adsorption studies of Cr(VI)

Effect of pH

The pH of the Cr(VI) solution is a significant parameters because of its different interaction with specific metal ions, reactive sites and surface charge of the adsorbent[40]. Therefore, the effect of pH on Cr(VI) adsorption was performed by changing the pH from 2 to 9 while other factors like concentration (50mg/L), dosages (0.05g in 100mL) keeping constant at time 40min and temperature 303K and presented in Figure 4a. The adsorption capacity efficiency maximum at lower pH for all nanomaterials and slightly decreased up to 6 but decreased sharply when the pH of the solution is above 5 of the solution. This phenomenon occurs due to the various reasons which are explained below. In aqueous solution Cr(VI) mainly exist as H_2CrO_4, $HCrO_4^-$, CrO_4^{2-}, $Cr_2O_7^{2-}$, etc[41]. At acidic pH (2 to 5), Cr(VI) exist manly as $HCrO_4^-$ and $Cr_2O_7^{2-}$ and above pH 5, it exists as CrO_4^{2-}. When pH is less than pH_{ZPC} (pH_{ZPC}= 5.32which was calculated using zeta potential studies at different pH and illustrated in Figure 4b), the surface of the adsorbents is positively charge that leads to protonation of hydroxyl groups of GO as well as metal (M^{n+}) present on GO surface. The adsorption of anionic $HCrO_4^-$ and $Cr_2O_7^{2-}$ species onto MgO functionalized GO based nanocomposites favors through electrostatic interaction, hence higher adsorption capacity was found at lower pH values. Similarly, when pH is greater than pH_{ZPC}, the surface of the adsorbents became negatively charged that leads to deprotonated which repel the Cr(VI) anionic species hence adsorption capacity decreases at higher pH (above 5) value[32,42]. The highest adsorption efficiency is found to be (achieved maximum adsorption capacity at pH=4) for MgO functionalized nanocomposite as compared to other prepared nanocomposite along with parent materials which was clearly shown in Fig. 4a. From the above explanation, it is confirmed that the adsorption capacity mainly depends on the electrostatic interaction of Cr(VI) anions with positively charge adsorbent surface and functional groups present on GO surface. The pH=4 was chosen the equilibrium pH and that used for all adsorption experiments.

Effect of contact time and adsorption kinetics

The reaction time is another important factor that effect adsorption capacity. So we have investigated the effect of contact time varying from 10 to 60 min while other affected parameters including Cr(VI) concentration (50mg/L), pH (4) and adsorbent dose (0.05g in 100mL Cr(VI) solution) and temperature (303K) were constant. Figure 5a shows the effect of time on Cr(VI) adsorption capacity on GO, MgO and GO-MgO nanocomposite. From this graph, It is observed that, the adsorption capacity increases with contact time and reached equilibrium at approximately 40 min for all the nanocomposite. This result is due to available of more surface binding sites after that the adsorption capacity became constant due to insufficient surface binding sites[42]. Further, the obtained adsorption data was fitted with two most common kinetic models i.e. pseudo first and second order kinetic model to better understanding the Cr(VI) adsorption process. Equation 3 and 4 are the mathematical expression of pseudo first order and second order respectively[32].

$$\log(q_e - q_t) = \log q_e - \frac{k_1 t}{2.303} \quad (3)$$

$$\frac{t}{q_t} = \frac{1}{k_2 q_e^{\,2}} + \frac{t}{q_e} \quad (4)$$

Where q_e (mg/g) is the equilibrium adsorption capacity and q_t (mg/g) isthe adsorption capacity at time t of Cr(VI) adsorption. k_1 (min^{-1}) and k_2 (g $mg^{-1}min^{-1}$)are the first and second order rate constant of respective kinetic models. Fig. 5b and c are the pseudo first order (t vs log (q_e-q_t)) and pseudo second order (t vs t/q_t) kinetic plots for Cr(VI) removal by GO, MgO and GO based MgO nanocomposite. The related parameters of these kinetic models were calculated using corresponding plots and listed in Table 1.

Based on the correlation coefficient (R^2) and comparison with the q_e calculated and experimental values, it was revealed that our experimental data best fitted with pseudo second order with higher R^2 and closer qe calculated and experimental value compare to pseudo first order kinetic model. Hence the chemisorption process was the rate controlling step[32,43].

CONCLUSIONS

In this present study, we have synthesized MgO, GO and GO-MgO nanomaterials by simple precipitation method by using magnesium nitrate as starting material and polyethylene glycol as stabling agent where sodium hydroxide is precipitating agent. Then obtained nanomaterials are calcined at 350^{0}C to form desire product. FESEM images indicate the formation of fine nanoparticles on GO surface. The formation of the phase and crystal structure is determined by XRD study. Further confirmation of formation is done by FTIR and Raman using the different peaks. Then, the three prepared GO, MgO and GO-MgO nanomaterials were used as adsorbent for removal of carcinogenic Cr(VI) from aqueous solution. From the adsorption study, it is found that among the three prepared materials GO-MgO nanocomposite is the most effective adsorbent for the adsorption of Cr(VI) from aqueous solution due to synergetic effect of GO and MgO. From the experimental results concluded that Cr(VI) adsorption is mainly pH dependent and maximum adsorption occur at pH=4 for GO-MgO. Again the adsorption data was fitted with various kinetics models and shown that Cr(VI) adsorption on GO-MgO follows pseudo second order kinetic model.

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Table-1: Pseudo- first-order and Pseudo- second-order kinetic parameters for Cr(VI) removal by NH_2-GO/ZnO-$ZnFe_2O_4$ and GO/ZnO-$ZnFe_2O_4$ nanocomposite

Adsorbent	q_e experimental (mg/g)	Pseudo-first order			Pseudo-second order		
		k_1 (min^{-1})	q_e, calculated (mg/g)	R^2	k_2 ($gmg^{-1}\,min^{-1}$)	q_e, calculated (mg/g)	R^2
GO	56.57	0.0072	44.24	0.912	0.0012	56.12	0.991
MgO	32.12	0.0065	26.02	0.862	0.0015	32.02	0.985
GO-MgO	72.92	0.0092	67.12	0.971	0.0009	71.92	0.999

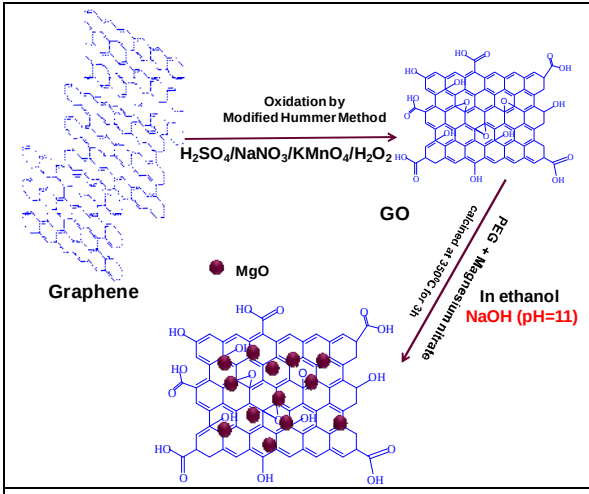

Figure-1: Synthesis route of GO based MgO nanocomposite.

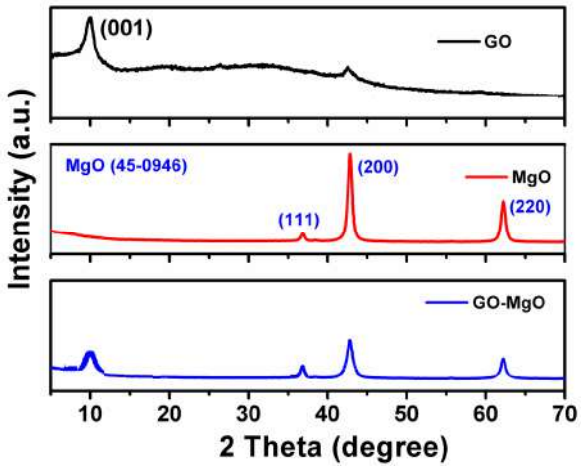

Figure-2: XRD pattern of GO, MgO and GO-MgO nanocomposite

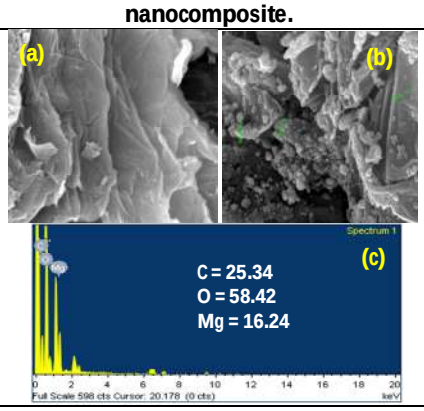

Figure-3: FESEM images of (a) GO, (b) GO-MgO and EDX spectra of GO-MgO nanocomposite

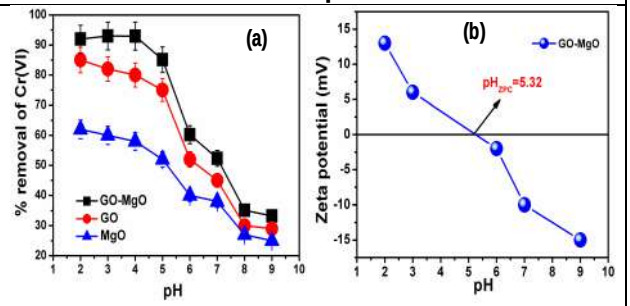

Figure-4 (a) Effect of pH on Cr(VI) removal on MgO, GO and GO-MgO; (b) Zeta potential study of GO-MgO nanocomposite

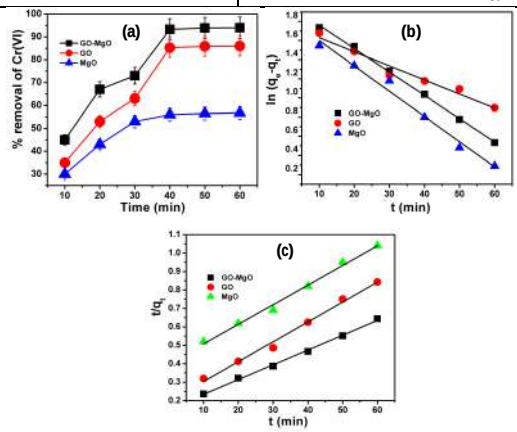

Figure-5: (a) Effect of time, (b) Pseudo first order and (c) Pseudo second order kinetics plots for Cr(VI) removal by GO, MgO and GO-MgO nanocomposite.

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RESEARCH ARTICLE

Role of Digital Marketing in Modern Era

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ABSTRACT

In the present period of mechanical progressions, marketing practices have been changed from traditional methods to digital method. Digital marketing is a device which can be utilized for developing the business internationally. With the assistance of digital marketing, a purchaser can likewise contrast an item and other item, and it additionally permits 24 hours of services to buy, even it permits clients to restore a conveyed item in the event that they are not happy with it. The conventional methods of showcasing are as yet brilliant however headway in market crusade, rivalry intricacy, buyer's assumptions, and market has constrained the organization to receive more powerful technique to reach and pull in shoppers. This paper will focus on advantages and disadvantages of digital marketing and how to anticipate digital marketing.

Keywords: Digital Marketing, importance, Digital marketing planning

INTRODUCTION

With increment in the quantity of web clients enhanced with the versatile and computerized transformation, presently the digital marketing has become indistinguishable piece of human existence. When contrasted with conventional methods of advertising computerized promoting offers benefits identified with reach, cost adequacy and proficiency. The absolute most basic computerized stage incorporates the dynamic utilization of web, sites, portable, TV, SMS and so on to appreciate imagination, development, dedication and enormous customer base the organizations are focusing and expanding the utilization of computerized stage to advance their item and services. Approaching purchasers and changing over them into potential possibilities has become a perplexing assignment. Finding some kind of harmony between ideal time, ideal spot, right item and right technique has truly become a test

for advertisers. Digital marketing, explicitly, alludes to 'Accomplishing advertising goals through applying advanced innovations and media. Digital promoting is about the utilization of web, electronic media and so forth to advance the item and increment its compass among purchasers. It is a coordinated showcasing exertion that requires web related and non-web related stage. A portion of the basic instances of digital marketing stage can be dynamic utilization of informal communication, TV; Search motor related promotion, SMS and other advanced advertising procedures and devices. Advanced advertising permits the buyer to connect with item/administrations as per their accommodation, need and inclination. Digital marketing guarantees moving toward the purchasers in ideal, significant and practical way. The advanced promoting measure is successfully utilized in both the force and push advertising methodologies. The message itself becomes viable once we are in the responsive mode. Authorization based advertising messages are incredible in light of the fact that dependent on its need or interest, the buyer itself decides to get the messages, instant messages or web feeds and in this way, there are high odds of its adequacy. Then again, if the shopper isn't intrigued yet the notice messages are as yet conveyed, they may not be that successful. This push methodologies of conveying undesirable data, subsequently, is less successful. Both, pull and push publicizing methodologies are conceivable in digital marketing. Sustainable Development Goals (SDGs), is one of the important aspects for economic development. SDG 9 is for industry, innovation and infrastructure. Digital marketing will bring innovation to the entrepreneurship. It will definitely fulfill the objective of SDG 9. Digital marketing will support in achieving sustainable development goals.

LITRATURE REVIEW

Digital marketing as a concept started from 1990. Promotion through web is considered as one of the important innovations for advertisement (Chaffey, 2009). Computerized media showcasing is an incredible asset utilized by associations and promoting supervisors to draw in buyers and construct brands to succeed (Fulgoni and Mörn, 2009) D.K Gangeshwar (2013) in his diary, "Internet business or web showcasing: a business survey from Indian Context", commented that the present created in web-based showcasing would be an important expansion to scientist and academicians and valuable hypothesis for experts, publicists and business visionaries. Web clients in India is going to increase 30 to 70 million in coming 5 years. 21st century will be more influenced by digital marjeting. Rathore, Pant, Sharma (2017), in their article "Arising patterns in Digital promoting in India" explained that the customers are looking through additional on web to track down the best items and administrations from the merchants around India. By various methods of computerized advertising like search engine optimisation (SEO), search engine marketing (SEM), content promoting, force to be reckoned with advertising, online business promoting, effort advertising, social promoting and so on the shopping rate of the clients have been expanded boundlessly.

Over the long haul the expression " digital marketing " has created from a specific term that portrays the marketing of goods and services using digital platforms - to a conventional term that depicts the strategy for consolidating advanced innovation to draw in buyers and make shopper propensities, support brands, keep up with clients and further develop income (Financial Times, lexicon.ft.com refered to in Kannan and Li, 2017). Henceforth, , digital marketing can be depicted as a nimble, innovation empowered structure by which organizations cooperate with customers and accomplices to create, interface, produce and hold an incentive for all partners (Kannan and Li, 2017). , digital marketing is the utilization of media gadgets, for example, mobiles telephones, PCs and different gadgets to arrive at purchasers through web-based media, sites, web search tools, applications and different strategies. , digital marketing has gigantic potential. One of the critical objectives of advanced advertising is to distinguish the way in which clients utilize arising innovation and fuse this knowledge for the benefit of the association, empowering the client to impart all the more effectively with their likely clients (S. Teixeira et al., 2018). It is additionally conceivable to support brand esteem, draw in new purchasers and further develop deals utilizing, digital marketing. Digital marketing can be on the web or disconnected (Bala and Verma, 2018).

E-Marketing advertisement increased through the help of TV, Radio, phone and also by electronic media (Rowley 2004). Reinartz and Kumar (2003) found that digital marketing decreases the advertisement cost. Company can reach

to the customers more easily through digital marketing. One of the most important benefits of digital marketing is that it will decrease the cost and will increase the profit of the company (Watson et al. 2002; Sheth and Sharma 2005). According to Chaffey (2011), E marketing will increase the reach out to target customers with low cost.

Giese and Gote (2000) tracks down that client data fulfillment (CIS) for computerized showcasing can be conceptualized as an amount of full of feeling reaction of changing power that follows utilization and is animated by central parts of deals exercises, data frameworks (sites), advanced items/administrations, customer support, after-sales service and company culture.

Objectives of the Study

- To understand the importance and challenges of digital marketing as a marketing communication system
- To focus on digital marketing planning

Advantages of Digital Marketing

- Global reach –Easily reach all over the world for new and also existing business
- Lower cost –It will reach to the customer at a very lower cost than the traditional method of advertisement.
- Trackable, quantifiable outcomes –Organisation can easily find how the customers are reacting to the web-based advertising. They can take action to increase the sales by using that information.
- Personalisation –They can get information about the client who is connected to the advertisers' site. Whenever the client visits the site, they can offer the product or service according to the customers' requirement.
- Openness –Advertisers can get client information by looking at the web-based media.
- Social currency –It can pass from client to client and subsequently get viral. Digital marketing movements can connect the promotion strategy in a better way.
- Increased conversion rates – Clients have to take a couple of snaps to purchase by using digital mode.

Disadvantages of Digital Marketing

Some of the challenges of digital marketing may include the following

- Skills and training –Organisations should have competent staff to work on digital marketing. Technology is changing too fast. So, there may be problem to get good employee to work on this. So, they need proper training.
- Time consuming –It requires more time for making content for the promotion. Its very important to calculate the profitability of the online promotion activities.
- More competition – As the company can reach the customers worldwide, they are also facing the rivalry worldwide. The competition is very high due to the digital marketing.
- Complaints & feedback –Any negative feedback or comment by the customers can easily reach to the number of other customers. It will harm the company's goodwill and image easily.
- Security and privacy issues –As the on-line fraud cases are increasing, the companies can be in problem. So, they have to be more careful while dealing with the client information and data.

Digital Marketing Planning

- Build relationships – By building digital associations with your client's organization can empower brand reliability and increment benefits. Consider content advertising strategies as a component of digital marketing campaign. Utilize a client relationship the board framework to improve focusing on and client support.
- Use client personas - By understanding client'smarketer can pick the correct channels to contact them with profoundly focused on, customized promoting correspondences. Perceive how to make client personas.
- Set SMART objectives - The aim of digital marketing campaign is explicit, quantifiable, attainable, reasonable and timely.

- Choose the correct strategies - There are wide scopes of digital marketing tactics strategies can be utilized by organizations, for example, email marketing and social media. Consider the target customer and aim to choose which strategies will be the best.
- Measure and improve – Organizations can utilize web investigation to decide how fruitful their strategies are. With the goal that they can change missions and track the outcomes to make enhancements.

Suggestions

The buyer should speak with the provider to affirm if the item appeared on the site will be comparative in shading, size and shape to the one to be conveyed. It is advisable to convey recorded as a hard copy through messages so it tends to be kept as reference in the event of any question. While surfing the inbox the buyer ought not to go to the bank's site which is reflected in the email as it very well might be a ridiculed email from programmer's gathering. In the event of paying on the web the purchaser should check minutely the URL of the bank address. The shopper should utilize virtual console while entering the client id and secret key on the bank's site in the wake of checking its location. Marketer should give first priority for safety and security of customers personal information, so that customers can rely on digital media and feel comfortable to do transactions. Company should take Customers feedback seriously and work accordingly.

CONCLUSION

Digital marketing is one of the most important methods to reach to the customers with a less time. Sometimes the customers can get some unconditional promise and also additional expenses for it. Now the customers are the ruler of the market as the competition is very high. The customer should believe and satisfied on the online promotion. More and more innovation are required in this sector. Digital marketing creates requirement in the customer's mind. Control to information protection by the organization and web-based media stage is touchy to keep up for empowering broad and mass use of advanced showcasing. Although more and more security problem is coming it is a necessity of the present era to move with digital marketing and innovations.

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RESEARCH ARTICLE

Entrepreneurs' Contributions to Economic Development and Growth

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ABSTRACT

Entrepreneurs are a unique breed of person. In even the most innovative economies, just a small percentage of the workforce starts a firm each year. Nonetheless, entrepreneurs, especially creative entrepreneurs, are critical to the economy's competitiveness. Entrepreneurial benefits, on the other hand, may only be achieved if the business environment is open to new ideas. Furthermore, authorities must plan for the possible loss of jobs that might occur in the medium term as entrepreneurs seek higher productivity through "creative destruction." In the meanwhile how to grow has been the key concern. Throughout the history of industrialization, growth and its relationship to economic success and social wellbeing have been taken for granted. This debate has taken place between huge corporations and society in the contemporary period. This narrative may be found in the dialectic between economics and sociology. Economics and sustainable development can provide a fresh perspective to the issue of economy and welfare through entrepreneurship.

Keywords: Growth, Economy, Entrepreneurs, Development, Entrepreneurship, Entrepreneurism

INTRODUCTION

Entrepreneurship is critical to economic growth (KritiKoS, A. S., 2014). In economies where entrepreneurs can operate with greater flexibility, develop their ideas, and reap the results, the benefits to society will be higher. When faced with significant regulatory impediments, entrepreneurs may relocate to more innovation-friendly countries or switch from productive to non-wealth-creating industries. Therefore, Governments must reduce red tape, streamline laws, and prepare for the negative impacts of layoffs in incumbent enterprises that fail as a result of increased

competition in order to recruit productive entrepreneurs. Entrepreneurship is a positive indicator of a strong economy (Ather, S. M., & Nimalathasam, B., 2010). Entrepreneurship is becoming increasingly important as a driving force for economic progress (Kourilsky & Esfandiari, 1997). According to United Nations Sustainable Development Goals, by 2030 it is required to achieve productive and complete employment and decent work for all men and women including young people and disabled persons (Envision2030 Goal 8: Decent Work and Economic Growth). In a place where there is no considerable economic activity, entrepreneurship takes on a different meaning and must be interpreted differently. It is characterised by the conditions associated with underdevelopment and does not arise from an industrial background with well-developed institutions to support and encourage it.

Entrepreneurship, according to a number of social scientists, is the main component that connects the socio-cultural environment with the rate of economic growth (Ather, S. M., & Nimalathasam, B., 2010). Recent evidence from developing nations throughout the world supports the idea that entrepreneurship may be encouraged via deliberate efforts (Ather, S. M., & Nimalathasam, B., 2010). There has also been widespread recognition that entrepreneurial development is critical not only to solving the problem of economic development, but also to solving the problems of unemployment, uneven development, economic power concentration, and profit diversion from traditional investment avenues. As a result, various initiatives by the government's development agencies and other organisations to promote entrepreneurship may be observed.

Entrepreneurial Inspiration

There is less motivation to foster new, enterprising businesses when the economy is doing well (KritiKoS, A. S., 2014). Why take a chance on something fresh and unproven when people and businesses are already generating money? Entrepreneurs frequently challenge existing organisations, and while this may seem unwelcome, established firms that are not pushed tend to grow complacent, willing to collect their earnings without investing in research and development to better their business. When imports enter, these stagnant businesses are the first to suffer, wilting quickly and unable to adjust to the competition. As a result, one of the advantages of entrepreneurship is that it challenges incumbents to do better during strong economic times.

When the economy is struggling, entrepreneurs are just as crucial, if not more so (KritiKoS, A. S., 2014). When unemployment is high and the economy is declining or stagnant, dynamic entrepreneurship may be able to assist in the recovery. New enterprises can improve demand by inventing novel goods or boosting competition, which might lead to the creation of new jobs and a reduction in unemployment. When entrepreneurs are regularly supported, in both good and bad economic times, all firms are kept on their toes, spurred to develop and adapt (KritiKoS, A. S., 2014). It's also becomes important here to note that entrepreneurship is not the same as running a small business (Afolabi, A., 2015). Small businesses are unquestionably an excellent vehicle for people to pursue their entrepreneurial dreams. The tiny business is an extension of the person in charge (Lumpkin and Dess, 1996).

Entrepreneurship, on the other hand, is not limited to those who establish or run a (creative) small business. Large-scale entrepreneurs, known as 'intrapreneurs' or 'corporate entrepreneurs,' also engage in entrepreneurial activities. Entrepreneurs provide the vitality that keeps economies healthy and thriving, even when some businesses fail. Entrepreneurship is not limited to capitalist economies. China's managed economy is starting to stimulate and facilitate entrepreneurship (KritiKoS, A. S., 2014). They've realised that entrepreneurial activities, which were formerly seen as a danger to the established system, are essential for economic competitiveness and long-term success.

The Link between Entrepreneurship and Economic Development or Growth

Entrepreneurship is commonly seen as good to economic growth and development (Afolabi, A., 2015).Over the last three decades, entrepreneurship has made a remarkable comeback in nations that have significantly reduced poverty (Naude, 2013). In reality, breakdown of the notion of entrepreneurship is required to comprehend the function of entrepreneurship in the process of economic progress (Wennekers &Thurik, 1999). Since Schumpeter's early

publications, the concept that entrepreneurship and economic progress are inextricably intertwined has gained traction (Afolabi, A., 2015). Economic growth is aided by a rise in the number of entrepreneurs. This influence is the outcome of their ability to communicate themselves in tangible terms, and more specifically, their willingness to create.

This inventive activity has previously been defined by Schumpeter, who distinguished five scenarios (as stated in Afolabi, A., 2015): (1) the launch of a new product – one that people are unfamiliar with – or a new quality of a product. (2) The introduction of a new technique of production, that is, one that has not yet been tested by experience in the branch of manufacturing in question, which does not have to be based on a scientifically novel discovery and may also exist in a new commercial approach of handling a commodity. (3) The creation of a new market, that is, a market into which the country's specific field of manufacturing has never before ventured, whether or not this market existed before. (4) The discovery of a new source of raw materials or semi-manufactured commodities, regardless of whether this source currently exists or must be generated. (5) The implementation of a new industrial organisation, such as the establishment of a monopoly position or the dismantling of a monopoly position. The Schumpeterian entrepreneur attempts to develop new profit prospects through his inventive activities. These possibilities may arise as a result of increased productivity, in which case their link to economic growth is obvious.

There are several conversations and disagreements about how entrepreneurship has aided economic progress, but it is critical to recognise the value of on-going innovation and competitive enhancement (Todtling and Wanzanbock, 2003). There has been a challenge identifying and measuring entrepreneurial forces, which has made determining the precise contributions to economic growth even more difficult. Furthermore, according to Carree and Thurik (2002), the concept of entrepreneurship is multifaceted and largely ill-defined. Because of the type of intermediary variables and relationships that exist, understanding the function of entrepreneurship in the process of economic growth will necessitate a framework (Bygrave and Minniti, 2000).

The finest examples of these intermediate factors include innovation, competition, which is primarily defined by company departure and entry, supply diversity, and the amount of energy and effort committed by entrepreneurs. Furthermore, Asc (2006) claims that entrepreneurship and economic growth have a positive link, while Henderson (2007) claims that entrepreneurship is increasingly being acknowledged as a main driver of economic progress. Entrepreneurs add value by commercialising new goods, creating new employment, and forming new businesses by combining current resources with inventive ideas (Afolabi, A., 2015). According to the Global Economic Monitor, countries with greater levels of entrepreneurial activity had stronger economic development. Entrepreneurs are, in a nutshell, the connection between fresh ideas and economic progress.

By boosting the speed and convenience of communication and interaction among the numerous economic players involved in the production cycle, innovative technologies are transforming the global economic landscape (Carayannis *et al.,* 2006). As a result, it is critical for implementing innovations. Many connections have been proposed in relation to the function of entrepreneurship in fostering economic growth. The role of the entrepreneur in implementing innovations as well as fostering competition is critical for economic success (Wennekers & Thurik, 1999). In view of the foregoing, Naude (2013) asserted that entrepreneurship will contribute to growth and job creation in advanced, emerging, and least developed economies alike. This is a legitimate expectation, as evidenced by recent historians, economics, and management science discoveries. With too many entrepreneurs, a country's ambitions may grow - it is widely known that as people's material wealth (or opportunity) rises, so do their aspirations. Entrepreneurs produce jobs, and we all know that unemployment is a big source of dissatisfaction. We also know that items provided by businesses, such as health and experience activities, contribute to increased happiness.

Entrepreneurship's Impact on Economic Development

Entrepreneurship is undoubtedly one of the most important strategies to encourage economic growth among the various options available (iED, 2020). Entrepreneurial endeavours are causing growth in an increasing number of nations throughout the world. It may appear to be a mammoth trip to go through as a start upper or a business owner who is only now beginning to comprehend the notion of entrepreneurship. People work hard, and their efforts may appear to be more difficult than they are. Entrepreneurs must understand that their work entails more than just making a profit and expanding their company to a larger scale. All of this personal and professional development has a societal benefit. Entrepreneurship is, without a doubt, the most important aspect that contributes to a community's economic growth in a variety of ways (iED, 2020). Some of the ways entrepreneurship contributes to economic progress are listed below (iED, 2020).

Job Creation

What is the most difficult challenge confronting today's young adults? Looking for a job. Indeed, the majority of young people are unable to find work that is either related to their skills or pays well. This is where entrepreneurship comes in. By definition, entrepreneurship can result in the creation of additional jobs. You are building a career for yourself as an entrepreneur. You will be recruiting additional individuals at the same time as your firm grows.

Contribute to the prosperity of local communities

Entrepreneurial ventures vary from other businesses in that they place a greater emphasis on the local community. An entrepreneur believes that his or her company will have a far greater influence on the local level. Entrepreneurs like to retain their enterprises as close to home as feasible, so contributing to the richness of local markets.

Contributing to the growth of local businesses

Entrepreneurs are not only producing employment and money on a local level, but they are also paving the road for new firms to set up. As a result, they contribute to the growth of local businesses while also bridging the gap between large corporations and small local businesses.

Introducing foreign opportunities to the local market

As a company expands, so do its opportunities. Exporting is a major step for any company, yet it is still every entrepreneur's desire to expand into new markets. Local communities can start exporting their products and form more professional cooperation through entrepreneurship. That is possible because of the basic principles of entrepreneurship.

The Way Ahead

Entrepreneurship is about profit-seeking desire, and when it succeeds, it enhances the economy and society in a unique way (Isenberg. D., 2011). The aim of the policymaker and public leader is to establish a virtuous cycle of entrepreneurship as a result of the spill overs. The quickest way to start this virtuous loop is to build, develop, cultivate, and evolve a geographically focused ecosystem that promotes entrepreneurship and its success. To do so, an independent team will be needed with the training, power, mandate, capacity, and resources to impact the ecosystem sufficiently and holistically before disbanding. From an economic policy standpoint, the fastest road to development is not through national innovation systems, national competitiveness, developing a knowledge-based economy, creating economic clusters, or attracting foreign direct investment. According to Isenberg. D. (2011), economic development strategies play a role at times, but entrepreneurship is either (a) a pre-condition for these strategies' success; (b) they are a complement to entrepreneurship; or (c) if implemented without an ecosystem perspective, they can be detrimental to entrepreneurship. These tactics may lose a lot of their usefulness if entrepreneurs — economic actors – are not involved. The quickest route is to cultivate an entrepreneurial environment in a planned and educated manner.

There is a lot of uncertainty, and responsible, educated testing and learning are necessary in any individual location, but isn't that part of the entrepreneurial process? Is the plan for the entrepreneurial ecosystem founded on good principles? Yes, the ideas are based on the most up-to-date research as well as the most comprehensive examination of practise. Are they capable of causing harm? Only the opportunity cost is a risk, and we know that leaders spend far more on initiatives with a lower likelihood of success. And the alternative of doing nothing or doing things we know don't work is unacceptably ineffective. Entrepreneurship is not a solution for society's ills, but it has enough spill overs and is causative enough that it should be considered a basic social benefit alongside education, security, welfare, energy, and health. If all of the scattered wisdom (research, theory, and practise) in the world could be gathered, we would have enough practical knowhow about how entrepreneurship develops in societies to know what kinds we need, how much is enough, and how to intentionally and strategically create enough of it in a given region to make it self-sustaining. As Ireland, Iceland, Israel, Chile, and China have demonstrated, entrepreneurship may emerge spontaneously in societies. However, it is already known that to get better outcomes, faster, and for less money than if it was left to chance. And it may be argued that the cost is so little, and the potential reward is so great, that it should be started immediately out with dozens or hundreds of projects. Entrepreneurship – long-term, ambitious, and on a large scale – will determine whether or not we live in a garbage dump in 2050. To paraphrase Victor Hugo, entrepreneurship is a concept whose time has come in all parts of the globe, and that no army is as powerful as an idea whose time has come.

Specific recommendations for local, state, and federal policies that contribute to the development of a supportive environment for entrepreneurship, according to Carland, J., &Carland, J. (2004), include:
Policies that reduce the regulatory and compliance burden of small and start-up ventures;
Policies that encourage and support private investment in start-up and growing ventures;
Policies that support and expand research and development activities in public and private institutions and organisations;
Policies that improve and expand education and training

CONCLUSION

Entrepreneurship has long been recognised as a powerful driver of economic growth. Various characteristics of entrepreneurship include 'innovation,' 'organization-building capacity,' 'gap-filling function,' 'input completion,' and so on. Individuals with these abilities are needed to lead and sustain the industrialisation process. As a result, efforts should be focused on finding and developing such entrepreneurial potential. Because entrepreneurial talent is a cultivable asset that can be developed and increased by education, training, and a favourable economic climate, policymakers and planners have turned their focus to entrepreneurship as a desired and achievable path to economic growth. Entrepreneurship is widely accepted as being crucial to the growth of a knowledge-based economy. The ideas which were presented above would be beneficial to practitioners, researchers, planners, policymakers, and academicians interested in entrepreneurship development.

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RESEARCH ARTICLE

Using Mobile App through Integrated NLP Services to Enhance Student Learning in Engineering Education

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ABSTRACT

Smartphones are becoming personal assistants due to their enhanced set of features like capabilities, services, and applications that they offer to them. In recent years, mobile applications with these emerging features are transforming the education industry. Students expect interaction and personalized learning as assets from mobile learning. Therefore, the development of intelligent mobile applications and motivating content development is one key aspect of mobile learning. In this article, we developed an intelligent mobile learning application that helps graduate engineering students in self-learning. In the form of documents, presentations, video lectures, and question banks, the learning application retains study material. It performs several automated tasks including automatic identification of important concepts, similar sentences, and concepts in the text, automatically analyzing the meaning of words, identification of questionable sentences, term extraction, and conducting a practice test for confidence building. To implement individual functionalities, multiple techniques were used. The evaluation of the mobile application was done in two ways. First, an evaluation of the mobile application based on its design structure and usage. For performing this task, 72 graduate engineering students have participated in the questionnaire-based feedback. Second, the Working of the individual modules is evaluated by three human experts.

Keywords: Automatic question generation, Mobile assisted learning, Self-learning, Text analytics, NLP

INTRODUCTION

According to UN SDG (United Nations Sustainable Development Goals), since 2000, there has been a gradual enhancement in universal primary education and also in the literacy rates [19]. In this scenario, the Mobile

technology provides a wide variety of possibilities, whether in the classroom or at home, to improve educational content and invent new ways of learning. Students today are more related than ever before to mobile phones and no longer want conventional learning methods such as reading textbooks and lectures in the same way as previous generations [16]. The following main advantages are uncovered by good mobile learning experiences: faster access to course material, more contact with other students and instructors, the opportunity to get more knowledge about the subjects studied, enhanced job quality, increased motivation. In the growth of mobile learning, the learning platform plays a critical role. The application should be more appealing than textbooks, promote easier comprehension of knowledge visualization, and provide additional material.

In engineering education, student interaction plays an important role and studies have shown a connection between the social interaction of students with the learning environment and positive academic achievement [15]. Educators have shown great interest in exploring ways of integrating mobile and wireless technology into teaching and learning in recent years. Various systems have been developed that use mobile devices to enhance teacher experience and input [17] and lecture communication, as in Scornavacca *et al.* [18], student contact and lecture participation [3]. Typically, this is accomplished in a face-to - face environment in which students come to the lecturer's office to receive the recommended academic advice and guidance in preparing each semester for learning achievement. The key initiative of this report, therefore, is to present the mobile application design system model in engineering education.

Intelligent text processing and web browsing that performs value content acquisition for student's individual-level learning supports the built mobile application. This encourages students to self-learn, quickly understand the concepts and enhance their examination results [2]. The system offers many features, including automatic recognition of the words, performing confidence-building trial exams, and automatic assessment. We evaluated the application in graduate engineering learning after growth. Specific functionalities of the device were tested and high precision was achieved by most of the modules. Moreover, the constructed framework is being tested by 72 engineering graduate students who used it as a self-learning application. Post-use input was provided via a questionnaire by the students. The feedback from the students shows that the scheme enables them to effectively master the concepts.

Related Work

Smartphone applications are available that are useful to lecturers. These apps enable them to coordinate course materials, rate assignments, improve learning goals, and better connect with learners. Grade Books for Professors are Google Spreadsheets that, either via a paid or free edition, are helpful strategies for coordinating and monitoring student grades. Using this quick and simple calculator helps to figure percentages, the Percent Calculator gets grades done harder, easier, quicker and stronger. The eClicker Polling System allows lecturers to ask their students during class about anything and anything. For Android devices, Voice Recorder is ideal, or iTalk allows teachers to make permanent records of lectures for students for any reason that does not make it to iPad users to class. In essence, Blackboard Mobile Learn provides a classroom app that can be used for smartphones and tablets on almost all platforms. The Smart Course requires subscribers to use digital textbook services and to have thousands of digital readings with unrestricted access to their phones and tablets [5].

Several scholars, including the writers in Cobb *et al.* [6], have been studying the use of SMS / MMS in classroom interaction systems. By encouraging learners to send feedback, queries or multiple-choice questions, such as SMS / MMS messages, active learning in the classroom is encouraged. This provision was found to enable shy or self-conscious students to engage, improve the relationship between learner and material, promote student interaction, and promote transparency in the classroom [12]. Some drawbacks remain, such as the cost of SMS / MMS, which can prevent this method from being widely adopted, as in Draganova [9], particularly from the point of view of the students, the aggregation of messages by the lecturer, and their real-time interpretation. Creation and testing of SHERPA, a mobile productivity platform designed for use in the classroom by both students and teachers. SHERPA

is intended to support teachers with different tasks in the administrative classroom, as well as to facilitate contact between colleagues.

METHODOLOGY

Experimental Design

As the research's first aim is to design a mobile application, we used a high-level python web framework called Django [1]. We had to define the features of the suggested framework for implementation. We discussed 72 graduate engineering students and three faculty, all interested in engineering teaching, to understand the framework requirement. We focused on recognising the obstacles a student encounters when he or she self-studies a subject from a science topic during the discussion. We have also described the areas where he or she focuses most during his examination preparation. The teachers were asked to point out the areas in which they put more time into teaching a concept or helping the student's study for the exam. We established from the discussion the general areas where most face problems. These are the sense of unknown words, long sentences being understood, scientific terms being remembered, a method without a diagram being understood, and essential parts being defined for analysis. All the students said that before the actual exam, a mock test is useful for building trust and knowing their weaknesses. From this research, the features of the proposed scheme were finalised. These are the meaning of unknown words, long sentences being understood, scientific terms being remembered, a system without a diagram being understood, and essential parts being defined for analysis. All students said that before the actual assessment, a mock test is useful for building trust and knowing their weaknesses. We finalised the features of the suggested framework from this report.

Tasks carried out by the Proposed System

The proposed learning application offers many features that enable students to learn. A text document is taken as an input. Then, the machine performs the tasks below:

- Provides context, if needed, of the words.
- List the main words.
- Abbreviations lists and their extensions.
- Provides pictures for different notions.
- Extracts from the text the entities and called entities.
- Identifies significant textbook chapter words.
- Performs trial examination, on request.
- Assesses the reactions of students.

Experimental Setup for System Evaluation

We are following two separate methods to test the proposed framework. As the framework consists of several independent modules and each module corresponds to a system function, the individual modules need to be evaluated. The first phase of the assessment, therefore, seeks to determine the performance of the individual modules. This evaluation is carried out by professional experts who are familiar with the functions of the modules.

We intend to evaluate the efficacy of the automated framework in enhancing the self-learning experience of graduate engineering students in the second phase of evaluation. For that reason, 72 graduate engineering students studying Computer System Architecture were provided with the system. For feedback on the submission, a questionnaire is prepared and given to the learners. We have selected the textbook Engineering Computer System Architecture by Morris Mano, 2nd edition, for the assessment. The programme operates on these sections and defines the important words automatically, retrieves relevant images, determines important sentences, and generates fill-in-the-blank queries. Three human specialists determine the consistency of these outputs. The accuracy of the relevant device modules is taken into account in these tests.

For the evaluation of sentence recognition, a similar human expert-based assessment is approved. To evaluate the quality of the automatic response evaluation module, a test data set is generated. For each question, the test set includes five long questions and 20 student responses. For the assessment, two human evaluators were hired. Subject experts are the evaluators. For the test-set questions, they first prepared model responses. The answers were measured on a 0 to 5 scale. For a correct answer containing all the required facts, there are 5 points and 0.0 for a wrong answer with no relevant facts. The average of two human evaluator ratings is taken into account as the gold standard score of a response. Then, those responses were reassessed by the machine. The system's precision is considered to be the proximity of the score generated by the system and the score of the human evaluator. The specifics of the method's implementation and assessment are discussed in the following pages.

System Implementation

Mobile Application for Computer System Architecture Learning

The details of the proposed application's implementation are explained here. A sample drawer of the developed mobile application is presented in Figure 1(a) and the whole chapter list is represented in Figure 1(b). The figure shows that there is a toolbox in the system that supports a set of features that the student is able to access. The complete list of system features is given in the section "Tasks carried out by the Proposed System". Later, the specifics of the techniques used for the implementation of these human features are discussed.

Word Meaning

In this research, as we concentrate on second-language students, the system contains a module represented in Figure 2 to provide the meaning of the words. Students find it difficult to understand or memorise unknown words. In order to help them develop a strong reading vocabulary, it requires more than having them look up words in a dictionary. Instead, learners need training to help them gain new word knowledge and develop strategies that will enable them to increase the depth of that knowledge over time. In order to help students, develop word knowledge in depth, we create an interface through which learners can get synonyms, antonyms, definitions, and examples of the word in use in phrases of a word(s). The system uses Word Net [13] to uncover glosses and synonyms of the word. For Computer System Architecture, however, the word may be a term; Word Net may not have a definition of it. So, a list of words and n-grams related to Computer System Architecture is identified by the system.

Important Terms Identification

Computer system architecture terms are identified using the term frequency * inverse document frequency (tf-idf). If in the current document the term frequently occurs but rare in other documents, the tf*idf score of a term becomes high [10]. We used parts of speech and named entity data during tf-idf computation, too. For the extraction of parts of speech and named entity information, we used the NLTK toolkit [4].

Additional Information on Term extraction

In the application, there is also a feature to provide additional information on the Computer System Architecture terms specified. If a student becomes interested in learning more about a term or concept, through the provided toolbox window, he or she may request more information from the system. The application then searches the query and retrieves the relevant webpages from a list of predefined websites. Basically, the search engine, effective web search, query formation, and trustworthy web sources may not be aware of a student. He or she may, therefore, unnecessarily visit several websites and waste his or her time on irrelevant documents. The tool helps him to find the information required effectively.

Important Sentences

For examination, all of the sentences in a chapter are not important. A subject question paper at the graduate engineering level contains different types of questions, including objective or factual questions (e.g. fill-in-the-blanks and multiple-choice questions), questions of the short-response type, and descriptive questions. Many learners, especially weak learners, often try to protect the marks against factual problems. Therefore, they often give a specific

focus during the preparation of the examination on the portions that are likely to generate objective questions. The system automatically identifies the phrases that contain a questionable fact, as the objective questions are formed primarily from facts embedded in the text. These sentences are considered and are highlighted as significant.

The approach we adopt for significant sentence identification here is based on the calculation of the similarity of sentences. We generate a reference set of sentences containing the question sentences and the sentences "point to remember." The textbooks often provide a section containing key points covered in the chapter; these are gathered. Objective questions are gathered from the current question papers and the set of practice questions provided in the exercise section of the textbook. These queries are translated to an assertive type using a series of Parse Tree-based guidelines. The parse tree was created with Stanford Parser [8].

All of these sentences, gathered from both sources, are essential for review. Other textbook sentences that are highly similar to these phrases are also identified and treated as significant. To compute the similarity, a combination of parse tree matching-based approach [11] and long short-term memory-based Infer Sent [7] is used. Infer Sent is a method of embedding sentences that provides representations of semantic sentences. To form a fixed-size vector, Infer Sent uses bidirectional long-term memory with mean-max pooling.

Conducting Sample Test: Generation of Question Paper and Answer Evaluation

A module for conducting a practice or trial exam is included in the system. The objective of the trial exam is to increase the student's level of trust. Automatically, the system produces the question paper. The scheme in the question document supports the factual question (fill-in-the-blanks). Factual questions are created from the questionable or factual sentences identified. In these sentences, key terms are included for Computer System Architecture. To form a fill-in-the-blank question, one of these words is blanked out. The interface for conducting demo exams is shown in figure 3. The learner can pick the syllabus and the type of questions for the mock test. The system also performs automatic assessments of student responses. For fill-in-the-blanks, with the student response, the system matches the right answer. This is basically a matching word or phrase. However, in the assessment process, not all words play an important role. So, in the bag-of - words model, we considered the words that have a high tf-idf score, nouns and noun phrases and selected them as important terms.

Evaluation of the Proposed Mobile Application

We are now evaluating the performance of the individual modules of the learning application proposed. We adopt the task 's manual assessment approach. We presented the evaluation strategy adopted in the study in the 'Experimental Setup for System Evaluation' section. In the following section, we discuss the details of the assessment.

Evaluation Metrics

Based on the type of information, different evaluation metrics were used. The accuracy of term identification is measured using the F-measure [14]. The harmonic mean of accuracy and recall (Eq. 3) is the F-measure or F1 score. Precision is the fraction of the relevant terms identified (Eq. 1). The recall is the fraction of relevant terms over the total amount of relevant terms (Eq. 2) that have been identified. The F-measure was also used to assess the identification of instrument names and the names of scientists. We use the percentage accuracy for evaluating scientist-invention and abbreviation-expansion pairs.

$$\text{Precision} = \frac{\text{Number of correctly retrieved terms}}{\text{Total number of terms retrieved by the system}} \quad (1)$$

$$\text{Recall} = \frac{\text{Number of correctly retrieved terms}}{\text{Total number of available terms in the documents}} \quad (2)$$

$$F_1 = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}} \quad (3)$$

Generating the Questions and Evaluating the Answers

The effectiveness of the identification of factual sentences depends on the performance of the automatic fill-in-the-blank (FIB) question generation. In addition, the factual or significant sentence selection module seeks to help students answer objective questions. A questionable fact ought to be included in an important sentence. Therefore, it is checked if the retrieved sentence contains any questionable facts in order to evaluate the significant phrase selection. The percentage of these phrases is taken as reliability. We observed in our experiments that the sentence selection module achieved 96.72 percent accuracy. Then, these phrases were converted into FIB questions by replacing one word with a blank. The key terms have received greater preference for question generation. Since the accuracy of the word identification is high, in question generation, we also achieved good accuracy. 70 system-generated FIB questions were tested by the evaluators and found that 65 of them were good questions; therefore, the accuracy is 92.86%.

Questionnaire-Based System Evaluation

A questionnaire provided to the graduate engineering students who used the application also investigates the effectiveness of the developed system. In this study, we also prepared a questionnaire to evaluate the students' acceptability of the suggested mobile application. We supplied it to 72 students of Computer System Architecture to evaluate the application. The application was used by these students as a self-learning application. They offered their feedback on the individual components and the overall system after their use. We studied various existing questionnaires to form the questionnaire and generated the questions that are appropriate for evaluating the individual modules and overall functionality of the application. Students provide feedback on a three-level scale for each question, agreeing, partially agreeing, and not agreeing. The students' responses to the questionnaire are summarised in Table 1. From the table, we found that the feedback achieved a high score for most of the questions. In summary, we found that in only 2 cases out of the total 576 responses (34.72 percent), the system did not agree. These values demonstrate that the system is efficient in meeting the students' needs.

CONCLUSION AND FUTURE WORK

For e-learning, an intelligent mobile application for learning is essential. For graduate level students, we created a mobile application for effective engineering education. The suggested application guides the students in various ways to learn the concepts effectively. The system provides the meaning of the unknown words; identifies important terms; performs a better learning practise test; identifies questionable phrases from the textbook. It is found that the system achieved reasonable accuracy in both evaluations of the effectiveness of the individual modules and of human experts. For future work, there are several instructions. Although the modules have been designed and tested using Computer System Architecture, we feel that the platform proposed is generic and can be applied in other subjects of science. By incorporating automatic MCQ generation, one can extend the application.

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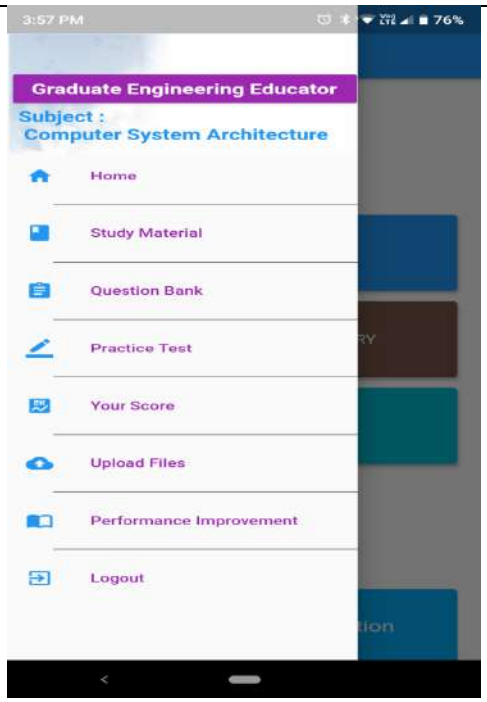
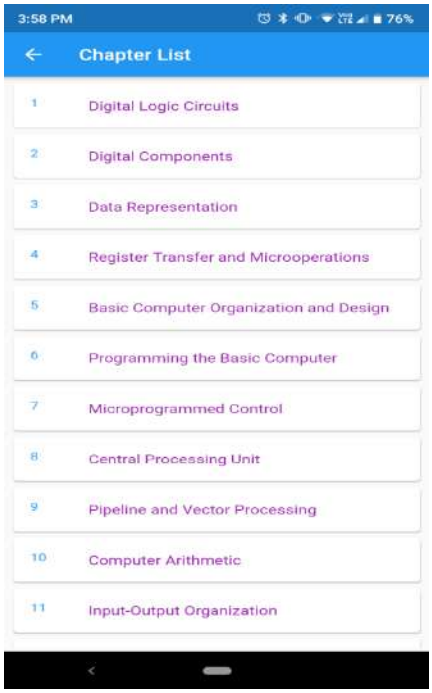
Table 1.Student feedback through Questionnaire – Total 72 Students

Sl No.	Questionnaire	Agree	Partially agree	Not agree
1	The learning platform is easy to navigate	64	8	0
2	Term identification is effective to identify and memorize the key concepts	70	2	0
3	The toolbox is helpful and properly oriented	58	13	1
4	The toolbox contains enough tools you require during the study	62	9	1
5	Important sentences are helpful in answering objective questions	68	4	0
6	The mock-test feature is useful	71	1	0
7	Overall you are satisfied with study material quality of the platform	70	2	0
8	You would recommend this platform to a friend	69	3	0



(a)



(b)

Figure 1. A sample view of the proposed mobile application (a) Drawer (b) Chapter list

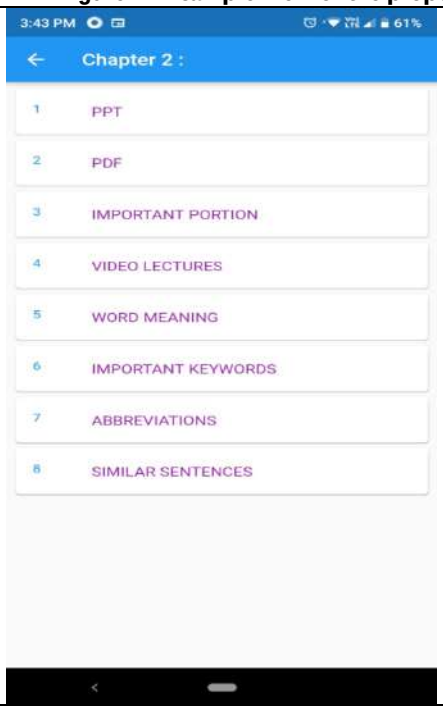


Figure 2. Front view of the study material of each chapter

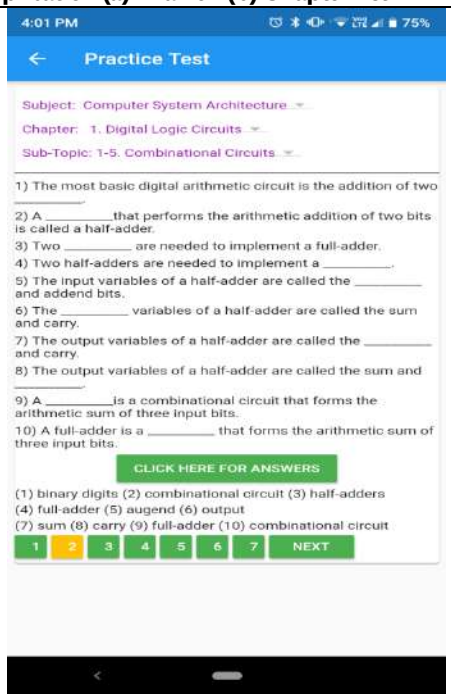


Figure 3. The interface for conducting demo examination by the mobile application

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RESEARCH ARTICLE

Biochemical Defense Strategy against Plant Pathogens

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ABSTRACT

Plants faced many challenges by both biotic as well as abiotic stresses. Of these, biotic stresses plant pathogens are gained importance to cause huge losses in terms of quality and quantity of yield. Many strategies have developed to combat the effect of plant pathogens. Among those, plant resistance is one of the important mechanisms against plant pathogens. Resistant varieties of plants contains more important biochemical weapons viz., total proteins, phenols, reducing and non-reducing sugars, peroxides and phenylalanine ammonialyase than susceptible varieties. Resistant plants showed low disease severity. It indicated that defense chemical weapons offers resistance to plants to defend the enemies.

Keywords: Plant pathogens, Resistant varieties, Biochemica weapons, Yield

INTRODUCTION

Plant defence strategies are either innate or artificial. In innate defence, plants are naturally checking the development of a particular pathogen(Hakeem Olalekan S hittu *et al*., 2019). This defence mechanism is classified into pre-existing and induced defence mechanisms. In all natural ecosystems, plants are surrounded by huge number of diverse potential living agents and different abiotic stresses. In general, plants protect themselves by triggering secondary metabolites. Secondary metabolites viz., terpenes, phenolics and nitrogen (N) and sulphur(S) containing compounds offer resistance to wide range of plantpathogens. The host surface acts a first line of defense against the pathogen. Prior to penetration or infection, host secreted some chemicals to protect themselves. Plants release various substances from the surface of above ground parts as well as through their root surface. Inhibitory substances show direct impact on micro-organisms or encourage selective groups to dominate the environment

which may act as antagonists to pathogens. Phytoalexens are toxic antimicrobial compounds. These are formed noticeable amounts in pants only after activation by phytopathogenic agents or by chemical or mechanical injuries in plants. Phytoalexins are formed during in-compatible interaction between host and the pathogen. The formation and accumulation of diverse storage proteins are closely related to plant defense since many of these proteins showed entomologic traits such as amylase and proteinase inhibitors, lectins and globulins. Proteinase inhibitor (PI) concentration in plant leaves is normally low but they can be actively triggered to elevated concentrations when plants are challenged by insects, mechanical damage or are exposed to exogenous phytohormones.

Diverse F Biochemical Molecules in Plant Disease Resistance

Arjunan *et al.* (1976) observed difference in protein content in sorghum leaves incited by *Helminthosporium turcicum*. Its value in healthy and infected leaves was 0.31 and 0.39 per cent, respectively in ten day old plant and 0.24 and 0.02 per cent, respectively in 60 day old plants. Nandagopal (1995) showed that the wheat genotypes exhibited resistant to leaf spot caused by *Exherohilum hawaiiensis* having less crude protein content than the vulnerable genotypes. The biochemical analysis of leaves of various varieties of mustard to *A. brassicae* exhibited that total phenol, O-dihydroxy phenol, total sugar, reducing sugar, chlorophyll content and flavonol contents were more in resistant genotype (*Brassica alba)* than vulnerable genotypes (Mathpal *et al*., 2011).Newton and Anderson (1929) found that wheat plants resistant to rust because of the formation of phenolics that check the growth of the pathogen. Phenol deposition was faster in incompatible host pathogen interaction than in the compatible interaction (Kiraly and Farkas, 1962). Tomiyama (1963) noticed that the formation of phenolics in diseased plants was a quite common event observed in several host pathogen combinations. The rise in phenolics content might arise from the liberation of phenol from their glucosides by the enzyme glucosidase of their host (Pridham, 1965). Relying on the assessment of phenols Bhatia *et al.* (1972) determined that the capability of tomato plants to combat infection incited by *A. solani* based on the quantity of phenolics in the leaf, stem and roots. Leaves of resistant plant variety exhibited moreamounts of total phenolics and orthodihydroxyphenolics than in leaves of the susceptible variety. Ramasami and Shanmugam (1976) noticed that Alternaria leaf spot resistant cotton seedlings exhibited more quantity of total and orthodihydroxy phenols than susceptible seedlings. Padmanaban and Narayanaswamy (1978) observed that *A. macrospora* affected leaves of cotton exhibited more phenolic content than the healthy leaves. Borthakur and Addy (1988) noticed that phenol concentration was less in the leaves of the rice cultivars infected by sheath blight pathogen. Singh and Srivastava (1988) noticed phenolics played a prime role in disease progress and disease resistance in moth bean plants. Borkar and Verma (1991) observed that the leaves of bacterial blight resistant cotton cv. 101-102B exhibited 69% total phenol more than the leaves of susceptible cotton cv. Acala-44. Sorghum genotypes resistant to foliar diseases contained more content of phenols than that of susceptible genotypes (Kalappanavar and Hiremath, 2000).Early blight of potato caused by *A. solani* was damaging to older leaves. The reduction of hexose content in older leaves favoured the disease development and the disease intensity was correlated with hexose level (Rowell, 1953). Horsfall and Dimond (1957) assigned a major role for sugars in disease resistance. They classified the diseases as high sugar diseases and low sugar diseases. Low sugar diseases occur severely when host sugar content is low and high sugar diseases occur when host sugar content is high. The intensity of attack by *A. solani* was more severe on the old senescent leaves of potato or tomato than on young ones. Generally high levels of total sugars, reducing sugars and non reducing sugars in the host plant are stated to be responsible for disease resistance (Jayapal and Mahadevan, 1968). *H. sativum* infected barley leaves recorded decrease in reducing, non-reducing and total sugars than the healthy leaves (Ramdayal and Joshi, 1968). Aggarwal and Khara (1983) observed mandarin infected with *A. citri* showed a decrease in total soluble solids, ascorbic acid, percentage acidity and total phenols. The reducing and non-reducing sugars were more in resistant cultivars than the susceptible cultivars of chickpea infected by Alternaria blight (Bhargava and Khare, 1988). Phukan (1993) reported that there was a gradual depletion in the total soluble sugar and starch content in the leaves of the potato cultivars infected by *Phytophthora infestans*. Tanmai (1997) found increased levels of sugars with increased severity of late leaf spot of groundnut. Further, she reported that the extent of increase was more in susceptible variety than in resistant variety. Non-*Bt* genotypes recorded higher amount of total protein but lower amount of total phenol and reducing sugars as compared to Bt genotypes infected with *A. macrospora* (Hosagoudar *et al*., 2008) while bacterial blight infected cotton plants recorded decrease in total protein, total phenol, total sugar, reducing sugar and non-reducing sugars (Hosagoudar and Chattannavar, 2008). Neeraj and

Verma (2010) observed that total sugars, non reducing sugars and total phenols were decreased in *A. alternata* infected leaves of *Raphanus sativus* than those of healthy leaves. Addy and Goodman (1972) observed increase in polyphenol oxidase and peroxidase activity in tissues of various plants following infection by viral, fungal or bacterial pathogens. Hossain *et al*. (1999) observed five time increase in the activity of peroxidase in *Colletotrichum gloeosporioides* infected mango leaves in comparison to healthy. Phenolic substances and PO contribute to the resistance of plants against pathogens (Jite and Tressa, 1999). Maiti and Basu (2009) observed the accumulation of the phenolic compounds in many of the host plants due to pathogen infection, which may be important in resistant reaction. In potatoes inoculated with *P. infestans*, there was an altered pattern of metabolism in both susceptible and resistant varieties. The phenol oxidizing enzymes were correlated with disease resistance in many crop plants (Schneider and Ullrich, 1994). The production of lignin is catalyzed by PO (Whitmore, 1978). Studies on quantification of biochemical changes in clusterbean using highly susceptible (IC 116835) and moderately resistant (IC 116903) genotypes against *A. cucumerina* var. *cyamopsidis* showed that activity of PO, PAL and quantity of phenols, flavanols and lignin increased with the increase in disease intensity and indicated important role played by these enzymes in defence mechanism against Alternaria blight in cluster bean (Joshi *et al*., 2004). Parihar *et al*. (2012) reported mustard genotypes viz., EC-399299, EC-399296, EC-399313 and PHR-2 infected with *A.brassicae* contained higher PAL and PO activity.

CONCLUSION

Plants are attacked by diverse pathogens that resulted in huge yield losses with respect to quality and quantity. To mitigate the effect of pathogens, using of resistant varieties is a superior strategy because inexpensive, ecofriendly and gave best results in the field compared to other methods. Resistant plant contains diverse chemical defence molecules to combat the effect of harmful pathogens(SDG 15:Life on land)

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RESEARCH ARTICLE

Synthesis of Alumina / Iron Oxide Mixed Nanocomposite using Combustion Method

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ABSTRACT

Combustion synthesis is characterized by highly exothermic reaction with temperature ranging from 500-3000 °C. These kind high temperature reactions are responsible to produce a wide variety of advanced materials like ceramics, intermetallics, metal-matrix composite etc. Due to strong heating, a pallet of ignited material will exhibit a combustion wave which propagates through the material in self–sustained manner. Here, we have synthesized Al_2O_3-Fe_2O_3 nanomaterial by using cost efficiftive and simple combustion method using aluminum and iron nitrate as starting material.

Keywords: Aluminium, Iron, Nanomaterial, Combustion method.

INTRODUCTION

Those materials whose structural elements - clusters, crystallites or molecules - have dimensions in the 1 to 100 nm range are referred as Nanostructure material. These materials over the past decade arises from the remarkable variations like electrical, optical & magnetic properties that occur as one progresses from an infinitely extended' solid to a particle of material consisting of a countable number of atoms [1-3]. They have also wide range of useful and unusual applications compared to conventional polycrystalline materials. Since past few decades there is increasing research interest in synthesis and processing of various nanostructure materials. Different types of nanostructured such as metal oxides, sulfides, selenides, tellurides & bimetallic materials have been reported in literature by various

research groups. Iron oxides & alumina materials are being used in a wide variety of applications such as catalyst, pigments, magnetic media, technical ceramics & biomedical applications [3-7]. At the other hand anisotropic nonspherical nanomaterials with their controllable sizes, shapes and crystallinity have drawn great attention, primarily due to their remarkable optical, electrical and catalytic properties, which are quite different from their bulk counterparts. Boehmite (γ-AlO(OH)) and its oxide derivative such as α -$Al_2O_3$and γ – Al_2O_3 have been studied extensively because they can be used as catalyst, adsorbents, flame retardants and optical materials. Arising out of their potential applications nanostructured alumina & iron oxide materials such as nanorods, nanotubes, nanopipe, nanofibre, nanowires, nanoflakes etc were prepared by different desirable synthetic roots like hydrothermal, sol-gel, combustion, microwave synthesis etc [8,9].

The definition of nanocomposite material has broadened significantly to encompass a large variety of systems such as one-dimensional, two-dimensional, three-dimensional and amorphous materials, made of distinctly dissimilar components and mixed at the nanometer scale i.e., less than 100 nm. The general class of nanocomposite organic/inorganic materials is a fast growing area of research. Significant effort is focused on the ability to obtain control of the nanoscale structures via innovative synthetic approaches. The properties that strengthening the general behavior of nanocomposite towards their substantial improvement includes mechanical properties e.g. strength, modulus and dimensional stability, decreased permeability to gases, water and hydrocarbons, thermal stability and heat distortion temperature, flame retardancy and reduced smoke emissions, chemical resistance, surface appearance, electrical conductivity and many others [10-15].

Nanocomposites differ from conventional composite materials due to the exceptionally high surface to volume ratio of the reinforcing phase and/or its exceptionally high aspect ratio. The reinforcing material can be made up of particles (e.g. minerals), sheets (e.g. exfoliated clay stacks) or fibers (e.g. carbon nanotubes or electrospun fibers). The area of the interface between the matrix and reinforcement phase(s) is typically an order of magnitude greater than for conventional composite materials. Core-shell or coated nanoparticles are also example of composite nanomaterials, which are essentially defined as particle containing a core and a shell and have dimension in nanometer range. Core-shell nanomaterials exhibits improved physical and chemical properties over their single componets counterparts and hence are potentially useful in a wide range of applications [12-14].

Aluminium oxide is the oxide of aluminium having chemical formula Al_2O_3 and amphoteric in nature. It is commonly called as Alumina. Alumina is the most widely used oxide ceramic material. Its applications are widespread, and include excellent mechanical strength at room temperature and high temperature, hardness, high melting point, chemical inertness, thermal shock resistance, large band gap and signifying its versatile features. On focus to its commercial application : it is used as a spark plugs, tap washers, pump seals, electronic substrates, grinding media, abrasion resistant tiles, cutting tools, bioceramics, (hip-joints), body armor, laboratory ware and ware parts for the textile and paper industries. Aluminium oxide can be prepared by several soft chemical methods such as precipitation, spray pyrolysis, sol-gel, organic precursors, hydrothermal method and so on [15-17].

Boehmite (AlOOH) is the oxy-hydroxy compound of aluminium, and is largely used as absorbent materials. It stays in orthorhombic dipyramidal system and a good catalyst for photochemical industry. However, it has been proven difficult to synthesize these materials with good crystallinity in aqueous solutions due to the very fast hydrolysis rates of alumina precursors therefore the reports on alumina nanostructures with well-resolved morphologies are limited. The synthesis of 2-D boehmite or alumina nanosheets (thickness under 100 nm) with uniform morphology and their assembled superstructures have not been reported so far. Especially, boehmite is also a crucial precursor for preparation of γ-alumina. Nano-sized alumina has potential for the preparation of ceramic catalysts, coatings, adsorbents and materials with photo luminescent properties because of its novel properties, such as high elastic modulus, thermal and chemical stability and optical characteristics. Therefore, the synthesis of nanostructured boehmite and alumina has received considerable research interest in recent years [10-17].

Iron oxide is the oxide of iron with different oxidation state of iron. Generally it is found in solid state having appearance of red-brown to black coloration. It is insoluble in water and stable at room temperature. In recent years, various α-Fe_2O_3 (hematite), Fe_3O_4 (magnetite) and FeOOH (goethite) nanostructures have been studied, including their shape-specific properties, synthesis methods, and potential applications on lithium ion battery electrodes, gas sensors, field effect transistor, catalysts, & gas sensing applications [12-15]. Goethite (FeOOH) is the hydrated iron oxide mineral found in soil by the weathering process of other iron rich minerals. It is generally having orthorhombic crystal system. It is one of the most important iron oxide surfaces, which incorporates a range of geo-chemically and environmentally important oxyanions and cations in its complex matrix. Besides that it is treated as an intermediate in the iron oxide preparation.

Different metals, metal oxides, sulfides, ceramic, core-shell and composite nanostructured materials can be prepared using a number of synthetic techniques, which are broadly classified into two categories, namely, physical methods and chemical methods. Among the chemical methods, the following are some important and commonly used techniques to prepare various nanomaterials.

Different synthetic methods:

- Chemical vapor deposition
- Hydrothermal synthesis
- Sol-gel technique
- Microemulsion technique
- Wet-chemical Process
- Combustion synthesis

However, in this report, we have focused mainly combustion synthesis for the synthesis of aluminium/iron oxide nanostructured material which are discussed below: Combustion synthesis: Scientists have known about these types of reactions for only three decades - in fact the first experiments were performed at ISMAN, in Russia, in the early seventies. From this research it was discovered that it is possible to drive a synthesis reaction in a self-propagating way [13-15].

Combustion synthesis is characterized by highly exothermic reaction with temperature ranging from 500-3000 °C. These kind high temperature reactions are responsible to produce a wide variety of advanced materials like ceramics, intermetallics, metal-matrix composite etc. Due to strong heating, a pallet of ignited material will exhibit a combustion wave which propagates through the material in self–sustained manner. Hence it is called as self–propagation because the process no longer requires the input energy. Combustion synthesis is a relatively new process and represents one of the most promising innovations in materials science [14-17]. The most important advantages of this process are: low energy requirements (no additional annealing is necessary), time saving (the entire process takes only a few minutes) and environmentally friendly (the combustion reaction by-products are N_2, CO_2 and H_2O). According to our aim of the experiment, we have generally studied the combustion synthesis by using urea as fuel and nitrate of alumina/iron as oxidiser by keeping their molar ratio 1:1.

Experimental details

Material used:

Following chemicals reused for synthesis of alumina/iron oxide mixed nanocomposite

a. Urea (fuel)
b. Aluminum nitrate ($Al(NO_3)_3.9H_2O$)
c. Ferric nitrate ($Fe(NO_3)_3).9H_2O$
d. Potassium hydroxide (KOH)

Synthesis of iron/alumina oxide mixed nanocomposite by combustion synthesis

Mixed iron/alumina oxide nanocomposite was synthesized by combustion synthesis keeping the oxidizers ($Fe(NO_3)_3.9H_2O$; $Al(NO_3)_3.9H_2O$) and fuel (urea) ratio 1:1 in milimolar proportion. In this work, in order to synthesize mixed iron/alumina oxide nanocomposite we have also maintained the ratio of $Fe(NO_3)_3.9H_2O$ to $Al(NO_3)_3.9H_2O$ as 1:1. For this synthesis, 3.08 g of $Fe(NO_3)_3.9H_2O$ and 2.86 g of $Al(NO_3)_3.9H_2O$ were added with 2.28 g of fuel urea (NH_2CONH_2) and brown gel precipitated appeared. To this, 5 ml distilled water was added and stirred until complete transparent solution appears. Then it was heated in a preheated furnace for half an hour at 400 °C. After heating, a dark browny red foams are obtained and grinded to get desired sample. To make a comparison, mixtures with $Fe(NO_3)_3.9H_2O$ and $Al(NO_3)_3.9H_2O$ milimolar ratio of 2/8 and 8/2 were prepared separately with correspondence amount of fuel urea in order to maintain fuel/oxidizer ratio 1:1. The schematics of combustion synthesis is represented below.

CONCLUSION

The studies as part of this project have established the precise protocol for the synthesis of mixed Alumina/Iron oxide nanocomposite.

- We have synthesized mixed nanocomposite of alumina/iron oxide by combustion method.
- keeping the oxidizers ($Fe(NO_3)_3.9H_2O$; $Al(NO_3)_3.9H_2O$) and fuel (urea) ratio 1:1 in milimolar proportion.
- The present work comes under the sustainable development goals (SDG) number 11 (Sustainable cities and Communities) and 12 (Responsible consumption and Production).

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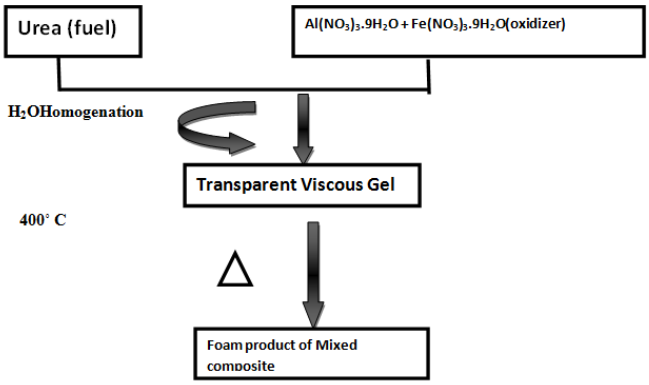

Fig 1.Schematic Diagram of Combustion synthesis

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RESEARCH ARTICLE

Interleukins: Functional Role in Cancer Immunotherapy

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ABSTRACT

Immune cells that are both innate and adaptive, along with cells and tissues that aren't immune interact through interleukins and associated cytokines. Both of them are crucial for the progression, advancement, and management of tumors. Interleukins can promote cancer growth and are also required for a successful tumor-directed immune response. Features of interleukins' could also be used for making immunotherapy more effective, increasing their efficiency while reducing side effects. The main goal of this study is to gain insights on the functional role of several interleukins (ILs) involved in accelerating pro-tumoural effects.

Keywords: Immune, interleukins, tumor, immunotherapy.

INTRODUCTION

The strong interaction amid the immune system and both normal as well as cancerous cells has been revealed by advances in cancer biology over the last century. These discoveries laid the groundwork for the idea of immune-surveillance, or even the immune system's ability to detect and remove abnormal cells. Immune-editing, on the other hand, narrates the immune system and cancer cells interact and shape each other, which finally leads to cancer development and progression [1,2]. Two important characteristics of cancer are immunological resistance and the occurrence of pro-tumoural inflammation [3]. The immune system contexture at the site of cancer at the time of presentation can determine the prognosis of colorectal cancer patients, which highlights its importance [4,5]. In the tumour microenvironment, immune cells and non-immune cells interact in the presence of cytokines. The Tumour

microenvironment in lung adeno-carcinoma, for example, has recently been shown to allow malignancy cells and immune responses will co-evolve [6]. Numerous interleukins are extremely significant in the genesis and tumor progression among the cytokines. The pleiotropic effect of interleukins in cancer is defined by a variety of biological sources, receptors, and signalling pathways, as well as potency. Interleukin intervention could be unique to each cell and extends initiation, progression, and control of tumor cells [7]. The discovery of the precise regulation of tumor immune mechanisms and escape opened the way for the development of novel, more drugs. In recent years, both fundamental and therapeutic cancer research has become fascinated in the therapeutic benefits of interleukins. The increasing number of clinical and preclinical researches demonstrates their promise as a medicinal agent and a goal. The growing number of preclinical and clinical studies demonstrates their promise as a target and a medicinal agent. Attempts to use cytokines have already been in medicinal studies as single therapeutic substances with modest performance, but are currently seeing resurgence in combination with the help of synthetic biology, genetics, and cell therapy [8]. The majority of the time, cytokine classification is based on homology in structure or receptors, as well as gene proximity, rather than their biological contribution to cancer, which is the focus of this study [9]. Interleukins will be considered in this review rather than their family ties, in terms of their biological importance in cancer. In this section, you'll find more information regarding cytokine classification. The turning points of the most recent interleukin-related findings pathways in tumor, and their utilization in medical care, will be covered in this review. We present an up-to-date review of trials in the clinic, recently licensed medicinal medicines, and preclinical breakthroughs. Mainly the focus of this review is on cancerous cells, but most of the exact concepts are applied to many diseases, as a result, it might be handy to all the readers in a wide range of subjects. The current study emphasizes the importance of critical proteins in maintaining human cell physiology and thus aligns with the objectives of one of the United Nations formulated Sustainable Development Goals (SDGs); SDG3 which ensures healthy lives and promotes well-being for all at all stages.

Carcinogenesis

Swelling that persists is recognized as a factor for the development of several cancers, including lung, cutaneous, esophageal, gastric, colorectal, and pancreatic cancers, as well as hepatocellular carcinoma [4]. The equilibrium state of a tissue is maintained by interleukins that cause the cells that are not immune to signal. Interleukin signalling in cancer cells, on the other hand, can develop into a pathogenic development of tumor's mechanism, metastatic dissemination, and the progression of cancer after an oncogenic event. Interleukin 1 is found to be related to inflammation-persuaded malignancy [10,11] . In case of inflammation that persists, immune and non-immune cells give rise toIL-1 Alpha and IL-1 Beta, which have lately received sight for their part in cancer biology [12]. Alarmins (Alarm cytokines) such as IL-1 Alpha (α) and IL-1 Beta (β) work on the IL-1 receptor (IL-1R) to activate and increase inflammatory reaction [9] . Pathogen-recognition receptors rapidly produce the IL-1 Beta precursor pro-IL-1 Beta in reaction to C-type lectin receptors, retinoic acid-inducible gene I protein (RIG-I)-like receptors, and molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs), and Toll-like receptors require inflammasome stimulation when caspase 1 cleaves them into their active state[13] . NLRs, RIG-I-like receptors, and Absent in Melanoma 2 (AIM2)-like receptors are all examples of nucleotide-binding oligomerization domain (NOD)-like receptors detect danger-associated molecular patterns, which stimulates the canonical inflammasome forms filaments of procaspase 1 and activates caspase 1, which subsequently inactivates pro-IL-1 Beta and pro-IL-18 to produce their active forms. [14]. According to new research, IL-33 has the ability to produce a self-producing carcinogenic microenvironment that encourages the spread of cancer cells [15] . On changing once the cells gain tumorigenic potential (also called tumor-initiating cells), as demonstrated in a squamous cell carcinoma model. Tumor-initiating cell releases IL-33, that increases tumor-associated macrophage infiltration and enhances transforming growth factor-β (TGF Beta) signalling, resulting in tumorigenic niche formation [15,16] .

IL-1 alpha andbeta can enhance the formation of tumorigenic mediators like nitric oxide and reactive oxygen species in the case of chronic inflammation [12,17] . IL1 marks the production of proinflammatory cytokines, like IL6, and initiates the the turning on of internal immune cells, activating the sequence of inflammatory processes [12] . Here, the outcome of IL1 is regulated by the phosphorylation of nuclear factor κB (NFκB), thereby activating the cytokine

inhibitor 3 (SOCS3) signal and enhancing the phosphorylation of the signal transducer. signal and recorder l recorder 3 (STAT3) [17,18] . Lately, oncogenic effects of IL1 cell type have been shown in mice that contain a blocking compound, colon epithelial cells with adenomatous polyposis coli, in which IL1 secretion is made up of monocytes, tumor stromal cells , epithelial cells and [19] . Working with IL1R in epithelial cells, IL1 directly promotes the destructive mutation of epithelial cells that mediate through the accumulation of nuclear NFκB. In addition, IL1 signaling in T cells triggers protoplasmic retention of IL17 and IL22 [19] This investigation is in line with previously reported protozoal effects on IL23 production by myeloid cells and the subsequent response of T helper 17 (TH17) cells to microbial products [20] . Likewise, in a mouse model lungs adenocarcinoma, IL1-dependent gene-induced production of myeloid 88 (MyD88) gene from myeloid cells activates γδ T cells to form an inflammatory loop requiring the secretion of IL17A and IL22 leads to the development of cells into cancerous tumours responsible for Trp53 and Kras mutation [21] .

IL22, activated by IL1 signature in cancer settings, is associated with the action of STAT3 and its cancer-promoting properties [22,23] . IL22 works with IL22R, which is specifically expressed in non-hematopoietic cells, to encourage the healing of a wound and the manufacturing of microbicidal peptides [23,24] . The most recent studies, on the other hand, emphasise two distinct characteristics in carcinogenesis [25]. Under homeostatic circumstances, IL22 is mostly produced by group 3 lymphoid cells (ILC3s) as well as to avoid tumour cell cycle, γδ T cells can restore DNA damage induced by genotoxicity inside the mucosal surfaces [25] . But, when its activities is unrestricted IL22binding protein (IL22BP), its natural deterrent, in a mouse model, IL22 exerts a protumorigenic impact of colorectal cancer [26] . T cells that produce IL22 are reported to accumulate in the lungs and intestines of human and mice models [22,27,28] . With STAT3 phosphorylation, IL22 supplies signaling for the growth and migration of damaging mutations and/or cells with oncogenic mutations, retaining their weight import. As revealed in human colon tissue and rat models of lung, pancreatic, and breast cancer mice, SRY (sex-determining region Y) box 2 (SOX2) and NANOG [29-32]. IL20 is known to behave in the same way to IL22. Protein 1 (PD1) decrease stimulates the immune system in hepatocellular carcinoma, breast, prostate, and oral cancer. For planned cell death in the pancreatic cancer [33] .

Damaged tissue and alarm cytokines are released, which cause the expression of IL6, IL10, IL11 and IL23 by myeloid cells and histocytes. Under homeostatic conditions, this leads to a cycle of self-inhibition to boost healing and reduce inflammation [34] . In turn, IL6 and IL11 are powerful regulators of inflammatory and innate responses [35,36] . Furthermore, IL6 is a development regulator and helps in metabolism [36]. These outcomes are because of the ubiquitinated transducer gp130 receptor subunit, this can isomerize to membrane IL6Rα or IL11Rα to trigger conventional cis signalling or the hydrophilic version of the receptor to cause non-classical converted signalling [37-40]. Janus kinase 1 (JAK1), JAK2, and tyrosine protein kinase 2 (TYK2) signalling are all activated by gp130. [38-40] , SHPTP2 (SHP2) is a tyrosine protein phosphatase that promotes tissue growth and repair, as well as SRC-Yes-associated protein (YAP)-Notch. [35,36,41]. In addition, the activation of phosphoinositide 3kinase (PI3K) - AKT - the interleukin signalling is integrated through mechanistic target of rapamycin complex 1 (mTORC1) signalling and cellular metabolism [35,36] . Classical IL6 signaling is considered essential for homeostasis, while transducing signaling has been shown specifically inflammation is amplified, and inflammatory carcinogenesis is promoted. [42-44]. STAT3 activation that is too high caused by an excess ofIL6 and IL11 in combination with the formation of cancers such as colon, stomach, pancreatic, and lung tumours is made possible by oncogenic genetic alterations. [45-48,49,50,51] . Myeloid cells produce IL1 and IL6,through the activation of hypoxia-inducible factor 1α (HIF1α), which activate PI3K-AKT-mTOR signalling, which changes their metabolism towards glycolysis and decreases oxidative phosphorylation, leading to an increase in IL1 and IL6 synthesis and aggravation of carcinogenic inflammation[52,53] . Note that dysregulated IL6 and IL1 signaling also contribute to cancer wasting.

Importantly, through angiogenesis, IL6 also induces vascular endothelial growth factor (VEGF) [34] . In addition, classical IL6 signaling through IL6R in lymphocytes promotes T-cell proliferation and lineage commitment to TH17 cells and T-follicular helper cells [43] . IL6 subdues the P3 junction box (FOXP3), TGFβ potential to induce regulatory T cell (Treg cells) development is being limited, allow TH17 cell differentiation, and amplify the anti-inflammatory

response transfected TH17 (ACT) cells, as demonstrated in a melanoma model of mouse[54]. IL23 is generated in response to DAMP at the epithelial barrier level[20] . Normally, it neutralizes anti-tumor activity of IL12, but has also been shown to directly promote tumor growth and angiogenesis. IL23 activates IL17 derived from ILC3 and committed TH17 cells, in a synergistic manner, inflammation is exacerbated by IL6, which causes epithelial cells to take in stem cells and go through malignant modification [20,55-57] . IL23 in addition with IL1, IL6 and IL21 can induce IL17 independently of T-cell receptor (TCR) signaling [12,18,58]. As demonstrated in mice models of skin and colon cancer, numerous microbial antigens can stimulate IL17 and cause allergic scarring, which can contribute to tumour formation [59-62] . Recruitment can be aided by signalling of IL17A and activate the epidermal growth factor receptor (EGFR) in skin stem cells, causing them to expand and migrate [62,63] . Thus, under conditions of persistent uncontrolled activation, inflammatory responses activate cellular programmes and it's possible that there's a direct correlation between cancer and this.

Growth and Development of Cancer

Malignant tumors have a number of characteristic features that Hanahan and Weinberg refer to as "cancer features" [64]. Markers of wound healing include proliferation, inflammation, angiogenesis, active invasion, migration and may therefore be Malicious use of cytokine signaling for the purpose of tissue repair [65,66]. Thus, IL1 promote inflammatory carcinogenesis, tumor invasion and angiogenesis [67]. Although stimulation of the NLR group pyrin-domain containing 3 (NLRP3) inflammasome has been widely described in cancer, the effects of NLRP3 activation and the production of IL-1 and its family member IL-18 varies from antitumor action to cancer progression and metastasis [68,69]. IL18 has been shown to promote angiogenesis through NFκB, which activates cancer cells activate VEGF, causing them to proliferate and invade, and suppressing programmed cell death and may cause cell-based immune suppression in the natural killer (NK) [70-73]. It also has the capacity to increase persistent carcinogenic inflammation, IL6 also promotes internal tumor progression pathways in cancer, which is responsible for the integration of many cancer symptoms [74]. IL6 activates PI3K - AKT, an active mitogen protein kinase (MAPK) / extracellular signal-regulating kinase (ERK), NFκB and STAT3 expression. These mechanisms increase the exposure of B-cell lymphoma 2 anti-apoptotic proteins (BCL2), B-cell lymphoma, BCLxL), forming protein-specific myeloid leukemia MCL1 and baculoviral repeat protein 5 inhibitor of apoptosis (IAP)) (BIRC5; also known as Survivin), avoids growth control, activates angiogenesis and metabolism, through VEGF production [74]. The phosphorylation of STAT3 in cancer cells is also influenced by other cytokines, like IL22, that promote cancer-promoting mechanisms [22,27,29,75]. In addition, prolonged STAT3 activation in cancer cells causes multiplication, matrix metalloproteinase production, and migration, all of which increase cancer resistance [34,76,77] . These effects are often related to the epithelial-to-mesenchymal transition (EMT), which is regulated by EMT transcription factors, such as zincfinger Eboxbinding (ZEB), SNAI1, SNAI2, SLUG and TWIST, and allows cell spread, separation, metastasis, and invasion [78-80] . EMTs enhanced by the integrated function of IL1β, IL6, IL17, IL22 and IL23 mediate invasiveness of many cancers. For example, the initiation of STAT3 by IL22 has been shown to regulate EMT markers of pancreatic ductal carcinoma and breast carcinoma in mouse models [30,32]. In addition, exposure for a long time to IL1β causes the involvement of MAPK-activating protein 1 (AP1) (ERK and JUN amino-terminal kinase (JNK)), resulting in epigenetic changes that induce persistent EMT phenotypes, consisting SLUG and ZEB2 transcription in lung cancer [81,82] .In invasive pancreatic ductal carcinoma, IL6 and IL11-mediated endocrine activation of STAT3 promotes EMT.IL35 in breast cancer and IL13-mediated STAT6 initiation in colorectal cancer[49,83-85] . IL23 uses the Wnt–βcatenin pathway to promote EMT in oesophageal cancer, while IL17-induced NFκB activation directly induces ZEB1 in lung cancer [86,87] . In many malignancies, IL8 activates PI3K, AKT, and mouse sarcoma (RAS) – quickly accelerated fibrosarcoma (RAF) – protein kinase (MEK)–ERK through PI3K, AKT [88] . However, in breast cancer cells, durable activation of ZEB1 by IL1 keeps them in a mesenchymal state and prevents metastasis [82]. To maintain their growth, cancer cells require a mesenchymal-epithelial transition. Considered altogether, our findings support the use of cytokine neutralizers to slow EMT-mediated cancer growth.

Immunosurveillance for Cancer

Innate Immunity

Although there are many carcinogenic factors that cause harmful cellular mutations continuously, by screening the immune system, our immune system detects and removes the majority of these altered cells [2]. Internal immune cells, like NK cells, naturally occurring T cells (NKT cells) and γδ T cells, which have a stored list of activation and "self-transformation" receptors [2] . Survivors of mutation can detect and reject altered cells. This process relies on the production of perforin, granzyme B and interferon γ (IFNγ) in these cells [89] . The latter result in apoptosis in tumor cells and the use of a large number of chemokines to trigger the activation of antibodies and the manufacturing of anti-cancer cytokines [2]. The multiplication, maturation, and cytotoxic effects of innate immune cells are mainly controlled by the IL2 family, namely IL2, IL7, IL15 and IL21, using receptors chromatophores sharing a common γc receptor subunit [8]. IL15 is a key cytokine for regulating NK cell biology, which is of main importance in the control of hematological malignancies [90] . IL15 is commonly co-presented with the IL15Rα subunit on the surface of APCs [8] . To activate signaling, the IL15–IL15Rα complex binds to the IL2Rβ–γ receptor complex shared with IL2 [8,91] . By interacting with its receptor on NK cells, IL15 initiates a chain of events that lead to the phosphorylation of serine-threonine kinase AKT. As a result, it causes the transcription factor X-box-binding protein 1 (XBP1) to accumulate and translocate into the nucleus, where the T-box protein is produced in T cells (T-bet), a crucial transcription factor for cytotoxicity. For differentiation, NK cells and TH1 cells were selected [90,92] . In turn, T-bet induces granzyme B for transcription and the genes responsible for NK cell proliferation, maturation, and survival[90] . Importantly, AKT activity downstream of IL15 induces priming homeostasis in cytotoxic T lymphocytes and NK cells (CTLs) [93]. APCs, like dendritic cells (DCs) and macrophages, are primed to make IL-12 by NK cell-secreted IFN, sharing one of its components with IL-23, p40 [8,56] . Importantly, APCs act as a connecting link between innate and adaptive immune responses, and cytokines control their recruitment, maturation, and activation [94] . APC-secreted IL-12 boosts IFN production in NK cells and thus antitumor activities [91,95,96] .

Statements and Declarations

Competing Interests

The authors declare that they have no conflict of interest.

Ethical Approval And Consent To Participate

It is a review article. No ethics approval is required.

Consent To Publish

Not applicable.

Human And Animal Rights

It is a review article. No animals were used in the study.

Availability Of Data And Materials

Not applicable.

Credit Authorship Contribution Statement

All the authors have substantial contribution for the preparation of the manuscript. Gagan Kumar Panigrahi and Aseema Rath conceived the idea. Data curation and writing: Aseema Rath, Annapurna Sahoo, Adyasha Pradhan, Roshni Prinkit Bal, Ankita Priyadarshini, Ipsita Sahoo, Jyotishree Acharya, Smruti Subhadarshinee, Bishnupriya Patalsingh, Shraban Kumar Sahoo and Gagan Kumar Panigrahi. All the authors have read and approved the final manuscript before submission.

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RESEARCH ARTICLE

Synthesis and Characterization of Zirconia Coated Silica Nanoparticles for Catalytic Reactions

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ABSTRACT

Silica nanoparticles and zirconia coated silica nanoparticles were prepared by Stober method and various subsequent methods. The nanoparticles obtained were characterized by XRD, SEM, EDAX and IR analytical techniques. The XRD study of pure ZrO_2 shows well crystalline characteristics with the presence of 100% monoclinic phase. The coated nanoparticles are found to be amorphous in nature. SEM study indicates the particles to possess disorder morphology with the particle are attached to each other through grain boundary to form agglomerated structure. The zirconia coated silica nanoparticles were used as an efficient catalyst for the synthesis of Bis(indolyl) methane under solvent free condition. The Bis(indolyl) methane were obtained with high yield and purity.

Keywords: Nanoparticles, Catalysis, Core-shell nanomaterials, Bis(indolyl) methane

INTRODUCTION

Enhance scientific research, upgrade the technological capabilities of industrial sectors Nanoparticles are essentially small clusters of atoms, which are about 1-100 nanometer in dimensions. The term nano derives from Greek word nanos, which means dwarf or extremely small. The prefix nano means one billionth (10^{-9}). Hence a nanometer is one billionth of a meter. Nanoparticles are essentially larger than individual atoms or molecules but are smaller than bulk solid. It Enhance scientific research, upgrade the technological capabilities of industrial sectors [1,2]. Hence, they are obeying neither absolute quantum chemistry nor laws of classical physics and have properties that differ markedly from those expected from the bulk materials. Because of their ultra fine size, high surface area and useful interfacial

defects nanomaterials are used as the key component for many areas such as electronics and optical devices, pharmaceuticals, paints, coating, superconductors, semiconductors and catalysis. Nanotechnology is the creation & utilization of materials, devices and system through the control matter at length scale less than 100 nm. It is recognized worldwide as key future technology that has the potential to unlock a new generation of materials & devices having revolutionary properties [1-5]. It is a multidisciplinary area where principle of physics, chemistry and engineering are combined to create new useful knowledge. The main physical and chemical properties of nanomaterials include high density, chemical inertness, high surface area to volume ratio. Extensive libraries of nanoparticles, composed of an assortment of different sizes, shapes, and materials, and with various chemical and surface properties, have already been constructed. The field of nanotechnology is under constant and rapid growth and new additions continue to supplement these libraries. The classes of nanoparticles listed below are all very general and multi-functional, however, some of their basic properties and current known uses in biotechnology, and particularly nanomedicine, are described here [5].

The synthesis of nanoparticles, their surface modification via core-shell and composite formation is attracting increasing attention arising out of its growing awareness in technological applications. The method of preparation of core shell and composite particles is a new direction in engineering. Recently, attempts have been made to prepare core shell (coated) and composite nanoparticles of organic-organic, organic-inorganic, inorganic-inorganic materials. Coated nanoparticles are essentially defined as the particles containing a core and a shell and have dimensions in the nanometer range [6-8]. Core-shell/composite nanoparticles often exhibit improved physical and chemical properties over their single-component counterparts, and hence are potentially useful in a wide range of applications. These core and shell nanomaterials can increase the luminescence quantum yield due to improved passivation of the surface and can be more physically robust than the bare organically passivated clusters. The scientific interest arises from the diverse attributes of core and shell nanoparticles as a model building block towards functional materials, including 1) size dispersity, 2) core and shell processability, 3) solubility, 4) stability and tenability, 5) capability of self assembly and 6) reactivity involving optical, electronic, magnetic, catalytic and chemical/biological phenomena. These core shell nanoparticles have applications in the areas such as microelectronics, quantum dots, optics, magnetic, photoactive devices and so on. The controlled synthesis of novel, uniform and stable core-shell and composite nanoparticles has been remained as a technical challenge for many years [9-10].

The synthesis and study nanoparticles, has become a major interdisciplinary area of research over the past 10 years. The size, morphology as well as the properties of nanoparticles basically depends on the methods of preparation. All the processes can be broadly divided into two processes, physical methods and chemical methods [11-15]. Among all chemical precipitation method is widely used due to simple set-up, less toxic and cost effective. In recent years, nanoparticles, coated and composite nanoparticles has been used in various fields of science, engineering and industrial applications by virtue of their specific, novel and useful properties. Heterogeneous catalysis represents one of the oldest and common applications of nanoparticles. Catalytic properties of nanoparticles are enhanced due to presence of large fraction of the reactive atoms that reside on the surface. There are many applications of metal, oxide and semiconductor nanoparticles in important area of applications such as three-way catalysis, fuel cells, cracking and reforming [16-20]. The main objective of the present study includes to synthesize zirconia by pH-controlled precipitation method, synthesize silica nanospheres by stober method, Coat the silica spheres with zirconia nanoparticles. Lastly to study and evaluate the catalytic properties of the SiO_2@ZrO_2 nanoparticles.

Experimental Details

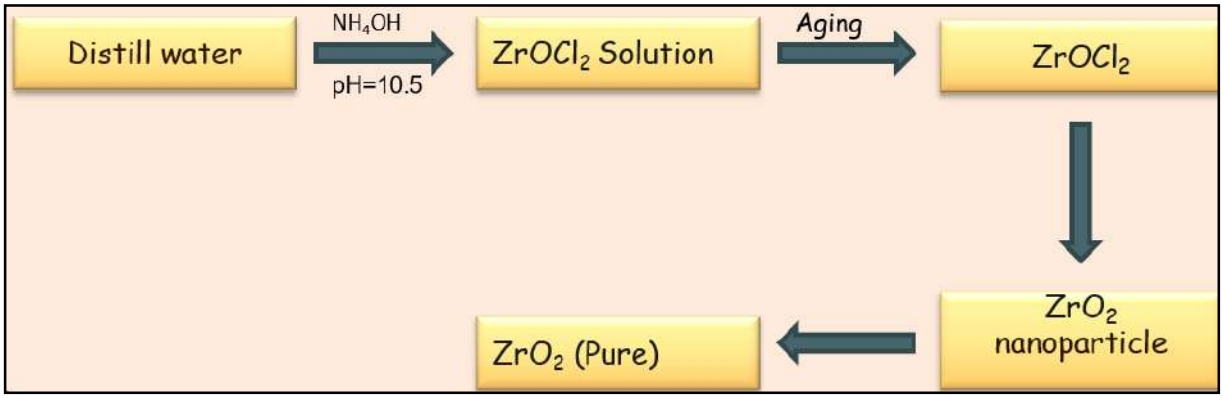
MATERIALS

The chemicals used in this experiment are $ZrOCl_2.8H_2O$, Tetra ethyl orthosilicate (TEOS), concentrated NH_4OH and ethanol solution. All the chemicals are used as received, without further purification. Distilled water was used throughout the experiment.

Synthesis Of Zirconia Nanoparticles

200 ml of distilled water was taken in a 1litre beaker over a magnetic stirrer with constant stirring. Then NH_4OH was added to adjust the pH about 10.5, After maintaining the pH, 13.05 gm of $ZrOCl_2$ solution was added in a dropwise manner with constant stirring and also maintain the pH of reaction mixture. Then the resulting nanoparticles was filtered and it was washed with hot distill water for 4-6 times. Finally, the nanoparticle was kept in oven at 100^{0}C for 12 hours followed by calcination at 400^{o}C for 2 hr at.

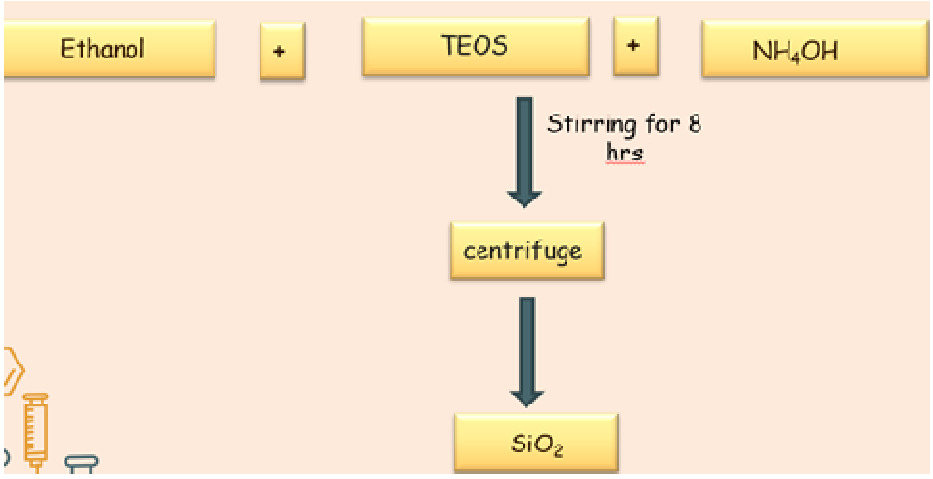
Schematic Representation



Synthesis Of Silica Nanoparticles By Stober Method

Silica particles were prepared by a simple one-step protocol which involves the condensation of tetraethyl orthosilicate (TEOS) in ethanol: water mixture under alkaline conditions at room temperature. First 20 mL of ethanol was taken in a 50ml beaker, and then 2ml of TEOS was added followed by 4ml of concentrated NH_4OH. After that it was stirred for 8 hour. The mixture thus obtained was centrifuged to get the silica nanoparticle.

Schematic representation:



Coating Of Zirconia On Silica Nanoparticle

In order to prepare silica nanoparticles, we have used the Stober synthesis in which first 20 ml of ethanol was taken in a 50 ml beaker then simultaneously 2ml of TEOS was added followed by 4 ml of NH_4OH and stirring was done for 8 hrs. After the obtained mixture was centrifuged, the silica nanoparticles were dispersed in distill water and $ZrOCl_2$ was added by making the medium alkaline by addition of NH_4OH to maintain the pH at 10-10.5. The solution

mixture thus obtained was filtered and it was dried at 100°C and then calcined at 400°C for 2 hr. The product was silica spheres which were coated by zirconia nanoparticles.

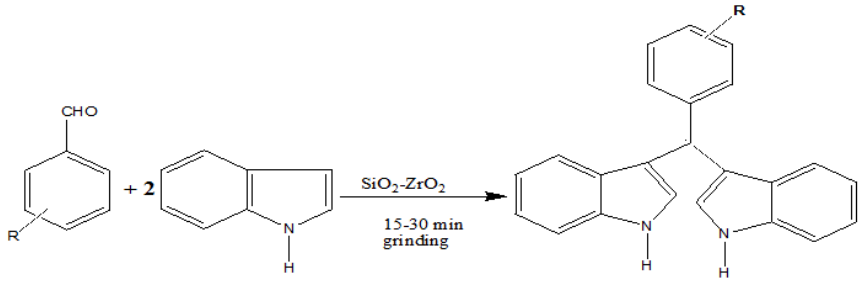
Characterization Of The Nanoparticles

The X-ray diffraction patterns of the samples were recorded on a Siemens D-500 diffractometer using Ni-filtered CuK_{α} radiation. The XRD measurements were carried out in the 2θ range of 20-70° with a scan speed of 2 degrees per minute using Bragg-Brantano configuration. Scanning electron microscopy pictures were taken using JEOL JSM-5300 microscope (acceleration voltage15 kV). The sample powders were deposited on a carbon tape before mounting on a sample holder for SEM analysis. The IR spectra of the samples were recorded (as KBr pellets) were recorded using a Perkin-Elmer infrared spectrophotometer with a resolution of 4 cm^{-1}, in the range of 400–4000 cm^{-1}.

Catalytic Organic Synthesis Reactions By Using SiO_2@ZrO_2

Synthesis of bis(indolyl) methane synthesis by click chemistry

The synthesis of bis(indolyl) methane was performed by mixing two mmol of indole and 1 mmol of aromatic aldehyde in presence of SiO_2-ZrO_2 catalyst (Scheme 1). The mixture was grinded by a mortar and pestle for the required amount of time. During the process the reactants change to liquid form and then solidified. The formation of the product was monitored by TLC. After completion of the reaction, the reaction mixture was treated with 15 ml of dichloromethane and then the catalyst was filtered. The product was recovered from dichloromethane solution and then recrystallized.



(Scheme 1)

RESULT AND DISCUSSIONS

XRD Study

The X-ray diffraction pattern of the silica, 41667irconia and the solica coated zirconia nanoparticles are shown in figure 1.

The pure zirconia prepared by this method was found to be well crystalline in nature with the peak positions corresponding to the presence of monoclinic phase. The silica prepared by the Stobber method in contrast is purely amorphous in nature. No well defined peaks are observed in case of the pure silica as well as he zirconia coated silica nanoparticles.

SEM/EDX

SEM/EDX analysis are done for silica and zirconia coated silica nanoparticles synthesized by stober's synthesis and subsequent modification. Figure 2 shows the SEM and the EDAX profile of the pure silica particles prepared by the Stober method. Te silica particles are of uniform size however, there are considerable agglomeration of the particles along the grain boundary resulting in the formation of the secondary particles. The EDX analysis also indicates the presence of elemental Si and O in the sample with a relative proportion corresponding to the SiO_2 particles. The SEM-EDX analysis of the SiO2-ZrO2 nanoparticles are presented in figure 3. The coated particles shows a completely

disordered morphology which is different from the silica particles. The EDX analysis indicate the present of silica as well as the zirconia particles in the composite sample.

IR Spectroscopy

The IR spectra of the zirconia coated silica particlde is shown in figure 3. The prominent band in the region of 3400-3600 cm^{-1}, corresponds the structural O-H stretching of the nanomaterials. In the bending mode region two bannds are observed in the range of 1500-1700 cm^{-1}, which is due to the O-h bending. In addition, the band at 900 cm^{-1}-1000cm^{-1} can be assigned to the Zr—O bond.

Catalytic Studies

The $SiO_2 \cong ZrO_2$ nanoparticles was used as a environmental friendly catalyst for the synthesis of bis(indolyl)methane. It was observed that the catalyst is quite active for the reaction with good yield of the products are obtained with in 10-30 minutes of mechanical grinding (Table 1). The electrophilic substitution reaction on indole with aldehyde give excellent yields in presence of the catalyst and the catalyst was found to be recyclable

CONCLUSIONS

The main conclusion of the present work is as follows Silica nanoparticles and zirconia coated silica nanoparticles were prepared by Stober method and various subsequent methods. The XRD study of pure ZrO_2 shows well crystalline characteristics with the presence of 100% monoclinic phase. The coated nanoparticles are found to be amorphous in nature. SEM study indicate the particles to possess disorder morphology with the particle are attached to each other through grain boundary to form agglomerated structure. The zirconia coated silica nanoparticles were used as an efficient catalyst for the synthesis of Bis(indolyl) methane under solvent free condition. The Bis(indolyl) methane were obtained with high yield and purity using the silica coated zirconia nanoparticles as catalyst.

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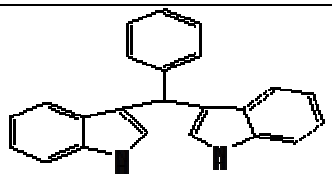
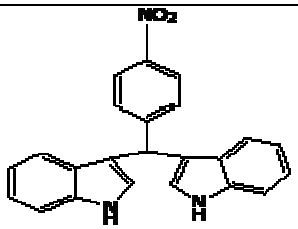
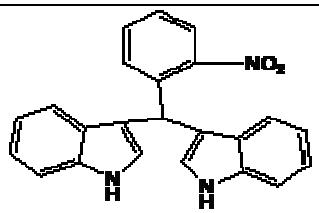
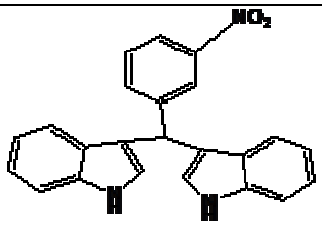
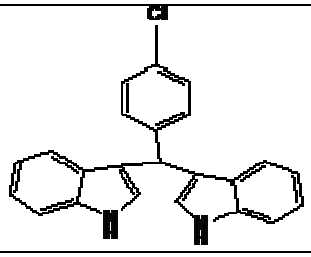
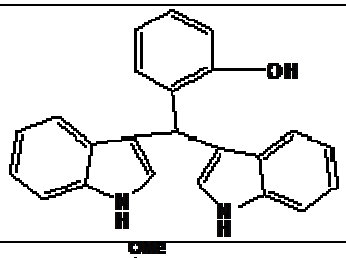
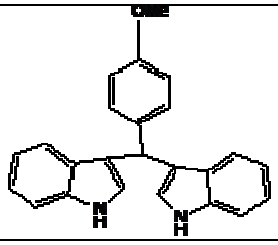
Table 1. Synthesis of bis(indolyl) methane in presence of SiO_2-ZrO_2 catalyst

Sl no	Aldehyde	Product	Time (min)	Yield (%)	IR (cm^{-1})
1	C_6H_5		30	65	3052, 1599, 1490, 792
2	4-$NO_2C_6H_4$		20	72	3052, 1593, 1506, 1487, 873
3	2- $NO_2C_6H_4$		20	90	3052, 1596, 1510, 1499, 886
4	3- $NO_2C_6H_4$		20	85	3052, 1595,
5	4-Cl C_6H_4		30	93	3052, 1617, 1486, 856, 786

6	2-OH C6H5		25	71	3454, 3050, 1156, 1610, 1434, 862
7	4-OMeC6H5		40	83	3053, 1608, 1454, 1244, 837

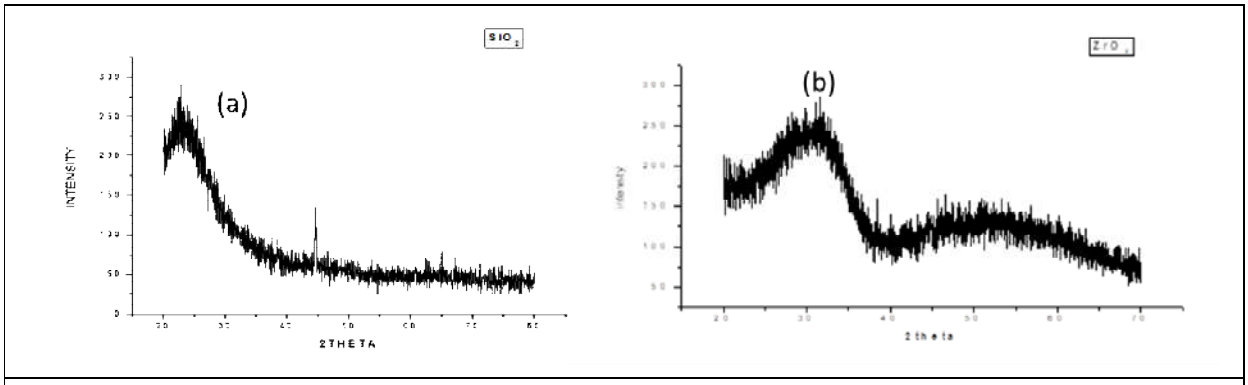


Figure 1. The XRD patterns of (a) silica, (b) Zirconia coated silica nanoparticles

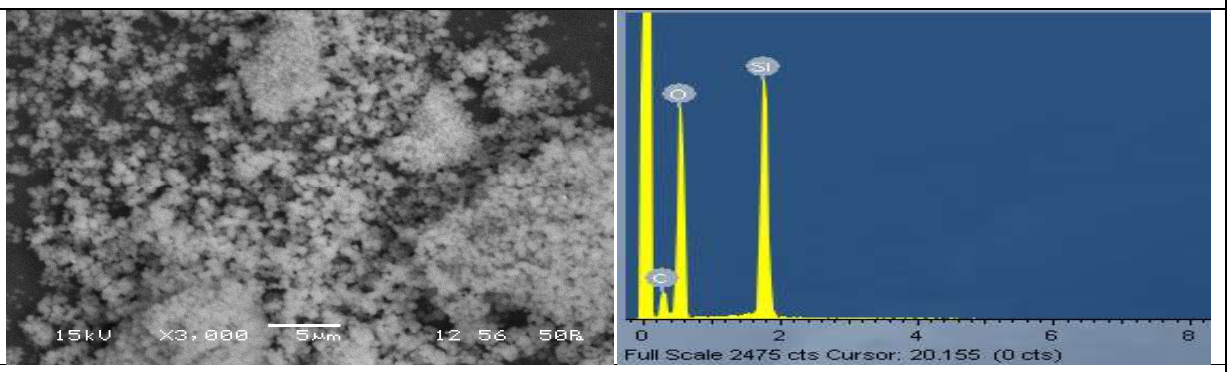


Figure 2. The SEM-EDX of silica particles

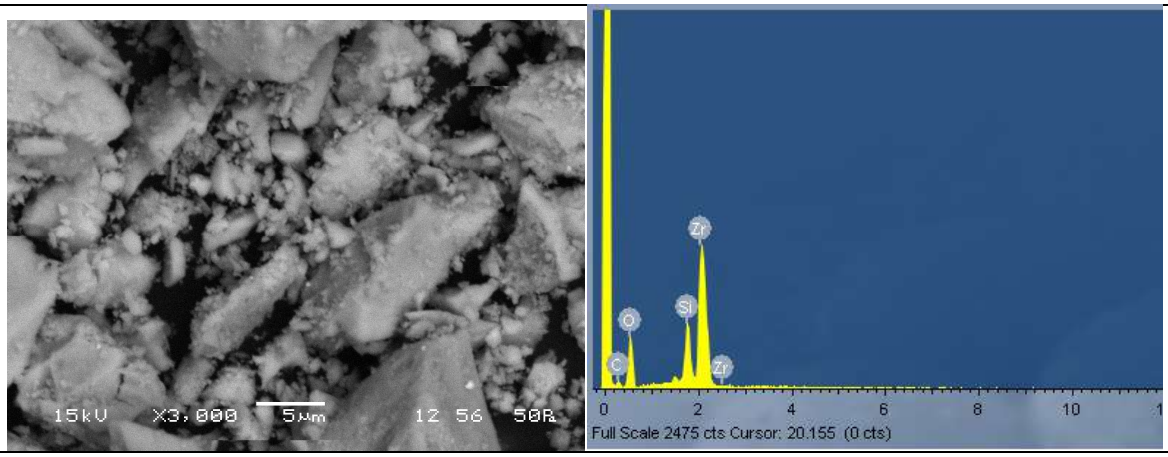


Figure 3. The SEM-EDX of SiO_2-ZrO_2 particles

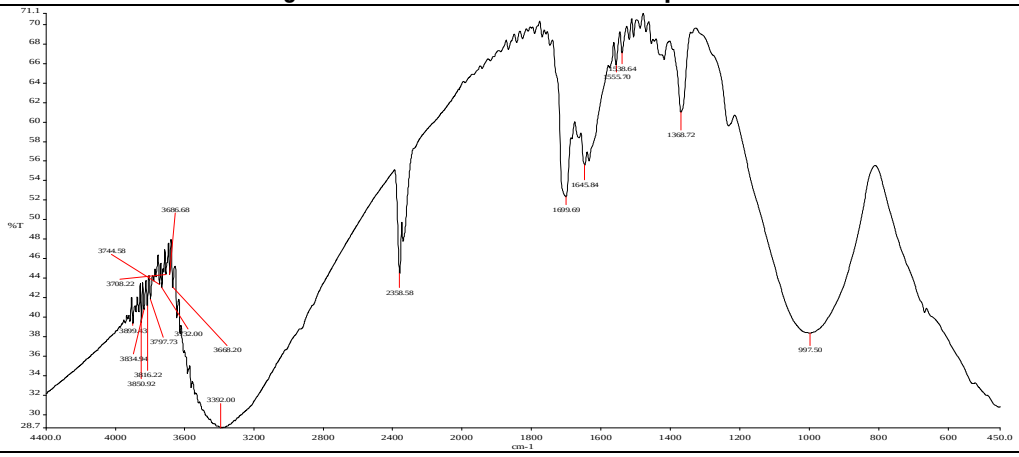


Figure 4. IR spectra of ZrO_2 coated SiO_2 nanoparticle

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REVIEW ARTICLE

Indian Traditional Plants used as Anti-cancer Agents and their Applications on Animal Models

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ABSTRACT

Cancer is a major health concern in both developed and developing countries. Several synthetic medications are used to treat the condition, but they have side effects, so researchers are looking into plant-derived chemotherapeutic drugs. As a result, a review of *In vivo* approaches for determining anticancer activities of natural compounds from medicinal plants has been attempted. Anticancer medicinal plants of Indian origin are reported in this review, together with extensive information on the portion used, the extract used, the type of model employed, and so on. These plants are still being utilised to treat cancers such sarcoma, lymphoma, carcinoma, and leukaemia. All of these plants could be used in *in vivo* investigations.

Keywords: Cancer, Herbal Approaches, Phytoconstituents, Anticancer, *In vivo* Animal models,

INTRODUCTION

Cancer is one of the top causes of morbidity and mortality in the world, with approximately 10 million fatalities in 2020, accounting for nearly one in every six deaths [1,3].Amongst different type of cancer: breast, oesophageal, lung, stomach, cervical, colon, rectum, ovarian and prostate cancers are the most frequent cancers. Breast, cervical, and ovarian cancers account for 34% of all cancer fatalities in women. Liver cancer, Lung cancer, oesophageal cancer, prostate cancer, and stomach cancer are the most common cancers among men[2]. Almost one-third of cancer fatalities are due to tobacco use, a high BMI, alcohol consumption, a low fruit and vegetable intake, and a lack of physical activity.It can be cured if caught early and appropriately treated. Cancer treatment has become a new field of study and is treated using both traditional and modern techniques. Different techniques like chemotherapy, radiation therapy, and surgery are some of the methods used to treat cancer [4]. All of them have some drawbacks. The usage of common chemicals has negative consequences and is hazardous [5,6]. However, since the problem remains, novel techniques to disease control are required, primarily because of the failure of existing chemotherapeutic techniques. Hence, new cancer preventive and treatment strategies are required to keep the

disease's death rate under control. Herbal therapy has evolved into a remarkably safe, nontoxic, and accessible source of cancer-fighting chemicals. Herbs are known to be able to counteract the effects of diseases in the body due to a variety of properties they possess [6]. There are numerous traditional herbal plants use in various parts of the world for their different pharmacological properties. We selected some Indian herbal plants for their anticancer properties. To induce apoptosis in cancer cells, metabolites derived from plant material are used. *Butea monosperma* (local name: Palash), *Terminalia chebula* (local name: Harida), *Andrographis paniculate* (local name: Green chiretta), *Podophyllum peltatum* (local name: Mayapple), *Catharanthus roseus* (local name: Periwinkle), *Zingiber officinalis* (local name: Ginger), and *Allium cepa* (local name: Onion), *Aloe vera* (local name: Aloe) are some anticancer medicinal plants that have been used traditionally for the anticancer benefits of their active components. Because of the introduction of new methodologies, the challenges associated with natural chemicals have been lessened, and interest in the utilisation of such natural substances in the pharmaceutical sector has grown [7,8].According to the World Health Organization, traditional therapeutic procedures are used by 80% of the world's population[9]. Hepatocellular carcinomas (HCC) are the world's fifth most common cancer, with a higher prevalence. Many research has been done on the treatment and prevention of HCC using herbal remedies, and it has been demonstrated that herbal components can affect all stages of HCC, including initiation, promotion, and progression [10,11]. This review focuses on the mechanism of action of a few Indian prominent anticancer plants, as well as active components, and its application in *in vivo* studies.

SOURCES AND METHODOLOGY

A systematic study of most relevant literature was retrieved through the electronic databases, Web of Science, Scopus, PubMed, and Google Scholar provided the most pertinent information. "Herbal medicines," "Anticancer activity," "Anticancer herbs," "Anticancer plants," "Mechanism of action," "Animal models," "*in vitro* activity," and "*in vivo* activity" were among the terms and phrases used in the search. After extraction and analysis using a combination of the above keywords/phrases and the inclusion criteria 200, relevant articles were found. Criteria were used in the articles choose certain selected anticancer plants, the phytochemicals of which are discuss in detail. Ten Indian traditional herbal plants were chosen for this study for which current articles were (a) *in vitro* and *in vivo* anticancer activities of herbal products, (b) anticancer activity of active ingredients from the plants, and (c) *in vivo* anticancer activity of herbal anticancer products were accessible. All of the data was compiled into a table, and the mechanisms of action were explained in subheadings and illustrated with various figures.

Selected Indian Traditional Herbal Plants And Their Anticancer Activities

Cancer is a malignant growth of body tissue or cells that is abnormal. A malignant tumour or malignancy is a cancerous development. A benign tumour is a non-cancerous development. The process of cancer metastasis is made up of a series of interconnected, sequential processes, each of which has a rate limiting step. Plants that are rich with chemicals that have chemo protective properties are being tested in clinical trials. Angiogenesis inhibition is a revolutionary cancer treatment method. This plant, when used correctly, can help with anti-angiogenic therapy and, as a result, cancer management.

Anticancer Activities Of Some Selected Indian Herbal Plant

Butea monosperma

In Tamilnadu, the plant *Butea monosperma* (L) Taub (Papilionaceae) is extensively distributed. It grows abundantly in open grassland and is distributed across mixed forests. Plantations can be grown on both irrigated and non-irrigated land. The leaves are naturally compounded. The three leaflets are abovate, with smooth margins, hairy abaxial surfaces, and glabrous adaxial surfaces. For feed, the green leaves are typically lopped. It's been observed that buffaloes fed Butea leaves produce more milk. They are used internally for flatulent colic, worms, and piles and are credited with astringent, tonic, diuretic, pimples, and tumorous [26,27,28].In a cancer model, the aqueous extract obtained from the dried flowers of B. monosperma was evaluated for antioxidative, anti-inflammatory, hepatoprotective, anti-proliferative, pro-apoptotic, and anticancer activities. It was found to inhibit cell proliferation

and accumulation of cells in G1 phase with significant induction of apoptotic cell death, implying promising anti-cancer properties. Furthermore, oral administration of the extract resulted in hepatoprotection in transgenic mice. [18].

Citrus medica

Citrus plants, which include fruits such as orange, mandarin, lime, lemon, sour orange, and grapefruit, belong to the Rutaceae family and appear to be a well-known promising source of various beneficial nutrients for humans. Due to the high volume of peel produced, citrus by-product processing could be a rich source of phenolic compounds and dietary fibre. Citrus fruit leftovers, which are usually dumped as garbage in the environment, could be used as a source of nutraceuticals. Such wastes are capable of providing significant low-cost nutritional dietary supplements due to their low cost and convenient availability [29]. The use of these bioactive-rich citrus leftovers could provide a cost-effective, environmentally friendly foundation for the development of new nutraceuticals or the upgrading of existing ones**.** From cancer cell start to promotion and eventually progression in the tumour microenvironment, substantial data suggests that flavonoids in citrus peel cover can prevent oncogenesis, proliferation, neovascularization, and metastasis while also triggering apoptosis [31]. Also, because of their plentiful antioxidants such as phenols, vitamin C, vitamin E, beta-carotene, and lipotene, these fruits and vegetables are considered to be the principal anti-cancer nutrients. Among these fruits, citrus is the most intriguing [19]. The anticancer impact of Citrus medica Linn. was investigated using the vital capacity test and the Ames test, with special emphasis on the utilisation of Salmonella typhimurium to identify antimutagenesis and anticancer levels of chemicals. Half-ripe and ripe fruit juices were found to have anticancer [30] and antimutagenesis effects in this study, with halfripe fruit juice being more effective than ripe fruit juice.

Aloe barbadensis

Aloe vera, a plant species in the Aloe genus, has been extensively explored for a variety of medicinal qualities, including antibacterial, antiviral, anticancer, immunoregulative, and hepatoprotective capabilities. It is a well-known natural chemical that was used in the tumour investigation. It contains polysaccharides, selenium, calcium, copper, zinc, chromium, and vitamins A, E, and C, as well as anti-inflammation, wound-healing, anti-hepatitis, and anti-gastric ulcer properties. Thus, Aloe vera's high anticancer and antimutagenic action could be attributed to the additive and synergistic antioxidant activity of phytochemicals such as flavonoids, triterpenoids, steroids, and others found in the plant [32].Although over 75 active compounds from the inner gel have been found, therapeutic efficacy has not been properly connected with each individual component. Aloe vera has been utilised for many centuries for its restorative and therapeutic characteristics. Many of the medicinal effects of aloe leaf extracts have been attributed to the polysaccharides found in the inner leaf parenchymatous tissue, but it is now thought that these biological activities should be attributed to a synergistic action of the compounds present rather than a single chemical substance. Glycoproteins (lectins) and polysaccharides are two aloe components that are said to have anti-cancer properties. A. Vera gel has been shown to have anti-tumor action in tests involving reduced tumour burden, tumour shrinkage, tumour necrosis, and longer survival [20].

Catharanthus roseus

Catharanthus roseus is a well-known medicinal plant that belongs to the Apocynaceae family and is high in alkaloids, which may be found in all parts of the plant. Two vinblastine and vincristine are dimeric alkaloids. Mostly prevalent in the upper portions of the body, substantial research has been done. It can be used to treat human neoplasma [33]. Vinblastine sulphate (Velban) is a drug that is used to treat Hodgkin's disease, as well as lymphocarcinoma, choriocarcinoma, neuroblastoma, and cancers of the breast, lungs, and other organs, in both acute and chronic leukaemia. Vincristine sulphate (Oncovin) stops mitosis in metaphase and is particularly successful in treating acute and lymphocytic leukaemia in children. Hodgkin's disease, Wilkins' tumour, neuroblastoma, and reticulum cell sarcoma are all treated with it. India is now the world's third largest producer of Vinblastine and Vincristine, and it exports these alkaloids to European countries [34]. In vivo/ In vitro, different percentages of methanolic crude extracts of Catharanthus were discovered to have considerable anticancer activity against a variety of cell types, with the greatest activity against multidrug resistant tumour types[21].

Podophyllum peltatum

Curcumin improved the anti-leukemic action of etoposide in Brown Norway rats with transplantable acute promyelocytic leukaemia (BNML) [30]. Rats were injected with leukemic cells and subsequently given curcumin (100–200 mg/kg) for 23 days. For the final three days of the experiment, etoposide (50 mg/kg) was given. Etoposide alone was found to effectively slow the growth of leukaemia in rats. Furthermore, when curcumin was given to rats at a dose of 200 mg/kg, it had an anticancer effect similar to etoposide. Furthermore, rats given 200 mg/kg curcumin followed by etoposide had a 1.57-fold tumour decrease and a higher reduction in spleen weight than rats given only etoposide [16].Podophyllotoxin is a non-alkaloid lignan isolated from the dried roots and rhizomes of *Podophyllum peltatum* or *Podophyllum emodi*. Etoposide (VP-16, epipodophyllotoxin) is a semi-synthetic derivative of podophyllotoxin (Berberidaceae). In 1983, the FDA approved etoposide for clinical use in the United States [36]. Despite the fact that etoposide was first created many years ago, it is still frequently used in the treatment of cancers such as small cell lung carcinoma[37], testicular carcinoma, leukaemia, adrenocortical carcinoma, breast cancer, and brain tumours [38].

Andrographis paniculate

The genus Andrographis, which belongs to the Acanthaceae family, is mostly found in tropical and subtropical areas [38]. *Andrographis paniculate* extracts and their major diterpenoid component significantly suppresses cell proliferation, induces cell cycle arrest, and induce cell apoptosis of various cancer cells. Andrographolide induced cell differentiation in mouse myeloid leukaemia cells, which showed strong anticancer activity. Various cell lines, including leukaemia, breast cancer, lung cancer, and melanoma cells, were found to be inhibited by andrographolide. Furthermore, through slowing cell cycle progression, this drug displays potent anticancer effect against human colorectal carcinoma LoVo cells. Various anti-cancer medicines decrease cancer cell proliferation by producing apoptosis, necrosis, cell-cycle arrest, or cell differentiation; others may have immunomodulatory effect, which involves activating the body's own immune system against cancer cells. Compounds that block several procancer processes are more interesting because they are more likely to inhibit a larger range of malignancies in a wide range of situations[22].

Terminalia chebula

Terminalia chebula Retz. (Combretaceae) is known in Tibet as the "King of Medicines" and is always listed first in the Ayurvedic materia medica due to its amazing healing properties and vast range of biological activity. *Terminalia chebula* Retz. fruit is used to cure a variety of ailments and disorders [39].In Swiss albino mice, an ethanolic extract of *Terminalia Chebula* fruit effectively suppressed tumour growth in EAC-induced cancer. The animals' haematological parameters are restored, tumour volume is reduced, and their longevity is increased as a result of this activity. These findings imply that *Terminalia Chebula* could be an effective cancer treatment [23].

Semecarpus anacardium

Semecarpus anacardium Linn. (Family: Anacardiaceae) is a plant used in Ayurvedic and Siddha medicine for its therapeutic properties. Its nut contains biflavonoids, phenolic compounds, bhilawanols, minerals, vitamins, and amino acids, according to chemical and phytochemical tests. This source's nut extract preparations are beneficial against a wide range of ailments, including arthritis, tumours, infections, and so on[40,41].When compared to EAC (Ehrlich Ascites Carcinoma) control mice, oral administration of *Semecarpus anacardium* nut extracts at a concentration of 200 mg/kg body weight reduced tumour area and volume in tumour bearing mice [24].

Mimosa pudica

Mimosa pudica Linn is a member of the Mimosaceae family. The entire Mimosa pudica plant is beneficial for a variety of pharmacological and biological functions. Mimosa pudica root and leaves have the highest pharmacological action as an anti-diabetic, antitumor, antitoxin, antihepatotoxin, antioxidant, and wound healer. Paste of leaves, Ethanolic extract of seeds are responsible for anticancer activity [42]. When compared to the control group, DCM extract at doses of 500 mg/kg, 1000 mg/kg, and isolated chemical at 2.5 mg/kg significantly reduced tumour volume and viable cell count while increasing nonviable cell count in dosage treated mice. The anticancer effect of *Mimosa pudica*Linn.

(Fabaceae) has been discovered to be attributable to the stimulation of macrophages, which are essential cells in the immune system [25].

CONCLUSION

This analysis of several Indian plants revealed that medicinal herbs have a significant anticancer potential. The majority of the time, this is accomplished via controlling signalling pathways. Inhibition of enzymes that slow tumour growth has been documented in numerous investigations. Many plants, both known and unknown, have anticancer properties that need to be investigated further. This article depicts the objective of "Ensure healthy lives and promote well-being for all at all ages," which is included in Sustainable Development Goal 3 and demonstrates the reduction of non-communicable disease i.e Cancer Mortality.

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Table:1 Some Selected Indian Traditional Medicinal Plant With Information On The Parts Used, The Extract Used, The Type Of Model Hired.

S. No	Common name	Botanical Name	Part or Constituent Used	Animal model	Dose Concent-ration	Std Drug compare	Ref.
1	Palash	*Butea monosperma*	Leaves (Ethanolic extract) Flowers	Swiss albino mice	200 and 400 mg/kg (p.o)	5-Fluorouracil (20 mg/kg/day i.p)	[12,13]
2	Lemon	*Citrus medica*	Citrus peel (water extract)	Swiss Albino mice	25 mg/kg (p.o.)	Vincristine (10 mg/kg) (p.o.)	[14]
3	Indian Aloe	*Aloe barbadensis*	Leaves	Swiss Albino mice	500 mg/kg (Topical and p.o)	Cyclophosphamide (50 mg/kg i.p)	[15]
4	Periwinkle	*Catharanthus roseus*	Leaves (Endophytic fraction)	Albino rats	200mg/kg and 150mg/kg (p.o)	(5-Flurouraci130mg/kg (p.o)	[17]
5	Mayapple	*Podophyllum peltatum*	Polyphenol (Curcumin)	Brown Norway rats with acute myeloidleukemia (BNML)	100 and 200 mg/kg (p.o)	Etoposide (50 mg/kg)	[16]
6	Harida	*Terminalia chebula*	Fruits	Swiss Albino mice	100 mg/kg and 200 mg/kg (p.o)	5-FU, 20 mg/kg/day, i. p	[23]
7	Bhilwa	*Semecarpus anacardium*	Nuts	Nude mice	200 mg/kg; body weight/day (p.o)	Cyclophosphamide (200 mg/kg; body weight/day	[24]
8	Mint	*Mimosa pudica*	Flower (Dichloromethane (DCM) extract)	Swiss albino mice	250 mg/kg, 500 mg/kg, and 1000 mg/kg (p.o)	Methotrexate at 2.5 mg/kg/day (p. o)	[25]

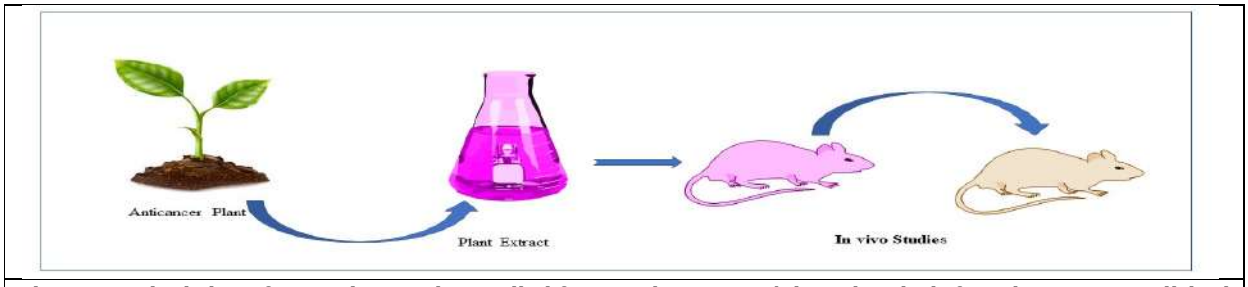

Figure 1: A depiction of general strategies applied for assaying extracts/phytochemicals from important medicinal plants for their anticancer activity in vivo constructed through Chembiodraw.

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RESEARCH ARTICLE

Global Scenario on the use of Biofertilizer

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ABSTRACT

Innovative cultivation lost its enduring due to overloaded apply synthetic manure and damaging or unfavorable insecticide further result of high amount price of farming, decrease food certainty and well-being. Finally reached the depletion in loam productivity or richness. Customers are discussed with their food sanctuary, enlargement of interest in rest farm production and catalogue registration contrasted with synthetic fellow paved the way to sharp investigation on the harvesting of manure and toxicant. In helping herb-growing-microorganism significance in supporting herb strength and extension as its reciprocal relationship in herb grow the solubility of Lucifer, ammonia and aqua uptake, withstand infectious disease and enrich yielding of phytohermones. Accordingly, that originate a considerable share out for continuous farming by the utilize of manure and toxicant that is the cooperation of biological science herb cultivator, herb physician and agronomists are required so as mature methods of biological yielding added save loam productive. Plant nutrients, macro nutrients on one hand and micro nutrients on the other hand, are the necessities for the generation of crop and production of foods to provide the fooding to the highly increasing population. Morti-Agricultural strategy currently are largly dependent on the organic chemical based fertilizers, which no doubt have the potentiality to feed the worldwide population but it never human health on one side and ecosystem on the other alternative to chemical fertilizer is the biofertilizer. As the name biofertilizer is amalgamation of the words that is" Bio" and" fertilizer", " Bio" refers to the biotic and "fertilizer" refers to a substance which when added to the soil increases the fertility and aids in the better growth and development of plants so "Bioferilizer" can be defined as a substance which includes the biofilms or the microbs which when added to the soil , conquer the rhizosphere on the internal portion an assist the growth and development of the plant.

Keywords: Agriculture, Microorganisms, Manure, Nutrients, Organic farming, Phytohormones, Sustainable, Toxicant.

INTRODUCTION

In global industry for manure is calculated to extend US$3.3 billion by 2025, operated by the increase in size center of authority global to decrease cultivation's maturity carbon footstep and build it new long-lasting (Gonet SS, Debska B,1999). The objective arrives in opposition to the background of protests complexed in weather interchange situation. Several advantages of biofertilizers increase its wide applications in sustainable agriculture .As the biological fertilization process relies on the supplement of organic inputs, living microbes like fungi and bacteria, it is highly essential for the healthy agriculture(Lal R,2011).The current study reviews the worldwide scenario of utilizisation of the ecofriendly biofertilizer is sustainable agriculture. During the last three decades the growth in the agricultural production increases by the use of different chemical fertilizer(Haynes RJ, 2005).These are not only causes the harmful effect in human beings but also effect in the quality of soil and the microorganisms, which are present in the soil and the ground water also(Gonet SS,1989).

Biofertilizer is one of the important and essential product for the growth and the development of the plant, and can provide the biofertilizer contains the microorganisms which are live bacteria, fungi and algae to enhance the nutrition. The microorganisms help in the enhancement of the fertility of the soil by fixing the atmospheric nitrogen, and solubilization of phosphate and potassium, and they are used in decomposition on the organic compound that are present in soil. The microorganisms enhance the production of growth promoting substance which affects the metabolic process of the plant (Fatunbi AO, Ncube L,2009). Biofertilizer proves to be economical, ecofriendly, more efficient productive and accessible to marginal and small farmers over the chemical fertilizers. In bacterial biofertilizer, the symbiotic and free living bacteria that contain Nif-gene which are capable for fixation of nitrogen. *Rhizobium* and *Azospirillum* are the important bacteria which enhance nitrogen to plant. Symbiotically by the formation of root nodules, the other free living bacteria like *Azotobacter, Kiebsiella* also used in N2 fixation (Marschner B, Kalbitz K,2003). Biofertilizer is added to the soil to conquer the rhizosphore on the internal portion of the plant and assist the growth and development of the plant by enhancing the contribution of primary nutrients ,biofertilizer or the micro inoculants guide the formation of atmospheric nitrogen through the process nitrogen fixation with the involvement of microorganisms so called Biological Nitrogen Fixation (BNF) aids in the solibilization of the plant nutrients like phosphorus, helps in the stimulation in the plant development through production of different plant promoting substance(Pejada M, Benipez C,2011) .

Besides bacteria, algae like *cyanobacteria* which are mostly used in biofertilizer and some fungi like *Mycorrhizae* (symbiotic association of plant root and soil fungus) play great role in inducing plant growth, mainly these microorganisms mobilize different types of nutrients like Cu, K, Al, Mn, Fe, Mg from the soil to the plant root(Li W, PanKW, Wu N,20014).The increasing number of different microbial preparation for agricultural use are mainly available in our market and also increasing the interest in their use in agricultural practice[9]. This goal comes in the against the backdrop of the challenges involved in fielding a growing global population in the midst of progressively climate change conditions (KiikkilaO, Karneva, 2014). As the increase in the production of food and crop there is a great need to make agriculture more resistant and efficient in an eco-friendly manner. The scenario is creating strong opportunity for biofertilizer, commercialization of crop probiotics will bring in massive opportunities for robust growth in the coming years (Zhao Y, LiW, Zhou Z,2005).

Application

In present day, the sustainability of agriculture is lost by the use of excess amount of chemical manure and pesticides, and it is also the cause of exclusive process of cultivation, insecurity of food and the result is loose of fertility in the soil. Importance of promoting plant is gained by the plant growth-promoting bacteria (Wu SC,Cao ZH et. al,2005). Soil quality and yield of plants are improved by biofertilizers. Pathogens are not allowed for growing.

They are environment-friendly and money making. Biofertilizers are natural fertilizers so they protect the atmosphere. *Azotobacter*, *Azospirilium*, *Rhizobium* and blue green algae are the biofertilizers which have been in use a long time. In leguminous plant, *Rhizobium* inoculant is used and in the crops like wheat, maize, potato, mustard and other vegetable plants, *Azotobacter* is used (Wilding LP,1995).

Methods of Application:

Seed Inoculation: The regular applying of bioferilizers is seed inoculation or seed treatment. 10% solution of jagerry is added. This mud is then spouted the seed and spread on the floor. This should be mixed properly and a thin layer is formed. The seeds are dried in shade area and then used. Biofertilizer is used as about 700gm for using the legume seed in a one-hactare area (Valarini PJ,Diaz MC *et. al,* 2003). Seedling Root Dips: Before transplantation in the field, the roots of transplanted plants are treated for half an hour. In this method, the seed is required for 1 area which areinoculed with 2-2.5kg bioferilizer. For this, the water is taken by a bucket and mixed up the biofertilizer perfectly. Then, the roots of seedling are dipped in this solution and the root is getting inoculate. Then the seedlings are displaced. This application is very acceptable for crops like onion, tomato, rice and flowers (JakubusM,Gajewski P,2013).

Main Field Application: The application is suitable for fruit crops, sugarcane and other crops where localized application is required. At the time of farming of fruit trees, in the ring of one sapling, 20kg of biofertilizer and compost is mixed up. After its maturity, the same quantity of biofertilizer is mixed with the ring soil of the seedling. Biofertilizers are applied in the soil for sometimes but it is required 4 to 10 times more. The inoculants need to be incubated with the well decomposed manure before using for 24 hours (ValariniPJ,Disz MC,2003). Self-Inoculation Or Tuber Inoculation: This application is completely used for *Azotobacter* biofertilizer. For one acre of land planting materials are required and sinked with the mixture. Similarly, if we are doing experiment with potato, then the tuber is emerged with the mixture and after the materials are dried in the shade, planting is done(KrasowiczS, Oleszek W,2011).

Environmental Impact: Wild animals are affected by fertilizers in less than in differentiation to the harm affected by pesticides. These are affected to the human health also. Blue baby syndrome is caused due to the drinking water of high nitrate concentration. It is also called as clinical methaemoglobinaemia (CoptyMK,Onay TT,2015) . Dust is the main cause to create the health problem by fertilizer. Lots of serious disease like cancer and gastric are originated from in questing of nitrate. Proper management is required by OHS, which is occupational health and safety. The occupational health and safety system of farmer assist guarantee the effective control of OHS threat, that averts the work related slash. Many hazards are occurring during the use of biofertilizer by farmers. The illness due to heat connection can be very dangerous. In every year, many employment become illness due to heard and it is also caused of dead but these are preventable (Zhu J,Zhang W,2011). Mostly use repitive motion in difficult position during the agricultural process. MSD means musculoskeletal injuries diseases. The nitrogen of the atmosphere contain in the soil and the leguminous plant's root by the use of bioferilizers and this is a continue process which are available to the crop (Liu E,YanC,Mei X,2010). The soluble form of phosphate is solublized by the help of biofertilizer. They rummage the phosphate from the soil layers. Production of hormones and anti-metabolites promotes the growth of root. Soil is mineralized by the help of decomposition of organic matter. The implement of biofertilizer in the soil increases the nutrients and yield capacity (Wang YJ,Zhang L,2015). The enormous use of various fertilizers like insecticide and pesticides will be creating bad impact to the soil and the environment. For the best economic value this is very necessary to decrease the use of hazardous compound like chemical thing, so biofertilizer has to be creating their own advantages for a green microbial revolution (De Santo AV,Moschetti G,2011).

CONCLUSION

The quality and quantity can be changed by the application of UG max. The permanent humus compound and the presence of plant nutrients are increased through the use of biofertilizer. For microorganisms preparations are heavily numbers are used that is accessible sell in markets and grow profit in that utilize in industrial working purposes. In addition a few number of uncertain outcomes of analysis are announced have led to extra exploration into the correspondence in the middle of the loam conditions and microbial fertilizers. It also helps for maintaining the soil fertility for a long time. The supplement of nitrogen to the plants is occurring by the help of bacteria in the soil, which play the vital role of nitrogen fixation and make the nitrogen into a soluble form. In modern agricultural process, variety types of technologies are development and play the beneficial role. The scenario of agricultural process will be changed in future by the use of chemical fertilizer and it is also affecting the global scenario that will be created a demand for biofertlizer in coming years. In developing countries, the food demand is high for the high production of food. People use very machinery and chemically processes, which affect the environmental threats in the future time. Escalation leads to high insert of nutrients that is in the form of animal feed. These insert thing is disclosed to the ground water and loses the gas to the atmosphere through the process of nutrient leaching. From enteric fermentation the methane emission will double in the period 1990-2050 due to medium scenario. An insignificant global source will be endured by the ammonia of animal waste. The correlated methane outpouring may be become a major global source. The growing fertilizer uses have not been estimated from the environmental aspects. Between the root of plants and the bacteria, fungi and cyanobacteria (the blue green algae) having symbiotic relationship. Both depend each other for their shelter and nutrients. Biofertilizers help to the maintain of replenishing the nutrients in the soil. The toxicity and imbalance of nutrients of soil are occurring due to the use of chemical fertilizer which is affected to the environment mostly. In nature containing effective microorganism, biofertilizer used organic which is originated from either root nodule or rhizospheric soil. In present situation, there are two reasons for the use of biofertilizer first one is having the crop productivity with increase of our ever population and second one is the use of chemical fertilizer is very effective for the soil and the environment also which leads to damage the soil and increase the other environmental hazards(SDG-15 Life on Land)

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RESEARCH ARTICLE

Green Synthesis of Fe_2O_3 Nanomaterial using *Azadirachta indica* (Neem) Leaf Extract

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ABSTRACT

Green Chemistry is the design of chemical products and processes that reduce or eliminate the use and/or generation of hazardous substances. The synthesis of nanoparticles using bio based substances has been proposed as a cost-effective and environmentally friendly alternative to chemical and physical methods. Green synthesis method also comes under the SDG goals number 3, 11 and 12. An environmental friendly and cost-effective method was used for the preparation of silver-iron oxide α-Fe_2O_3 nanomaterials using Neem (*Azadirachta indica*) leaf extract.

Keywords: *Azadirachta indica*, Iron oxide, Nanocomposite

INTRODUCTION

Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a bulk scale or larger scale [1]. It is the science of objects with smallest dimensions ranging from a few nanometers to less than 100 nanometers. Nanoscience is the emerging field of material science with huge potential to bring benefits for mankind in areas as diverse as drug development, water decontamination, information and communication technologies, and the production of stronger, lighter materials [2].

Nanomaterials are those materials having atleast one of their dimensions at nanoscale range. Nanomaterials can be of zero dimension (e.g., nanoparticles), one dimension (e.g., nanofibers, nanotubes, nanorods, nanowires), two dimensions (e.g., nanofilms, nanolayers, nanocoatings), or three dimensions (e.g., dispersion of nanoparticles, bundles of nanowires, and nanotubes as well as multinano layers) [3,4].

Technology can be defined in more similar words as the ability of taking advantage of the progress of science to create novel opportunities for practical applications. Technology is the driving force for benefitting the mankind since it is an ultimate source of providing a wealth of novel materials, devices, and the machines capable of improving the living standards [5]. The technology at nanoscale that is already with us is that of microelectronics, material science and these technologies are "evolutionary nano". The nanotechnology whose form and importance is yet to be explored which is undefined is "revolutionary nano", that is, technologies emerging from new nanostructured materials (e.g., buckytubes) or quantum dots. Today, it is believable that the revolutionary nanoscience exists in the laboratories and that new forms of nanotechnology can change the face of the planet. It is possible that some day, this revolutionary science will change its course towards some other new technology and will going to scale up the benefits provided by nanoscale research [6,7].

A very broad definition says nanomaterials as those which have structured components with at least one dimension less than 100nm [8]. Materials like graphene, thin films, or surface coatings are two dimensional nanomaterials. Materials that are nanoscale in two dimensions (are extended in one dimension) include nanowires and nanotubes. Materials that are nanoscale in three dimensions are particles, for example quantum dots (tiny particles of semiconductor materials). Two factors cause the properties of nanomaterials to differ significantly from other materials: increased relative surface area, and quantum effects. These factors can change or enhance properties such as reactivity, strength and electrical characteristics [9,10]. Nanoparticles are defined as solid particles with a size in the range of 10-1000nm. These particles have at least one dimension smaller than 1 μm and potentially as small as atomic and molecular length scales (~0.2 nm) [11]. Nanoparticles are of great scientific interest as they are, in effect, a bridge between bulk materials and atomic or molecular structures. Scientific research on nanoparticles is intense as they have many potential applications in medicine, physics, optics, and electronics. Metal Nanoparticles can be synthesised by various processes including laser ablation, condensation from vapor, thermal decomposition, and wet chemical reduction of the corresponding metal salts, sol-gel methods, and hydrothermal synthesis [10-12].

Nanocomposites are multiphase solid materials where one of the phases has one, two or three dimensions of less than 100 nanometers (nm), or structures having nanoscale repeat distances between the different phases that make up the material [15]. Broadly speaking, it can include porous media, colloids, gels and copolymers, but is more often consider the solid combination of a bulk matrix and nanodimensional phase(s) differing in properties due to dissimilarities in structure and chemistry. The mechanical, electrical, optical, and thermal properties of nanocomposites differ largely from the component materials. Due to enhancement in physical and chemical properties, nanocomposites find various industrial applications in food packaging, medicine Photocatalysis, sensors, electronics, nanophotonics, controlled drug release, automobiles etc [12].

Iron oxide naturally occurs in three different mineral forms, hematite, magnetite and maghemite. As the mineral known as Hematite, Fe_2O_3 is the main source of iron. Hematite crystallizes in lattice in rhombohedral lattice system. Fe_2O_3 can also be obtained in various polymorphs. α-Fe_2O_3 has the rhombohedral, corundum (α-Al_2O_3) structure and is the most common form. Fe_2O_3 nanoparticle size ranges from 1-100 nm. Fe_2O_3 nanoparticles have diverse application as in case of magnetic resonance imaging to provide enhanced contrast in visualizing the presence of tumor. Also Fe_2O_3 can be used to as vehicle for targeted drug delivery as well as coating for nanoscale anti cancerous drug and for magnetic data storage. Apart from these Fe_2O_3 nanoparticles are also used in industries coatings, plastics, nanowires, nanofibers, and textiles and in specific alloy and catalyst applications [7,12].

Green Chemistry is the design of chemical products and processes that reduce or eliminate the use and/or generation of hazardous substances. The synthesis of nanoparticles using bio based substances has been proposed as a cost-

effective and environmentally friendly alternative to chemical and physical methods. Plant-mediated synthesis of nanoparticles is a green chemistry approach that connects nanotechnology with plants. The extract obtained from leaves, barks, and seeds are widely exploited for catalyzing a synthesis. The present scenario, where much effort are being paid towards searching green alternatives for conventional synthesis method has driven the research to a new scale where exploiting nature in more judicious way has shown a bright future for green synthesis [8-12].The Sustainable Development Goals (SDGs), also known as the Global Goals, were adopted by the United Nations in 2015 as a universal call to action to end poverty, protect the planet, and ensure that by 2030 all people enjoy peace and prosperity. The 17 SDGs are integratedthey recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. The beauty of this work is its full fill the SDGs number 3 (Good Health and well-being), 11 (Sustainable cities and Communities) and 12 (Responsible consumption and Production).

MATERIALS AND METHODS

Materials

All chemicals were analytical grade and thus used as received without doing any further purification. $Fe(NO_3)_3$ and Ethanol were purchased from were purchased from Merck, India. For all adsorption experiments, distilled water (DW) was used.

Preparation of plant extract

Fresh leaves of *Azadirachta Indica*leaves were collected from the campus of CUTM BBSR and were washed meticulously with water to remove any dirt and impurities and are then rinsed with distilled water to remove ionic impurities. The washed leaves were then cut and crushed using mortar and pestle, distilled water is added in 5:1 ratio. This solution is gently heated to about 60-80^{o}C for 10 minutes and cooled down at room temperature. The solution is filtered and centrifuged for 5 minutes at 4000 rpm. The obtained plant extract is ready to use. Extract can also be stored for 2-3 days if required.

Preparation of Fe_2O_3 nanomaterial

To prepare Fe_2O_3nanomaterial, firstly 0.1 M$Fe(NO_3)_3$ solutions are prepared using DW. After complete homogenization of the solution, leaf extract is added drop wise to the solution using a burette with constant stirring in approximately 1:1 ratio for about 15 min. After complete formation of precipitate, solution is kept for undisturbed again for 45 min and then it is centrifuged for 5 min at 4000 rpm. The precipitate obtained is washed thoroughly with DI water and alcohol for removal of ionic impurities followed by Acetone to remove any organic impurities. Formed precipitate is then oven dried followed by combustion at 400 ^{o}C for 12-14 hours. The overall synthetic procedure is shown in Fig. 1.

CONCLUSIONS

Green Chemistry is the design of chemical products and processes that reduce or eliminate the use and/or generation of hazardous substances. The synthesis of nanoparticles using bio based substances has been proposed as a cost-effective and environmentally friendly alternative to chemical and physical methods. An environmental friendly and cost effective method was used for the preparation of silver-iron oxide α-Fe_2O_3 nanomaterials using Neem (*Azadirachta indica*) leaf extract.

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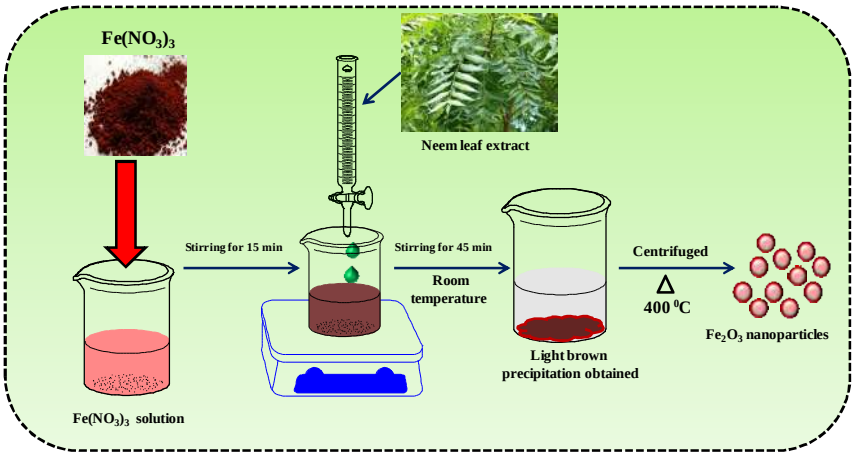

Fig. 1. Green synthesis of Fe_2O_3 nanoparticles using *Neem* leaf extract.

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RESEARCH ARTICLE

Effect of pH on Adsorption Efficiency of Methylene Blue Removal using MgO Decorated Graphene Oxide Nanocomposite

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ABSTRACT

In this present study, we have synthesized MgO, GO and GO-MgO nanomaterials by simple precipitation method by using magnesium nitrate as starting material and polyethylene glycol as stabling agent where sodium hydroxide is precipitating agent. Then obtained nanomaterials are calcined at 3500C to form desire product. FESEM images indicate the formation of fine nanoparticles on GO surface. The formation of the phase and crystal structure is determined by XRD and HRTEM study. Further confirmation of formation is done by FTIR and Raman using the different peaks. Then, the three prepared GO, MgO and GO-MgO nanomaterials were used as adsorbent for removal of carcinogenic Methylene blue (MB) dye from aqueous solution. From the adsorption study, it is found that among the three prepared materials GO-MgO nanocomposite is the most effective adsorbent for the adsorption of MB from aqueous solution due to synergetic effect of GO and MgO. From the experimental results concluded that MB adsorption is mainly pH dependent and maximum adsorption occur at pH=9 for GO-MgO.

Keywords: Graphene oxide, Magnesium, Adsorption, Methylene blue, Nanomaterials

INTRODUCTION

In the modernized society, the water pollution is a major global problem intimidating the life system, which accounts for a large number of diseases and death by consuming contaminated water. There are various types of water contaminants such as inorganic pollutants like arsenic, cadmium, chromium, fluoride, lead, mercury etc. and organic contaminants like acrylamide, phenol, benzene hexachloride, carbon tetrachloride and different organic dyes like

congo red, methyl blue, methyl orange etc. [1–4].From environmental safety point of view, the removal these inorganic contaminants from waste water effluent before discharging into natural water stream are extremely important [5–8]. Several processes like reverse osmosis, precipitation, activated carbon filter, membrane separation, ion exchange, photocatalysis, adsorption, solvent extraction, nanofiltration etc. have been used. Among them, adsorption is the most commonly used method, due to its low cost, simple operation and design requirements, low residual product generation, its lack of interaction with toxic substances and possibility to reuse the adsorbent[9–11]. The nano sized metal oxidead sorbents are known to be the promising candidates for removal of inorganic pollutants from aqueous media, due to their large surface areas and high reactive sites[12–14]. Due to environmental friendly and cost effective metal oxide (mainly Aluminium, Iron, Magnesium etc.) nanocomposites can be used in various field including catalyst industry, gas sensors, solar cells, adsorption and so on[15–19].They are classified as the promising ones for heavy metals and fluoride removal from aqueous systems. Many investigations have shown that metals oxide nanomaterials are good adsorbents. However, nano sized metal oxide adsorbents aggregate during adsorption process, and because of their small size,it is difficult to separate from waste water and it is also decreasing the adsorption capacity. In order to decrease the aggregation behavior of nanomaterials, easy separation and improve the adsorption capacity resent research focused on development of engineered nanomaterials mounted onto high surface area Graphene oxide nanosheet substrate [20,21].

Graphene is one of the most fascinating advanced carbon-based nanomaterials having a two dimensional honeycomb sp^2 carbon lattice, large theoretical surface area (2630 m^2/g), excellent chemical inertness, high transparency, enormous electron mobility, good thermal conductivity and remarkable elasticity [22–24]. Therefore, graphene is considered a favorable material for various applications such as sensors, transistors, catalysis, and environmental pollution treatment. Graphene Oxide (GO) is an oxidized derivative of graphene which contains epoxide, hydroxyl, and carboxyl groups. These functional groups lead to the negative charge, hydrophilicity and easy dispersion of GO in aqueous solutions. These characteristics make GO a potential candidate for the removal of different pollutants by adsorption [25,26]. Due to its large surface area and presence of large number of functional groups, GO can be used as an excellent platform to grow various nanoparticles. In addition, GO also helps in preventing agglomeration of nanoparticles therefore it can be effectively used as template/precursor for the growth of different kinds of nanoparticles. In case of functionalization of graphene oxide with metal oxide nanomaterials, graphene not only serves as a highly conductive support material but also provides a large surface for the dispersion of metal oxide nanoparticles [6,27,28].Now-a-day, surface modified GO by using different organic, inorganic groups and polymer has also been used for removing environmental inorganic pollutantsto achieve high adsorption efficiency because these functional group can form stable chelates with heavy metal ions. Metal oxide, based on functionalized graphene oxide nanocomposites has received more attention in the adsorption field due to achieve high capacity and electivity in the last few years [29–33].

The Sustainable Development Goals (SDGs), also known as the Global Goals, were adopted by the United Nations in 2015 as a universal call to action to end poverty, protect the planet, and ensure that by 2030 all people enjoy peace and prosperity. The 17 SDGs are integrated they recognize that action in one area will affect outcomes in others, and that development must balance social, economic and environmental sustainability. Countries have committed to prioritize progress for those who're furthest behind. The sustainable development goals (SDGs) are designed to end poverty, hunger, AIDS, and discrimination against women and girls. The creativity, knowhow, technology and financial resources from all of society is necessary to achieve the SDGs in every context. So, it is important to develop a system that satisfy the maximum goals of SDGs.

The main objectives of this research work are to synthesize different types of mixed metal oxides nanomaterials decorated onto GO substrate by using cost effective method. Studies on the formation, structure, surface morphology, surface area and crystallite size of prepared graphene-based nanomaterials by using FT-IR, XRD,FE-SEM and BET surface area analytical techniques. Environmental application of these GO based nanocomposite materials towards adsorptive removal of dye molecules from aqueous solution. The beauty of this work is its full fill

the SDGs number 3 (Good Health and well-being), 6 (Clean water and Sanitation), 11 (Sustainable cities and Communities) and 12 (Responsible consumption and Production) and 14 (Life below water).

MATERIALS AND METHODS

Materials

All of the chemicals were of analytical grade and used without further purification. Graphite powder (300 mesh), Poly ethylene glycol (PEG; Mn=20,000), Magnesium nitrate hexahydrate ($Mg(NO_3)_2.6H_2O$) and Methylene blue dye were bought from Sigma Aldrich (USA). Ethanols (C_2H_5OH), Sodium Hydroxide (NaOH), Hydrochloric acid (HCl),potassium permanganate ($KMnO_4$), hydrogen peroxide (H_2O_2, 30%), sulfuric acid (H_2SO_4, 98%)were purchased from Merck (INDIA). A standard 1000 mg/L concentration of Methylene blue solution was prepared by adding appropriate amount of MB in 1000 mL of double distilled water. The desired MB solution was prepared by dilution of this stock solution.

Preparation of Adsorbent

Synthesis of GO

GO was prepared from graphite powder according to modified Hummer's method by oxidation treatment of GO [34]. Briefly, 3 g of graphite powder and 3g of sodium nitrate were dissolved in 75 mL of sulfuric acid (98%) and stirred for 2h in ice bath. After that 9g of $KMnO_4$ was added slowly under continuous stirring conditions for another 2h. The temperature of the reaction mixture was increased to 98 °C and continuously stirred for 12 h. Afterward, the suspension was cooled to room temperature and mixed with ~100 mL water followed by 30mL of 30% H_2O_2 and sonicated for half an hour to exfoliate GO into single layers. The diluted mixture was then centrifuged for 15min at 10,000 rpm. The solid residue was washed with 5% HCl and distilled water several time for complete neutralization followed by vacuum-dried at room temperature for 12 h, to obtain GO powder.

Synthesis of MgO nanomaterial

Co-precipitation method was used to synthesize MgO composite nanomaterials[35]. In this method, $Mg(NO_3)_2.6H_2O$and polyethylene glycol (PEG; MW: 20,000) were dissolved in 70 mL of ethanol with 1:2 mol ratios of Mg and polymer respectively (where PEG was used for controlling the size of the nanocomposite). Then 2M NaOH was added dropwise to the mixture up to pH 11 under magnetic stirring. After 3h of vigorously stirring, the white precipitated reaction mixturewas obtained. After that the prepared sample was washed several times with ethanol and distilled water and then dried at 60^0C for 4 hours. Then the dried sample was calcined at 350^0C for 3hours with heating rate 10^0C /min to form MgO nanomaterials.

Synthesis of GO-MgO nanocomposite

A simple one step co-precipitation method was used for the synthesis of GO-MgO nanocomposite in which $Mg(NO_3)_2.6H_2O$and polyethylene glycol (PEG; MW: 20,000)acted as the MgO precursor where GO is the supporting material (shown in Figure-1). In this synthetic procedure, 0.5g of GO was spread uniformly into 30 mL of ethanol by ultrasonication for 1 h. In another beaker, 30 mL of ethanolic solution of$Mg(NO_3)_2.6H_2O$and PEG with 1:1:2 mol ratios of Mgand PEG was taken and stirred vigorously for 60 min. After that, the GO suspension wa sadded to the above solution with stirring. Then the pH of the reaction mixture was adjusted up to 11 by drop wise adding of 2M NaOH solution under stirring. Then black colored composite was obtained and It was separated by centrifugation and then continually washed with distilled water and ethanol, and then dried at 60^0C for 4 hours. Then the prepared sample was calcined at 350^0C for 3hours with heating rate 10^0C /min to form GO-MgO nanocomposite.

Characterization

The crystalline structure of the prepared GO based composite nano adsorbents was studied by using a PAN analytical powder X-ray diffractometer (XRD) with Cu Kα radiation (l) 1.54156 A^0. The X-ray scanning rate was 10^0/min with a step size of 0.05^0. The functional groups of the prepared composites were characterized by Fourier

transform infrared spectrometry (FT-IR) on a Nicolet IR100 Spectrometer in the range of wave number from 4000–400 cm^{-1}.Nova Nano SEM 450 Field emission scanning electron microscopy (FE-SEM) was used to understand the morphology of prepared nanocomposites and It is worked at an acceleration voltage of 15-20 kV. The selected area electron diffraction (SAED) pattern and diameter of the prepared nanocomposite was observed using a high resolution transmission electron microscope (JEM-2100 HRTEM, Make-JEOL, Japan) with an acceleration voltage of 200 kV. The elemental composition was determined using energy-dispersive X-ray spectrometry (EDX).The specific surface area and pore size distribution (PSD) of the nanocomposites were found using nitrogen adsorption/ desorption isotherms which was performed at liquid nitrogen temperature in an automated physisorption instrument (Autosorb-iQ, Quantachrome Instruments).

Adsorption Experiments

In order to investigate the removal of Cr(VI) a number of adsorption experiments were performed by changing pH and dose. All the adsorption studies 0.05g of adsorbent was used in 50mL of 100 mg/L MB solution in 100 mL of blue capped glass bottles with a fixed time of continuous shaking using a thermostatic orbital shaker at 200rpm. After adsorption experiment, the composite nano adsorbents were detached out using a centrifuge with 8000 rpm for 15 min, after that the adsorbent free solution was collected for analysis. The MB concentrations after adsorptions were determined by a UV-visible spectrophotometer (UV-Shimadzu 2450) with maximum wave length at 664 nm. All the above experiments for MB removal were carried out at room temperature. The equilibrium adsorption capacity (q_e in mg/g) and percentage of removal efficiency (%R) were obtained using equations 1 and 2 respectively[36].

$$q_e = \frac{(C_0 - C_e)V}{m} \quad (1)$$

$$\%R = \frac{(C_0 - C_t)}{C_0} \times 100 \quad (2)$$

Where C_0 (mg/L) and C_t (mg/L) are the concentration of MB initially and at time t respectively. C_e (mg/L) is the equilibrium concentration of MB in aqueous solution. V (L) and m (g) are the volume of solution and mass of the adsorbent respectively.

RESULTS AND DISCUSSION

Characterization of Nanocomposites

Fig. 2 reveals the XRD patterns of GO, MgO and GO-MgO nanocomposites. The peak at 2θ=10.85° **was confirmed the formation of GO from graphite powder.** The XRD pattern of MgO contains characteristics peaks at at 2θ=37.05°, 43.42° and 62.1° belong to the plane (111), (200), and (220) respectively are index to cubic structure of MgO according to JCPDS no. 45-0946 [37]. For GO-MgO all the above peaks are found but the peaks intensity decreases due to the polycrystalline nature of composite [38].

In order to examine the presence of functional groups in nanocomposites, FTIR measurements were conducted. Figure-3 shows the FTIR of GO, MgO and GO-MgO. For GO, the peak at 3468 is due to stretching vibration of O-H group. The peaks at 1730, 1620, 1430 and 1050 cm^{-1} are ascribed due to oxygen containing group of GO and correspond to stretching vibration of C=O group, vibration of C=C in aromatic ring, stretching vibration C-OH group and stretching vibration of C-O of epoxide group respectively[20,39]. The bands at 467 cm^{-1} correspond to Mg-O stretching vibration respectively in GO-MgO. Some peaks of GO are vanished in case of GO-MgO due to the formation of nanoparticles on the GO surface through some functional group.

The FESEM image of the GO (Figure-4a) showed the characteristic wrinkled and sheet-like structure with smooth surface. The FESEM image of the GO-MgO nanocomposite is shown in Figure-4b, which clearly indicates that nano particle was formed onto the GO layers with different morphology compare to GO.Figure-4c shows the SEM-EDX spectra of GO-MgO, from this figure we have confirmed that the prepared composite contains Mg, C and O with

16.24, 25.34 and 58.42 weight percentages respectively. We have also performed the nitrogen adsorption–desorption isotherms and BJH pore size distributions studies of the prepared GO-MgO sample and the results are shown in Figure-5.Isotherm plot of this composite represents a type II isotherm curve having surface areas 62 m^2/g The pore size distribution of GO-MgO nanocomposite in the inset of Figure-5 is calculated from the isotherm plots with BJH method, which shows that the poresize is 4.6 nm.

Effect of pH on Adsorption efficiency of MB

Figure-6 shows the effect of dose on %removal of MB by GO, MgO and GO-MgO nanocomposites. The %removal increases with increase in dose up to 0.07g for all three materials. The increase in % removal may be because of increase in the sum of active sites with adsorbent dosage. However, further increase in the adsorbent dose, the %removal all most constant because at higher adsorbent dose the concentration of MB molecules present in solution are not enough to cover all adsorption sites. Thus equilibrium adsorbent dosage for MB was 0.07 g and this amount was used for all adsorption experiments. Further it is also found that GO-MgO has more adsorption efficiency compare to GO and MgO due to more active sites

As pH can change the surface charge and properties of adsorbent, hence pH of the solution is an important parameter that can greatly affect the MB adsorption on adsorbents surface [39].The effect of pH ranging from 2.0 to 10 on the adsorption efficiency of MB on GO, MgO and GO-MgO are shown in Figure-7a. From this Figure, it is clearly observed that, the maximum efficiency achieved at higher pH value (pH=9) for MB for all materials. For better understanding the above phenomenon, the pH_{ZPC} value and structural formula of MB at different pH were considered. As seen in Figure-7b, the pH_{ZPC} value was 5.32. The pH value is greater than 5.32, the surface of the adsorbent become negative. As we know MB is a positively charge dye and it attract more at pH greater than 5.32 by electrostatic interaction between MB and negatively charge adsorbent surface that achieved higher adsorption at higher pH and lower adsorption value at lower pH[40,41]. Here also we found that GO-MgO has achieved more adsorption efficiency compare to GO and MgO.

CONCLUSIONS

In this present study, we have synthesized MgO, GO and GO-MgO nanomaterials by simple precipitation method by using magnesium nitrate as starting material and polyethylene glycol as stabling agent where sodium hydroxide is precipitating agent. Then obtained nanomaterials are calcined at 350ºC to form desire product. FESEM images indicate the formation of fine nanoparticles on GO surface. The formation of the phase and crystal structure is determined by XRD study. Further confirmation of formation is done by FTIR and Raman using the different peaks. Then, the three prepared GO, MgO and GO-MgO nanomaterials were used as adsorbent for removal of carcinogenic MB dye from aqueous solution. From the adsorption study, it is found that among the three prepared materials GO-MgO nanocomposite is the most effective adsorbent for the adsorption of MB from aqueous solution due to synergetic effect of GO and MgO. From the experimental results concluded that MB adsorption is mainly pH dependent and maximum adsorption occur at pH=9 for GO-MgO.

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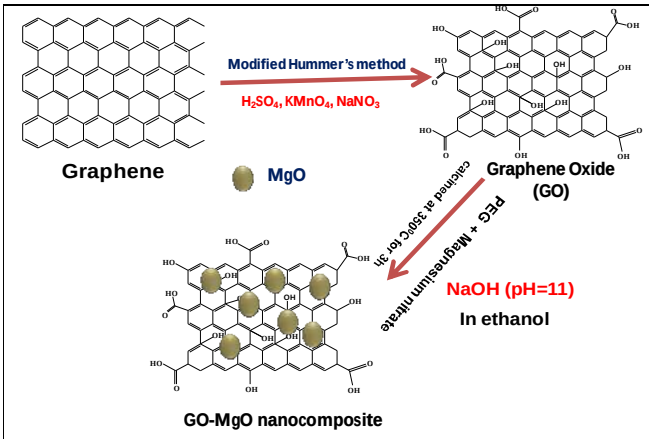

Figure-1: Synthesis route of GO based MgO nanocomposite.

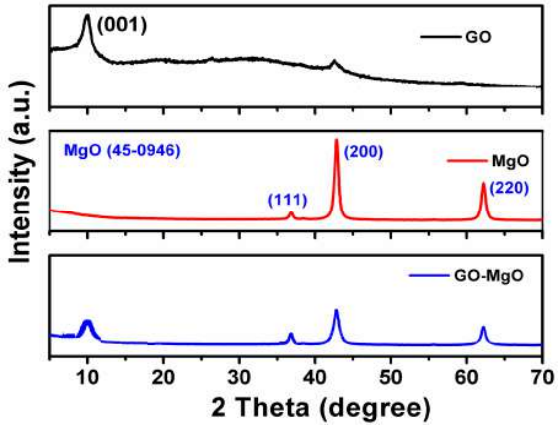

Figure-2: XRD pattern of GO, MgO and GO-MgO nanocomposite

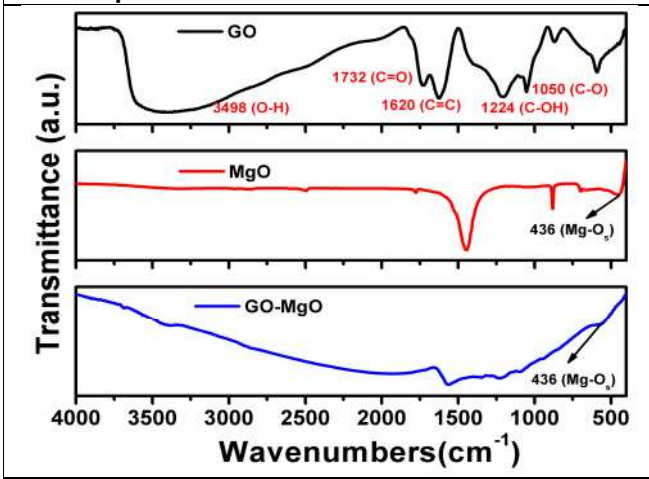

Figure-3: FTIR spectra of GO, MgO and GO-MgO nanocomposite

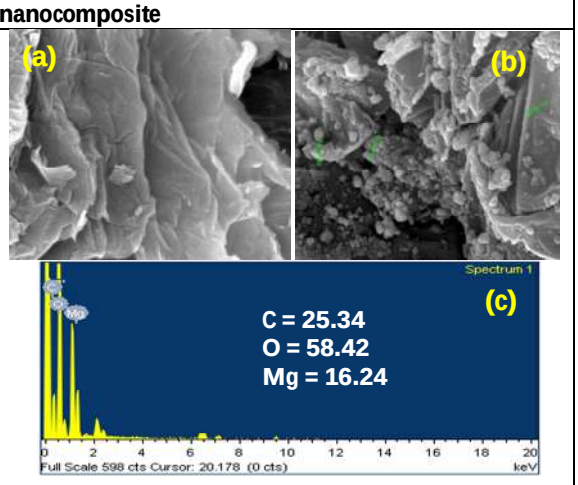

Figure-4: FESEM images of (a) GO, (b) GO-MgO and EDX spectra of GO-MgO nanocomposite

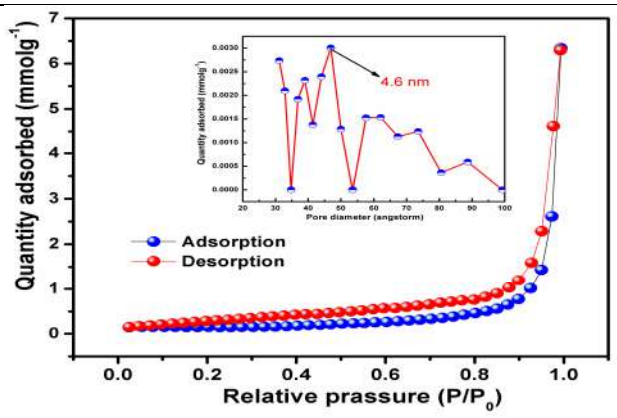

Figure-5: The nitrogen adsorption–desorption isotherms and BJH pore size distributions of GO-MgO nanocomposite

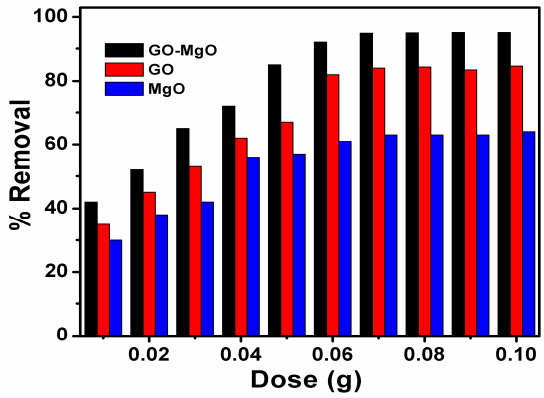

Figure-6: Effect of adsorbent dose for MB adsorption on GO, MgO and GO-MgO

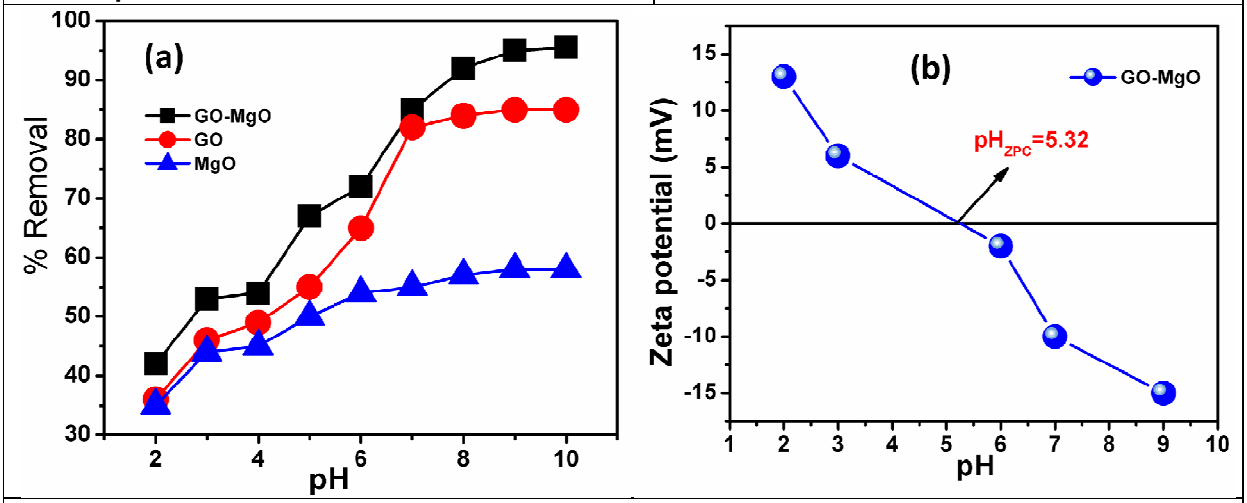

Figure-7 (a) Effect of pH on MB removal on MgO, GO and GO-MgO; (b) Zeta potential study of GO-MgO nanocomposite

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RESEARCH ARTICLE

Innovative Entrepreneurship to Reinvigorate the Economy of Odisha in the Realm of COVID-19 Pandemic

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ABSTRACT

One of the most vital driving elements behind a successful economic system is innovation. Cutting-edge and inventive entrepreneurs are adding new dimensions to economic growth and advancement in today's competitive and progressive world. Odisha's economy has been well-designed, with an emphasis on global infrastructural development, innovative academic culture, and appropriate training options for the essential talent. Between 2011-12 and 2017-18, the state's economy grew at an excessive rate, with the state's GSDP increasing at a CAGR 10.20%. Odisha's economy is constricting as a result of the present COVID-19 crisis. Since April 1, 2020, the COVID-19 pandemic has spelled disaster for the Micro, Small, and Medium Enterprise (MSME) sector in Odisha, with 3,207 units shut down. However, firms in the post-COVID age are expected to operate in a very different way, with a lot of room for innovation. In the coming years, the Odisha government wants to produce as many MSMEs (micro, small, and medium companies) as possible. Despite a number of hurdles, the startups that have sprung up in recent years have not only brought new ideas to the table, but they have also evolved into key job providers in the state, helping to boost the economy. The purpose of this research is to look into the relationship between entrepreneurship, innovative entrepreneurship, and economic development in Odisha. The paper's main goal is to highlight the major impediments that entrepreneurs encounter in wake of recent government policy. This critical assessment serves as a basic analytical framework for regulators and entrepreneurs in Odisha who want to make the state self-sufficient.

Keywords: Economy, innovative entrepreneurs, key barriers, self-reliant Odisha, startups.

INTRODUCTION

Innovation and entrepreneurship are two essential drivers of economic growth in the contemporary environment. Innovation is defined as the introduction of a new or considerably upgraded product, service, or process, a new

marketing technique, or a new organisational method in company processes, workspaces, or external relationships. Entrepreneurs, on the other hand, are business owners who seek to generate or expand economic activity by identifying and pursuing new goods, methods, or markets (Bashir, Akhtar, 2016). When entrepreneurship and innovation are joined to build new firms based on fresh novel ideas, it is referred to as inventive entrepreneurship (Stefan, Comes, Szabo, & Herman, 2012). Because innovation is the bedrock of job creation, productivity growth, and entrepreneurial initiatives, competition heats up, forcing businesses to keep inventing or risk dying or having their products commoditized. Innovative economies are more productive, resilient, and adaptable to change, resulting in a higher quality of life.

As a result, it is a major engine of economic development and growth (OECD, 2015). At the moment, creative and modern start-ups are attempting to disrupt current sectors. Existing businesses, on the other hand, relies on creative skills and practices to stay afloat. Interesting ideas can be turned into viable start-up businesses through innovation and ingenuity. These days, a start-up must come up with new ideas and concepts in order to develop not only products but also services that satisfy changing tastes and preferences (Nanda, 2020). Entrepreneurship is defined as a creative and innovative response to the environment, as well as the capacity to recognize, establish, and execute on a business opportunity. In today's global environment, sustainability or innovative idea-based entrepreneurship demands stakeholders to update their processes. Traditional or out-of-date businessmen conducting ordinary tasks, on the other hand, have not been recognized as entrepreneurs. Entrepreneurship has the power to change an individual's growth structure as well as the economy's prosperity and progress (Manocha, 2012). Because they build or own their highly specialized market niche and have high-capacity development potential to increase the region's economy as a result of globalization, innovative firms are the "hidden champions" (Litz, 2013).

Odisha is an Indian state in the east recognized for its unique culture, abundant wildlife, natural resources, ancient sites, and various handicrafts, all of which provide potential for various organizations. When it comes to entrepreneurship in Odisha, Bhubaneswar, Cuttack, Rourkela, Brahmapur, and Puri have all emerged as start-up destinations. The Odisha government wants to create 0.4 million jobs by fostering 0.15 million MSMEs during thefiscal year 2015-19. An entrepreneurial development policy is being finalized by the MSME department. The state's fast-growing start-up culture is aided by the presence of world-class educational institutions and industrial behemoths. The state's youths are talented, energetic, and creative. When talking with corporate think tanks, it is discovered that several cities in Odisha are excellent places to start and validate customers (Padhi, Senapati, Priyabadini, Pradhan, 2018).

Innovative Entrepreneurship Environment in Odisha

According to research by Dun & Bradstreet, the state is one of India's fastest growing economies, with growth expected to reach 12% by 2020 (Dun & Bradstreet, Inc. - Financials - Annual Reports and Proxy Statements, 2020). Bhubaneswar, the capital city of Odisha, has been awarded the best place to do business in India this year by the World Bank. Odisha's Micro, Small, and Medium Enterprises department has around 20,000 firms registered. Through inventions and wealth contributions, entrepreneurs make significant contributions to the growth of society and the economy. In an effective innovative start-up entrepreneurship environment, innovation, as well as high-growth entrepreneurship supportive mechanisms, has played a critical role in creating start-up enterprises. Startup Odisha, with the motto "A New Wave of Innovation," is an initiative of the Government of Odisha that aims to create a world-class "Startup Hub" in the state. Notably, the measure provides incentives and exemptions that go beyond the Central Government's creative entrepreneurship strategy, or any other current policy in Odisha. The goal of the initiative is to unleash the potential of women entrepreneurs in Odisha by fostering at least 33 basis points of startups with female founders as well as co-founders. Its objective is to help Odisha become one of India's top three startup locations by creating a holistic innovative startup environment (Start-up Odisha, 2022). Odisha Youth Innovation Fund (OYIF) was founded in 2013 with the sole objective to support technological innovations and the development of successful business models by youths from various sections of society which are need-based, simple, cost-effective, and long-term (Youth Innovation Fund, 2022). In collaboration with other State and Central

Government agencies, state government arms such as the Directorate of Industries and the Odisha Khadi & Village Industries Board may be useful in fostering firms based on creative ideas, particularly developments in the rural artisan sector.

Obstacles Faced by Entrepreneurs of Odisha during COVID-19 Pandemic

The Covid-19 epidemic has had a significant influence on economics all throughout the world, with most economies experiencing economic decline. The global economy is expected to expand by 6% in 2021-22 and 4.9% in 2022-23. According to the IMF, India's GDP would develop at a rate of 9.5% this fiscal year and 8.5% in 2022-23. Due to the impact of the second wave of the pandemic and the potential of following waves, the recovery in 2021- 22 is expected to be slower than previously planned. In the case of Odisha, the GDP is estimated to increase by around 9.5% in 2021-22 and by nearly 9% in 2022-23 (Finance.odisha.gov.in, 2022). The state government's strong restrictions to limit the spread of Covid-19 had a substantial influence on the state's economy in the early stages. In 2020-21, Odisha's per-capita income is predicted to be Rs. 1,02,156, though it is low as compared to the year 2019-20 when it was from Rs. 1,04,566. The state's per-capita income is expected to drop 2.30 percent, compared to a 5.41 percent drop nationally. Despite the devastating impacts of Covid-19, the state's sectoral makeup is virtually unchanged from the previous year (Das, Das, Chinara, Orissa Economics Association, 2020).

In 2019-20, the agricultural, industrial, and service sectors contributed 21.27 %, 36.26 %, and 42.47 % of the Gross State Value Added (GSVA), respectively, compared to 21.38 %, 37.92 %, and 40.70 % in the previous year. From 2012-13 to 2020-21, the state economy is predicted to grow at a 5.72 % annual average rate, compared to a national average of 5.01 %. These factors support the view that the state's economic foundation has steadied, and as a result it is capable of managing financial risks and staying on the path of prudent fiscal management, with an emphasis on all-round socioeconomic development for equitable growth (Economic survey-2020-21, 2022). The pandemic has taken a toll on Odisha's entrepreneurs, the bulk of whom are part of an early-stage ecosystem, but they are fighting back with new ideas and initiatives. Despite the fact that many businesses in Odisha experienced layoffs, wage cuts, and temporary closures, and some had financial difficulties during the lockout, many have recovered successfully. The vast majority of businesses have adjusted to the new normal and are developing new strategies, goods, and services to deal with the post-covid market conditions. The challenge has been accepted, and the entrepreneurs' attention has shifted. Several people have started developing covid-related products and accessories to deal with the current situation. The state government has being urged to launch a startup revitalization package by entrepreneurs (News and News, 2022).

Area to Reinvigorate the Economy through Innovative Entrepreneurship

Odisha is now relying on creativity to establish itself as India's tech hub. A growing number of entrepreneurs are choosing Odisha, particularly the capital Bhubaneswar, as their base of operations, demonstrating that innovation can come from anywhere. The fund will encourage innovations in any area that aim to increase productivity and profitability, market share, provide additional job opportunities, and improve the environment, with the focus areas listed in table 1. Odisha is rich in mineral reserves and has a huge mineral potential. Odisha accounts for 10-14% of mineral manufacturing in terms of geographical dispersion. In the fiscal year 2009-10, revenue from mining reserves amounted to Rs. 2020.71 crore. As a result, the state provides a number of opportunities for mineral-based firms to start up. In India, Odisha ranks third in cashew nut cultivation, production, and processing by producing between 1,00,000 and 1,25,000 metric tonnes of cashews every year. It accounts for more than a quarter of the entire raw cashew nut production. Odisha's raw cashew nut industry generates Rs. 950 crores in income. As an outcome, the conversion of raw cashews into kernels yields an additional Rs. 250 crore in revenue.

As a whole, Odisha's cashew nut industry generates Rs. 1200 crores every year. Jute is one of India's most important cash crops in the east. Jute has a wide range of applications, thus producing jute and jute-based products could be a viable business venture. Odisha's traditional cottage industry is handloom and handicraft. Odisha's handloom business is made up of artists from rural and semi-urban areas, the bulk of whom are women from economically disadvantaged backgrounds. The availability of local resources, cost-effective labour, inexpensive capital, exclusive

craftsmanship to make the items, and expanding demand around the globe are all advantages of Odisha's handloom and handicraft sector. Odisha's textiles are known for their exquisite weaves, which give it a distinct personality. As a result, Odisha's handloom sector has enormous potential for generating significant money and providing employment opportunities for rural artisans. Odisha has huge potential to play a key role in the nation's eco-tourism sector, thanks to its diverse and beautiful natural resources. Despite being jeopardised by the COVID -19 epidemic, the Odisha government's eco-tourism programme has shown to be effective. During the years 2016-17 and 2018-19, the state government invested around Rs. 34 crores on eco-tourism projects. The state's growing domestic and worldwide demand for eco-tourism has also aided in providing job and livelihood assistance in a variety of fields, including housekeeping, hospitality, conservation, and other related roles. As a result of the development in eco-tourism, the state now offers a plethora of economic prospects (Top 5 Innovative Ideas of New Business in Odisha, 2022).

The Pareto Optimality Law was used along with Juran's 80/20 rule to identify the key sectors of the Odisha economy. A statistical decision-making technique named as Pareto analysis is commonly used to select a small number of sectors, known as the Vital Few Sectors that have a significant impact. It is based on the Pareto principle, which suggests that efforts should be focused on the VFS that contribute 80% of total net district domestic product so that the remaining Trivial Many Sectors, which contribute 20%, will gain naturally from greater NDDP. Using Juran's 80/20 rule, the VFS and TMS originating from 17 sectors contributing to the NDDP for the state of Odisha as a whole were detected (Chand, 2020). Figure 1 demonstrates that out of the total of 17 sectors that contribute to NDDP, four primary sectors, namely Agriculture & Animal Husbandry, Trade, Hotel & Restaurant, Other Services, and Construction, are the most important and require more focus for creative entrepreneurship. As a result, if the state economy is to be revived, these industries will require more attention.

CONCLUSION

After the third wave of COVID-19, Odisha is gradually opening up the economy to save livelihoods and produce money for its population. According to the findings of this study, innovative entrepreneurs are not yet a significant engine of economic growth in Odisha since they do not have enough opportunities to compete with large corporations. The study reveals that the most justifiable strategy for the growth of innovative entrepreneurship in Odisha is cooperation across different types of groomed enterprises in order to overcome their deficiencies, enhance existing opportunities, and activate innovation and entrepreneurial skills. The State Government should devise particular policy measures to provide chances for semi-skilled and skilled adolescents by establishing innovative rural companies in every Panchayat and ULB, according to the report.

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Table 1. Focus areas for innovative entrepreneurships in Odisha.

Sr. No.	Focus area
1	Active citizenship and community engagement
2	Education and life skills
3	Environment, sustainable use and conservation
4	Gender justice and equality
5	Globalization and technology
6	Health and wellbeing
7	Heritage, culture and diversity
8	Skill development, entrepreneurship and employment
9	Sports and physical education

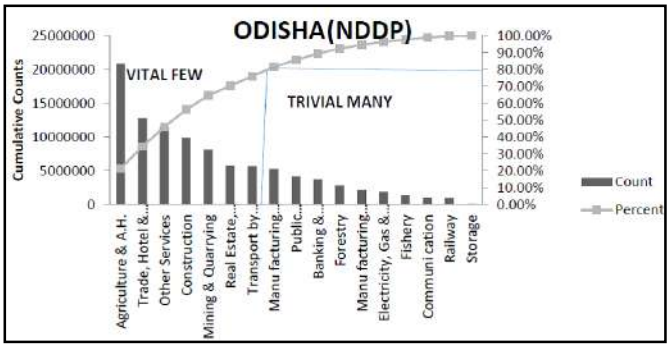

Figure 1. Pareto curve of Odisha (Chand, 2020).

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RESEARCH ARTICLE

An Insight on *Globba* L: A Less Explored Genus

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ABSTRACT

The Genus *Globba* L. is the third largest genus of the family Zingiberaceae ranked afterpolyphyletic genera Alpinia Roxb. and *Amomum* Roxb. The genus is represented by 110species globally and 17 species in India. Members of the Globba are widely distributed intropical and sub-tropical regions, including Asia (India, China) with the highest diversity centre in the Southeast Asia region. The members of the genus characterised by unique phytochemical profile in addition they exhibits good antioxidant and antimicrobial activities. Phytochemical investigation revealed the presence unique bioactive compounds i.e. Globbanol-A, Globbatones-A and B, 16-oxo-(8)17-12-labdadien-15, 11-olide1andbenzofuran-2-carboxaldehyde in *Globba*. Members of the genus *Globba* exhibit remark able antioxidant potentials as compared to the reference standard-ascorbicacid (AA) and butylated hydroxytoluene (BHT). Different species of *Globba* having prominent ethnomedicinal significance as they are used in treatment of various ailments such as Post-partumflatulence, Conjunctivitis and eye abrasions, Asthma, mouth ulcer Leucoderma, hoping cough, Food poisoning, relive the pain ofscorpion sting, also as Analgesic and Antipyretics.

Keywords: Zingiberaceae, Globba, Globbatones, Globanol-A, Antioxidant potentials, Antimicrobial activities.

INTRODUCTION

The Plant Kingdom is the storehouse for natural drugs and possesses a rich reserve of unexplored bioactive compounds which can be further used for therapeutic purposes. Herbal medicine has a long history of usage and has been part of the indigenous treatment of any human civilization. About four billion people (80% of the World's population) of the developing world rely upon the alternative health care system and they form an integral fraction of their tradition and culture. (Bandaranayake, 2006). The most generalized view for the use of traditional herbal medicines is that it is an inexpensive, locally available, common belief it is safer to use than chemical (synthetic) medicines, satisfies a need of more personalized health care, and allows for a greater approach to health individually. (Benzie IF,2011.). The genus globba is very diverse in its composition and comprises of over 100 species.

It is the third largest genera of Zingiberaceae behind s Alpinia and Amomum. Generally, found in the tropical and subtropical parts of the Asia. Globba are rich in aminoacids, cardiac glycosides, and fatty acids. As of which they can be widely exploited for therapeutic purpose. For example, the tuber extract of G. bulbifera, shows antimicrobial and antioxidant properties. anti-inflammatoryproperty is exhibited by G. malaccensis, the essential oils of G. sessiliflora shows antipyretic activity.(Kumar,2017)

The Genus *Globba* L. is the third largest, genus of the family Zingiberaceae (Williams et al.,2004) ranked after polyphyletic genera *Alpinia* Roxb.and Amomum Roxb. (Williams et al.,2004). and consists of about 110 species, distributed in South China, India and Malaysia (Takano & Okada, 2000; Larsen et al.,1998; Smith,1988), The genus is represented by 14 species In India and is almost confined to all states, but greatest number occurs in North-East India (Sabu,2006). The members of the genus characterized by unique phytochemical profile in addition they exhibits good antioxidant and antimicrobial activities. This review presents various aspects of Globba, which includes ethnobotanical, phyto chemistry, antimicrobial and antioxidant activities. The therapeutic properties of this genus are well explored in this investigation, which paves a new way for novel drug discovery. This study will open avenues for sustainable development of good health and well being .

Ethno medicinal Usage: Different species were used in treatment of disease.

The phytochemistry of the genus Globba has received more attention in recent years. The presenceof carbohydrates, α-amino acids, reducing sugars, glycosides starch's, proteins steroids, alkaloids, flavonoids, saponins, tannins, terpenoids, coumarins, phenols, , and phlobatannins were found in phytochemical investigation of *Globbaarracanensis* (Ohnmaretal.,2020). Phytochemical investigation of methanolic extracts of Globbamarantina revealed the presence of alkaloid, cardiacglycosides & steroids and absence of saponin, anthraquinone (Naznin et al, 2019). Phuong et al.(2020) found completely new compounds; Globbanol A (polyoxygenated cyclohexene), crotepoxide & boesenboxide (cyclohexene derivatives) along with a 2'-hydroxy-4,4', 6'-trimethoxy- chalconein Phytochemical analysis of rhizomes of Globbapendula Roxb. These compounds for the first timereported from the genus *Globba.* Maulidiana (2009),has isolated two new naturally occurring compound, i.e, 16-oxo-(8)17-12-labdadien-15,11-olide1andbenzofuran -2- carboxaldehyde and other known compounds including iso andrographolide, indirubin, vanillin, vanillic acid, 2(3H)-benzoxazolone, as well as β-sitosteryl-β-D-glucopyranoside, β-sitosterol, and 7α-hydroxysitosterol.Which has enhanced the secondary metabolite list.

GC and GC-MS analysis of essential oil obtained from rhizome of *Globba sessiliflora* found to be rich in oxygenated sesquiterpenes (65.8%), β-eudesmol (27.6%). caryophyllene oxide (9.7%), τ-muurolol (8.3%), γ-eudesmol (6.4%), (6E)-nerolidol (4.1%), (E)-sequisabinenehydrate(2.4%),1-epi-cubenol(2.6%)andβ-bisabolenol(2.2%).Otheroxygenated sesquiterpenoids were found to be less than 1% (Ravendra et al., 2017).Two new homodrimane sesquiterpenoids, globbatones A and B and one 16-norlabdane diterpenoid, globbatone C, were isolated from the chloroform extract of *Globbas herwoodiana* rhizomes. (Prema et al., 2020). GC-FID and GC/MS analysis of essential oils obtained by hydrodistillation whole plantbody of *Globbas chomburgkii* revealed presence of24 compounds; b-caryophyllene (31.7%), caryophyllene oxide(10.3%), hexadecanoic acid (7.6%) and a labdane-type diterpene 13,14,15,16-tetranor labd-8(17)-en-12-al(6.6%) were the major constituents of the oil (Raj et al.,2010).

Antimicrobialactivities

Members of the genus *Globba* has been traditionally used for the treatment of throat infections andbeen reported to inhibit the broad range of pathogenic microorganisms including gram positive, gramnegativebacteria. Acetoneand petroleum ether extracts from the leaves of *Globba arracanensis* Kurz. exhibited highly antimicrobial activity against eight test organisms named *Agrobacterium sp.,Bacillus subtilis, Candida albicans, Escherichia coli, Micrococcus luteus, Pseudomonas aeruginosa, Salmonella typhi and Staphylococcus aureus.*with zone of inhibition>18mm.(Ohnmaretal.,2020).

Antioxidant activity

Antioxidants includes a wide range of compounds, they mitigates harmfuleffects of free radicals by reducing them.

Hence they have protective function in our body againstoxidative stress. Yaowachai (2020) found the rhizome of the tissue cultured derived plantlets of *Globba globulifera* had the highest DPPH radical scavenging assay (93.55%) and lowest IC50 (0.46mg/ml) and DPPH scavenging ability is more correlated with total phenolic contents (r = 0.913), andless correlatedwith total flavonoid content (r = 0.894). The methanolic leaf extract of G. marantina showed moderate antioxidant activity ((IC50=145.80μg/ml)) as compared with those of the standards, ascorbic acid (IC50 = 100.27μg/ml) and BHT (IC50 = 113.89 μg/ml) observed by (Naznin et al., 2019).

CONCLUSION

In recent years, ethnomedicinal studies of different species of the genus *Globba* received much attention as it brings various traditional uses to light.. Phytochemical study revelled presence of potent bioactive compoundsspecific to the genus *Globba* were Globbanol A , Crotepoxide, Boesenboxide along with a 2'- hydroxy-4,4',6'-trime thoxy-chalcone (chalcone,). Pharmacological screenings of the explored *Globba* as a medically potent genus As the pharmacologists are looking forward todevelop new drugs from natural sources, development of modern drugs from the member of Globba can be emphasized for the control of various diseases. A systemic approach should be developed for more exploration of novel compounds in globba and their therapeutic properties. As this will show a way to designing of a new drug.

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Table 1: Depicting the ethnobotanical usage of Globba species

Species	Vernacular Name/Common name	Part use	Traditional uses	Method usage	Reference
Globba leucantha Miq	Malaysia: Merian darah	Root	Post-partum	Decoction Taken orally	(Onget al.,2011)
Globba pendula Roxb.	Indonesia: pedas(in South Sumatra) Malaysia:Meroyan Tinggal	Root	Post-partum flatulence	Decotion taken orally	(Ong etal.,2011; Priyadiet al., 2010)
	Indonesia; Tepus: Pemulih	Exudates	Mouth ulcer	Raw	(Azliza etal., 2012)

Globba marantina Linn.	India: Kattumanjal	Rhizome	Post-natal care of mother and child	Ten grams of fresh Rhizome is made into a paste with equal amount of fresh or shade dried rhizome of *Dioscorea tomentosa*	(Muthukumarasamy et al.,2004)
		Leaves	Conjunctivitis and eye abrasions	Aqueous extract of leaves is used as eye drops against severe conjunctivitis	(Verma et al.,2010)
		Rhizome	Leucoderma	Fresh rhizomes crushed, mixed with Pongamia seed oil and paste applied On white spots	(Ram et al.,2004)
Globba clarkei Baker.	India: Silaadha Chakma, (In Arunachal Pradesh)	Rhizome	To cure cough	Rhizome extract mixed with leaf extract of *Adhatoda vasica* is taken orally	(Tusharetal.,2010`)
	India: Globba-tong(Nagaland)	Rhizome	Food poisoning	Juice of rhizome and the decoction seed's is taken orally for food poisoning	(Jamir,2012)
Globba multiflora Baker.	India: Belah (Nyishi Arunachal Pradesh)	Rhizome	Analgesic and Antipyretics	Crushed rhizome applied locally on wound	(Tushar et al.,2010)
Globba multiflora Wall.ex Baker	India: Hiching (in Reang)	Rhizome	Hoping cough	Decoction	(Shil et al.,2014)
Globba patens Miq.	Malaysia: Merianbiasa	Root	Post-partum	Decoction taken orally	(Ong etal.,2011)
Globba orixensis Roxb.	India-Gada (in Odisha)	Rhizome	Scorpion sting	Paste applied externally	(Das andMishra,1988)

Phytochemistry

	India: Globba-tong (Nagaland)	Rhizome	Food poisoning	Juice of rhizome and the decoction seed's is taken orally for food poisoning	(Jamir,2012)
Globba multiflora Baker.	India: Belah (Nyishi Arunachal Pradesh)	Rhizome	Analgesic and Antipyretics	Crushed rhizome applied locally on wound.	(Tusharetal.,2010)
Globba multiflora	India: Hiching (in Reang)	Rhizome	Hoping cough	Decoction	(Shiletal.,2014)

Wall.ex Baker					
Globba patens Miq.	Malaysia: Merianbiasa	Root	Post-partum	Decoction taken orally	(Ong etal.,2011)
Globbaorixensis Roxb.	India-Gada (in Odisha)	Rhizome	Scorpion sting	Paste applied externally	(Das andMishra,1988)

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RESEARCH ARTICLE

An analysis on Prospects for Entrepreneurship in Cashew Sector of India

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ABSTRACT

The cashew processing industry supports everyone from growers to dealers to wholesalers to processors to supermarkets and retailers. Cashew processing has historically been a labor-intensive industry that has employed a large number of rural women. The sector is classified as traditional due to the presence of minimal technology in the processing of cashew nut. The domestic cashew nut market includes collecting cashews from villages and distributing them among small-scale processors. As India has a competitive advantage in the production and processing of cashew nuts, the cashew processing industry presents a great potential for entrepreneurs. Despite the fact that the industry provides ample business potential, it faces several problems due to global competition from other nations and a variety of other issues. Despite the fact that entrepreneurs are required to invest large sums of money as working capital in order for their businesses to run properly, they do not have access to rapid loans. As the input costs have grown greatly, a decline in pricing of the finished items produces huge losses for the entrepreneurs. Strategies for increasing production & productivity of cashew are development of compact and dwarf high yielding cashew variety suitable for high density plantation, Massive replanting programme to replace senile and unthrifty orchards, development of cost effective cashew production technologies, increasing productivity by adopting improved cashew production technologies.

Keywords: Cashew Processing Business, Entrepreneurship Development, Issues, Problems

INTRODUCTION

In India, the number of new entrepreneurial initiatives has exploded in recent years (Sabrina, 2019). The Indian government has made a number of efforts to encourage entrepreneurship in the nation, including initiatives such as Make in India, Start-up India, Stand-Up India, and the Mudra Scheme. The Indian entrepreneurial sector has enormous potential to improve numerous attributes that are important for successful entrepreneurship, such as intensity in ideas, willingness to take risks, agility in business operations, and the capacity to make quick decisions and brave leadership. As a result, India has a compelling need to support entrepreneurs as never before. Moreover, as per the UN Sustainable Development Goals, it is required to increase the accessibility of small scale and other industries to affordable financial services like easy credit and to integrate them with value chain and markets (Envision2030, Goal 9: Industry, Innovation and Infrastructure).

The cashew business is a classic export-oriented industry that serves to earn foreign currencies and increase the country's share of the gross domestic product. The cashew industry is an agricultural one. The sector is classified as traditional due to the presence of minimal technology in the processing of cashewnut. The domestic cashew nut market includes collecting cashews from villages and distributing them among small-scale processors (Stevelal, 2018). Rural entrepreneurship is gaining traction as a new field of study for assisting agricultural growth (Koyana, S., & Mason, R. B., 2017). Because cashew processing falls within the classification of agro-based industries in India, encouraging entrepreneurship in this field is simpler. It has the ability to employ a large number of rural residents and provide a significant source of income for them. The cashew processing sector employs over three lakh people (V. V. GiriNational Labour Institute, 2014), the majority of whom are women (95 percent) from socioeconomically disadvantaged populations in rural regions.

Challenges

Due to a variety of factors, cashew entrepreneurship has not been particularly popular with new entrepreneurs in India. One of the causes seems to be that finding employees to work in cashew manufacturers has grown increasingly challenging for businesses (Bhat, V., 2019). Workers don't really chose cashew processing as a career field because of the hazardous working conditions in cashew factories (Lamble, 2013). Shelling, peeling, and grading steps of the processing process typically demand women employees to crouch for 7 to 8 hours each day, which is harmful to their knees, stomach, and backbone. Workers' skin discolours as a result of the very acidic oil generated during the cashew shelling operation, which causes dermatitis and blistering (Eagleton, 2007). As a result, governments and supervisory agencies should make enhancing the workplace environment and safety laws a key priority in order to attract new workers and businessmen to this business. Female workers would be less likely to leave if the workplace environment and safety rules were improved. Entrepreneurs frequently encounter the problem that, although working for lower rates than males, female workers are more erratic in their work schedules. Because of their various family duties, this irregularity exists. Furthermore, they assist other members of the family in farm work throughout the typical agricultural season. As a result, business owners must create a safe workplace environment for female employees in order to reduce their turnover rates. The 21st century brings challenges which make entrepreneurial skills inevitable for the entrepreneurs (Pattanayak and Padhy, 2020). The responsibility lies with the entrepreneurs themselves as well as on the policy makers, administrative agencies and institutions of higher education to facilitate the process of skill acquisition by the present and aspiring entrepreneurs.

Entrepreneurs confront additional difficulty relating to their working capital, in addition to the difficulties of a higher turnover rate of female workers (Ramachandran, 2019). The amount of operating capital necessary to run a processing firm is still rather large. Working capital is the money that a company needs to conduct its day-to-day operations. It reveals the operations efficiency and economic health of a company. According to Nwude, E. C., 2016agro-based enterprises (cashew being one of them) require lesser fixed capital and more working capital to run. Around half of the cash must be spent in working capital to maintain the processing units running throughout the year (Kamath, 2016). As a result, entrepreneurs must be supplied with timely credit facilities in order to meet their

units' working capital needs. Entrepreneurs are required tomake regular use of technology for taking business decisions including marketing decisions, as they have been no longer in physical contact with their teams and stake holdersin recent times (Pattanayak and Padhy, 2021).

Many businesses in Kerala fail due to the large sums necessary to maintain operating capital, as well as other reasonable reasons, as well as a few other states, have turned down their processing units (Das, M. 2000). The cost of raw materials, processing, and labour has risen dramatically in recent years. Because input costs have risen significantly, a decline in finished product prices results in significant losses for businesses. However, the government has made every effort to resurrect these processing plants and eliminate bottlenecks in the business.
Many ambitious entrepreneurs might be stopped from leaving the business due to a lack of financial support if industry bottlenecks are removed and accessible financing is made available (Mund, C.S., 2020). Financial institutions do not provide enough funding to new businesses. Lending to budding enterprises is always hazardous for banks (Thampy, A., 2010). Only a few young entrepreneurs who are fortunate in obtaining funding from family members, relatives, or via subsidies are able to begin their businesses on a small scale. If banking processes for credit are streamlined and adequate quantities of credit are offered at concessionary rates, new entrants will find it easier to enter the market.

There was a constant emphasis on streamlining banking procedures for lending and giving loans to businesses at reduced rates. In contrast, a series of events that occurred in 2016 dealt a devastating damage to cashew nut businessmen across the country. When the union government slapped a 9.4% import charge on raw cashew nuts in 2016, the cashew sector took a hit (Ameerudheen, 2018). In the same year, worldwide raw nut costs jumped from $800 a tonne to $1800 per tonne, rendering raw nut imports too expensive for processors. Many entrepreneurs saw this as an effort to smother the country's expansion of MSMEs (Micro, Small, and Medium Enterprises). Many entrepreneurs began to close their processing operations after 2016. Cashew businesses around the country began failing on their bank debt in the same year. To collect their loans, the banks used the provisions of the Sarfaesi Act. The Sarfaesi Act of 2002 authorises banks to seize hypothecated assets in order to recover their loan debts (Jose, 2017). Extending more financing to loss-making divisions, according to bankers, was not a good idea. Instead of collecting entrepreneur's hypothecated property to recover bank dues, it is urgent to inject more money to recoup the loss-making units.

In addition to providing additional funding to restore loss-making units, it is also critical to shield cashew entrepreneurs from worldwide market pricing concerns. Entrepreneurs that turn raw nuts into polished kernels run the danger of losing a lot of money (Bhat, V., 2019). Establishing business in this industry, according to the entrepreneurs, is extremely dangerous, and some even equate it to gambling. This view is widespread due to the market's high volatility in cashew kernel pricing. They purchase the raw materials and begin processing operations while keeping in mind the current market rates for kernels. They make educated guesses regarding the market pricing that will exist when their items are ready for sale. They make a lot of money if their prediction is correct, but they lose a lot of money if prices are so low. As a result, the government should develop a robust risk management system that enables entrepreneurs to obtain critical technical information such as input prices, output prices, productivity, and current market dynamics.

Opportunities

India's inbuilt strength is its diversified agro-climatic conditions, which are beneficial to a wide range of crop cultures, including cashew farming. Cashew and its by-products have a well-defined domestic and global market, which needs large-scale cashew farming (Bhoomika, 2018). The cashew processing industry supports everyone from growers to dealers to wholesalers to processors to supermarkets and retailers. Cashew processing has historically been a labor-intensive industry that has employed a large number of rural women (D' Silva and Bhatt, 2021).

As India has a competitive advantage in producing and handling of cashew nuts, the cashew processing industry presents a great potential for entrepreneurs. The soil and climate of India are ideal for cashew farming. Compared to every other nation in the globe, India has the most territory dedicated to cashew farming (Karthickumar, 2014). After basmati rice, spices, and tea, cashew is India's fourth most significant export item (Ameerudheen, 2018). India has surpassed the United States as the world's largest consumer of cashew kernels (Nair, 2015). This demonstrates the industry's enormous potential for sustaining entrepreneurship and innovation.

As it belongs within the agro-based industries group, the cashew processing industry is highly adapted to sustaining entrepreneurship and innovation. Agriculture is directly or indirectly tied to agro-based industry. By connecting the industrial and agricultural sectors, these industries perform a critical role. The cashew nut business, out of all sorts of agro-based enterprises, has the greatest potential to absorb extra rural labour. Following independence, the government launched a slew of entrepreneurship development initiatives aimed at improving entrepreneurs' skills and abilities. In the latest budget, the government announced a number of incentives for entrepreneurs who want to start an agro-processing business. For example, the 9.4 per cent import charge that was levied in 2016 has since been reduced to 2.5 per cent (Ameerudheen, 2018), allowing businesses to import large amounts of raw nuts from other nations. To foster entrepreneurship in the business, Bhoodes (2019) suggests that governments explore totally eliminating import duties and providing interest-free credit for the first five years.

Even though it may appear impracticable to waive import duties and provide interest-free loans, there is a better answer that exists in the ever-increasing market requirements for cashew nuts throughout the world. In recent years, there has been a significant increase in the demand for cashew (Boafo , J. and Lyons , K. (2021). From being seen as a luxury item, it is now regarded as a healthful and necessary item. Cashew nuts will always have a market, regardless of how much are grown and processed. The whole world's cashew crop could be devoured in 60 days if everyone on the planet ate only one cashew each day, not even a handful. So, even if the entrepreneurs raise processing capacity to its maximum, marketing and selling will not be an issue. As a result, funds earned from successful cashew nut marketing and sales may be successfully utilised to intervene and favourably improve the livelihoods of many impoverished women workers, particularly in rural regions. The Indian cashew business employs more than one million people, the large bulk of which are women (Bhoodes, 2019). Cashew processing will always be a labor-intensive industry, as procedures such as peeling and grading always will require some human work. The advantage of employing women in processing units for entrepreneurs is that women are plentiful in rural regions and may be employed for a profit.

Strategies for increasing production & productivity of cashew are development of compact and dwarf high yielding cashew variety suitable for high density plantation, Massive replanting programme to replace senile and unthrifty orchards, development of cost effective cashew production technologies, increasing productivity by adopting improved cashew production technologies (Mohana and Nayak, 2018).

CONCLUSION

Cashew nuts should be promoted across the world by the government and various cashew boards. The goal for farmers and politicians should be to produce sufficient raw nuts to fuel the processing plants. Transfer of technical know-how on processing procedures, as well as timely financial rewards from the government in the form of financing and subsidies, will go a long way toward assisting businesses in expanding their processing capacity. Due to a variety of factors, cashew entrepreneurship has not been particularly popular with new entrepreneurs in India. One of the causes seems to be that finding employees to work in cashew manufacturers has grown increasingly challenging for businesses. Entrepreneurs are required tomake regular use of technology for taking business decisions including marketing decisions, as they have been no longer in physical contact with their teams and stake holders in recent times. The 21st century brings challenges which make entrepreneurial skills inevitable for the entrepreneurs. The responsibility lies with the entrepreneurs themselves as well as on the policy makers,

administrative agencies and institutions of higher education to facilitate the process of skill acquisition by the present and aspiring entrepreneurs.

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RESEARCH ARTICLE

Identification of Some Penicillium Species by using Morphological Characteristics from Aquaculture and Agriculture Waste Contaminated Water Bodies

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ABSTRACT

In the current study our aim to investigate the presence of human pathogenic opportunistic mycotoxins producing fungi in river water which is used as water resource for local habitats. The objective is to detect mycotoxins producing *Penicillium* species by using morphological characteristics. In our present study conducted at Ganagalawanipeta village river water (Srikakulam, Andhra Pradesh) which is contaminated by agri & aqua culture wastes, a wide variety of Mycotoxins producing fungal species were detected. 30 samples were taken for period of six months for their screening and occurrence. This article focuses on *Penicillium* genus identification by using several morphological characteristics. The samples were inoculated on Potato Dextrose Agar (PDA), Sabouraud Dextrose Agar (SDA) and other specified culture media like, Czapek yeast agar (CYA), Malt extract agar (MEA), czapekdox agar (CZ) followed by incubation at 25°c and 37°c. The most commonly identified 4 species of *Penicillium* are *P.expansum, P. chrysogenums, P. commune, and P. funiculosum*. The results of present study suggest that the river inhabitants in particular research site Ganagalawanipeta village are at a greater risk of getting life-threatening fungal infections which may lead to various morbidities. Our future goal is to study the aflD gene which has a role in monitoring the bio-synthetic direction of penicillium biosynthesis. This could thus be a good a target gene for inactivation, to develop efficient means of penicillium control by using RNA silencing technology.

Keywords: *Penicillium*, filamentous fungi, environment, RNA silencing, Technology

INTRODUCTION

Fungi are ubiquitous organisms that are widely distributed in nature., 50,000 to 250,000 known species of fungi a limited number of species are responsible for diseases [1,2]. The most problematic species are *Candida spp., Aspergillus spp., Cryptococcus spp., Penicillium spp.*,[3,4.] *Penicillium* is a very large and ubiquitous and diverse genus occurring worldwide which currently contains 354 accepted species [5]. Many species are common contaminants on various substrates and are known as potential mycotoxins producers, in the food industry where they produce a wide range of mycotoxins. Correct identification is therefore important when studying possible *Penicillium* contamination of food, feed and water. Human pathogenic species are rare, however opportunistic infections leading to mycotic keratitis, otomycosis and endocarditis (following insertion of valve prosthesis) have been reported [6]. filamentous fungus causing the serious post harvest disease known as blue mould in harvested apples, peaches and hazels [7].

River water contaminated due to man-made activities like agricultural and aquaculture practices. Aquaculture activities are major impact on water resources-they are biological, physical and chemical. Physically there is a lot of pressure on water, biologically it introduces exotic species, pathogens and diseases. Several studies have suggested an important role for waterborne fungi to endanger human health [8,9,10]. The consumption of fungi-contaminated drinking water has, as far as is known, not caused acute disease, at least in immuno-competent individuals. However, there is a risk of superficial or localized infection in healthy individuals and more severe and invasive infection in immuno-compromised patients. Some species also have the potential to cause allergic reactions and diseases. There is number of reasons to suggest that water should be considered as a potential transmission route for pathogenic or allergenic fungi. However, a number of other environmental sources exist. Aerosolisation of spores or fragments of hyphae from water has been particularly investigated as a pathway of exposure.

Generally Identification of the fungal species is based on the morphological characteristics of the colony and microscopic examinations [12]. *Penicillium* taxonomy is complex and ever evolving, the genus is easily identified by its characteristic conidiophore, but species identification and differentiation is complex, for it is traditionally based on a range of morphological features [13]. Macro-morphological features which are considered include conidial and mycelial color, colony diameter, colony reverse color, production of exudates and soluble pigments, presence of sclerotia and cleistotheciaseriation, shape. Micro-morphology characterization is mainly dependent on size of vesicle, conidia and stipe morphology, presence of Hulle cells, and morphology of cleistothecia and ascospores [24]. Morphological features have to be determined under standardized laboratory conditions by trained mycologists, to obtain an accurate identification. Molecular methods are improving and become more rapidly available, microscopy and culture remains commonly used essential tools for identification of fugal species. The present study was taken up to search out the diversity of opportunistic fungal pathogens in the river water that is still being used by the people living in the village Ganagalawanipeta and then to check out the rate and relevance of fungal infections in the population actively engaged with various activities related to the river water.

MATERIALS AND METHODS

Description and research site

The village Ganagalawanipeta mainly depends on the river Nagavali for drinking, agricultural and aquaculture purposes. This river surrounded by 100 acre land cultivated for aquaculture practices [15]. The polluted water is discharged into the channels from the upstream aquaculture ponds that same water is used by downstream human and animal consumption.

Collection of water samples

30 water samples collected from 5 different sites for a period of 6 months, from October 2020 to March 2021. The water samples were collected from the site of investigation in sterile screwed bottles, at five different sites of the waste water disposed area. pH of the samples measured, the samples are deposited in refrigerator until used. Plastic containers, which were previously sterilized with 70% alcohol and rinsed with distilled water. At the river, the containers were rinsed thrice with the river water before being used to collect the samples.

Isolation of fungi

Water samples were obtained from different sites were serially diluted five folds and then spread plate technique were followed for the isolation of fungal species in the study, spreading 0.1 ml inoculate from the serial dilution tubes on the petri dishes containing the potato dextrose agar (PDA) for the genus level identification..

Medium of growth

Penicillium isolates were identified up to genus level on potato dextrose agar (PDA) and Sabouraud Dextrose Agar (SDA), to improve the sensitivity and specificity of routine culture approach for identification of species level, we used some differential media including, Czapekdox agar (CZ) Czapek concentration 10.0ml, K_2HPO_4 1.0gr, sucrose 30.0gr, agar 17.5gr, distilled water (DW) 1.0 lit MarenA.Klich CBS-2002, czapek yeast agar (CYA) czapek concentration 10.0ml, K_2HPO_4 1.0gr, powdered yeast extract 5.0gr, sucrose 30.0 gr, Agar 15.0gr and DW 1.0 lit., malt extract agar (MEA) powdered malt extract 20.0gr, Peptone 10.0gr, Glucose 20.0gr, Agar 20.0gr, DW 1.0 lit and czapek yeast 20% sucrose agar czapek concentration 10.0 ml, K_2HPO_4 1.0gr, powdered yeast extract 5.0gr, sucrose 200.0gr, agar 15.0gr, Dwater 1.0 lit. (Bandh et al., 2012)[24]

Inoculation and incubation

1 ml of each sample was homogenized aseptically and diluted to 10^{-5} dilution. Series of sterile petri plates were taken and 1 ml of sample was transferred from each dilution. These dilutions are then plated onto agar media and incubated. About 15ml of agar media previously melted and maintained at 45 ± 1 °C was poured on to it. The time elapsing between the end of the preparation of the initial suspension and the moment when the medium is poured into the dishes does not exceed 15 minutes. Inoculates with the medium were mixed carefully and allowed it to solidify. A control plate was prepared to check the sterility of plates that were incubated at 25± 1 °C. The colonies were counted on each plate after 4,5 and 7 days of incubation. After inoculation on several replicate agar plates, the plates were incubated at 25 °C to promote the growth of fungal colonies . Three-point inoculation was also carried on 80mm Petri dishes, an accepted standard technique for cultivation and for the morphological identification of *Aspergillus, Penicillium* and other related genera [16]. The three-point inoculation was done by using glass Petri dishes inoculated with very low quantities of conidia using glass needles, incubated at different temperatures upside down for 7 days to prevent spread of conidia all over the plate and growth of the colonies. .

Culture and identification

Penicillium isolates were identified up to genus level on potato dextrose agar (PDA) and Sabouraud Dextrose Agar (SDA) results showed in Figure 1. To improve the sensitivity and specificity of routine culture approach for identification of species level, we used some differential media. We used Riddle's classic slide culture method for microscopic study of standard strains and most of our isolates [17]. Deposited a drops of lactophenol mounting fluid at the center of a clean glass slide. Cellophane tape strips cut about 3 cm long from the stock roll by using forceps while handling the tape. Dissecting the needle will aid in freeing the tape from the forceps. The adhesive side of the tape is applied to the surface of a sporulating fungus colony, dense mass of hyphae and spores will be collected. The tape was removed from contact with the fungus colony and applied adhesive side down, to the drop of mounting fluid on the glass slide [14]. The tape gently rubbed with a smooth, flat instrument to express air bubbles. Examined the tape mount microscopically under the oil immersion objective with oil [14]. Microscopic characteristics for the identification were conidial heads, stipes, color and length vesicles shape and seriation, metula covering, conidia size, shape and roughness also colony features including diameter after 7 days, color of conidia, mycelia, exudates

and reverse, colony texture and shape, phialide shape and branching pattern observed and compared the morphological characteristics of tested *penicillium* isolates with those of the standard specie.

RESULT

During the period of 6 months, most commonly identified 4 species of *Penicillum* are *P.expansum, P. chrysogenum, P. commune, and P. funiculosum* by using differential culture media like CZ, CYA and MEA for their growth. Some *Penicillium* species were obtained from the contaminated water samples which were collected from research site aquaculture wastewater, agricultural waste disposed area and river water. The result showed that in this study *P.expansum* (46%), *P. chrysogenum* (33.0%) and *P.commune* (11.0%) and *P. funiculosum* (10.0%) were most common isolated species. Macroscopic and microscopic features used for identification of *penicillium* species are shown in Table-I and Table-II. Fungal morphology was characterized by using standard *penicillium* strains. Morphological features of colonies on culture media as well as microscopic characteristics of the strains were studied further. Morphological characteristics of macroscopic are shown in Table-I, Result showing the most common conidia color of the fungal colonies was green and yellow. Reverse color of the colonies was white to cream, some more colors like yellow, pale brown, brown and yellow orange were also shown by the conidia and reverse side of the isolated fungal strains. The colony diameters shown by different species ranged between a minimum of 25 mm and a maximum of 44 mm are macroscopic features of these identified fungal species in differential culture media. On different specific media macroscopic features of fungal strains show different characteristics of color, reverse color and colony diameter.

Microscopic characteristics showing in Table - II that the conidia shape shown by the strains was globose, ellipsoid, subglobose and pyriform with ornamentation of conidia and stipe as smooth, coarsely roughened and finely roughened. Moreover, the phialide shape was Flask-shaped, ampulliform and cylindrical, branching pattern was Monoverticillate, Bi-verticillate, Ter-verticillate and Quarteverticillate. The conidia length, conidia width, stripe length and stripe width varied between 3.0 to 4.0 µm, 2.5 to 3 µm, 45 to 310 µm and 2 to 3.5 µm, respectively. On different specific media microscopic features of fungal strains show different characteristics

DISCUSSION

The presence of these terrestrial molds in water supports the paradigm that their deposition is attributable to contamination of the water body due to the entry of contaminated waste sewage from the agriculture and aquaculture practices. Due to the increased human population, safe drinking and recreational waters remains one of the most important present and future plans. Fungi are not mentioned in the present regulations that define water quality, they are constantly isolated from water microbial communities [18]. Surface water resources include rivers, streams and lakes that can be used for drinking water and household activities. but they may also serve recreational purposes [19,20,21]. During recreational activities, people are exposed to fungi via direct skin contact and through inhalation of aerosols [18]. The latest literature regarding the surface water with the presence of ascomycetous species of Cylindrocarpon, Microsporum, Phialemonium, Rhinocladiella, and fungi from subphylum Mucoromycotina [19,22,23]. In this study we used morphological method with differential culture media for identification of important specie like *Aspergillus* and *Penicillium* Generally culture required five or more days is required for identification of these fungal species. In our study using differential media like CYA and SDA with macroscopic and microscopic characteristics of fungal growth on these culture media. Further studies would be helpful in clarifying the media and conditions that are most effective for the recovery and identification.

CONCLUSION

The aim of present study was to identify human opportunistic fungal pathogens in river water of Nagavali, Ganagallawanipeta village. We found four most commonly identified *penicillium* species by following traditional approches. There is a crucial gap of information about the presence of mycotoxins producing fungi occurrence in natural water reservoirs. In this regard, non-target screening and suspected screening are needed strategies using techniques based on HRMS. However, the efficient application of these approaches is dependent on further research and development of specifically designed libraries.

SDG 15: Life on Land:
Identification of mycotoxin producing fungi is of great importance as they contribute to toxicity in foods and water.

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Table 1. Morphological characters of fungal colonies on CYA

Name of fungi	On CYA		
	Colour of conidium	Reverse colour	Diameter (mm)
P.expansum	Dull green	White to cream, green	27
P. chrysogenum	Yellow	Pale brown	38
P. commune	White to cream, yellow	Brown	23
P. funiculosum	Green	White to cream	35

Table II : Microscopic characters of fungal colonies on differential culture media observed through MAGNUS compound microscope

Name of fungi	Conidia length (µm)	Conidia width (µm)	Conidia shape	Conidia ornamentation	Stipe length (µm)	Stipe width (µm)	Stipe ornamentation	Phialide shape	Branching pattern
P.expansum	3.1	2.5	cylindrical shape	Smooth	310	3	Smooth	Flask-shaped, (ampulliform, with constriction)	Bi-verticillate
P. chrysogenum	3	2.8	Globose, Ellipsoid	Smooth, Finely roughned	260	3.4	Coarsely roughened Warted	Flask-shaped, (ampulliform, with constriction)	Quarte verticillate
P. commune	3.5	3	Ellipsoid, Pyriform	Smooth	320	3.5	Smooth	Phialide shape	Mono verticillate
P. funiculosum	2.9	2.4	Globose, Subglobose	Coarsely roughened	38	2.5	Coarsely roughened	Cylindrical	Ter-verticillate

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RESEARCH ARTICLE

Molecular Interaction in Binary Mixtures containing N,N-Dimethyl Formamide and n-Butanol

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ABSTRACT

The acoustic studies of the interactions between alcohol molecules and water-soluble polar solvent DMF are significant for under standing the relationships between structure and function polar molecules like DMF, and for explaining the mechanisms of interaction of alcoholic OH group with an electro negative moiety. In this piece of work Ultrasonic velocity, density and viscosity have been measured at 298K, 308K, 318K and 328K form a mixture of N,N-dimethylformamide(DMF) and n-butanol, the frequency being maintaine data constant value. The experimental data have been used to calculate the acoustical and thermo dynamical parameters like a diabatic compressibility, free length, free volume, internal pressure, acoustic impedance, Gibbs free energy.

Keywords: acoustic studies, electro negative moiety, N,N-dimethylformamide, thermo dynamical parameters, a diabetic compressibility, free length, free volume, internal pressure, acoustic impedance.

INTRODUCTION

Ultrasonic studies provide a wealth of information about the state of liquids. The measurement of ultrasonic velocity in pure liquids and mixtures is an important tool to study the physiochemical properties of the liquids and also explain the nature of molecular interactions. The practical importance of liquid mixture a ther than single component liquid systems has gained much importance during the last two decades in assessing the nature of molecular interactions and investigating the physio-chemical behaviour of such systems **[1,2]**. Ultrasonic investigation of liquid mixtures consisting of polar and non-polar components is of consider able importance in understanding the physical nature and strength of molecular interaction in the liquid mixtures **[3]**. For a better understanding of the physio-chemical properties and the molecular interaction between the participating components of the mixtures, ultrasonic

velocity together with density and viscosity are measured at different temperatures for different concentrations of the components in the mixture. Ultrasonic velocity and the derived acoustical parameters like adiabatic compressibility, free length, relaxation time, acoustic impedance, etc., provide valuable information about the molecular environments. This has been studied for various binary and ternary mixtures **[4-17]** with respect to variation in concentration of the liquids and temperatures.

In the present paper, variation of various parameters of binary mixtures containing n-Butanol and N,N-dimethylformamide (N,N-DMF) at different temperatures have been studied for different concentrations

DMF (C_3H_7NO) is a versatile compound. It is a non-aqueous solvent which has no hydrogen bonding in pure state. Therefore, it acts as an a protic, photophilic medium with high dielectric constant and it is also considered as a dissociating solvent. DMF being a polar molecule results in dipolar and induced dipolar interaction between it and chlorobenzene in addition to dipolar-dipolar interaction between its molecules. DMF is primarily used as an industrial solvent. DMF solutions are used to process polymer fibers, films and surface coating to permit easy spinning of acrylic fiber to produce wire enamels and as a crystallization medium in the pharmaceutical industry. n-Butanolisa primary alcohol with the chemical formula C_4H_9OH and a linear structure.butanol is used as a raw material for coating resins, butyl carboxylates such as butyl acetate, butylacrylate, and glycol ethers. On the other hand, it is widely used as a solvent because many organic materials are soluble in it. The ambitious and progressive agenda of the Goals presents a huge opportunity to foster, support the emergence of and experiment with new forms of innovation for sustainable development.

EXPERIMENTAL SECTION

The chemicals used in the present work were analytical reagent (AR) and spectroscopic reagent (SR) grades with minimum assay of 99.9% were obtained from E-Merk Ltd (India). Various concentrations of the binary liquid mixtures were prepared in terms of mole fraction

Solution-1(S_1)⇒n-Butanol:N, N-Dimethyl formamide=1:9 Solution-2(S_2)⇒n-Butanol:N, N-Dimethyl formamide=2:8 Solution-3(S_3)⇒n-Butanol:N, N-Dimethyl formamide=3:7 Solution-4(S_4)⇒n-Butanol:N, N-Dimethyl formamide=4:6 Solution-5(S_5)⇒n-Butanol:N, N-Dimethyl formamide=5:5.

Velocity Measurement

The velocity of ultrasonic wave in the binary mixture have been measured using multi-frequency ultrasonic interferometer with an high degree of accuracy operating at 11 different frequencies (Model M-84) supplied by M/s Mittal Enterprises, New Delhi. The measuring cell of inter ferometer is a specially designed double walled vessel with provision for temperature constancy. An electronically operated digital constant temperature bath (Model SSI-03 spl) supplied by M/s Mittal Enterprises, New Delhi, operating in the temperature range -10^{o}c to85^{o}c with an accuracy of ±0.1 Kh as been used to circulate water through the outer jacket of the double walled measuring cell containing the experimental liquid

Density Measurement

The densities of the liquid mixtures were measured using a digital meter named, "Micro viscometer, Model-Lovis 2000 ME".

Viscosity measurement:

The viscosities of the ternary mixture were measured using an Oswald's viscometer calibrated with double distilled water. The Oswald's viscometer with the experimental mixture was immersed in a temperature- controlled water bath. The time of flow was measured using a digital racer stop watch with an accuracy of 0.1sec. The viscosity was determined using the relation,

$\eta 2=\eta 1(t2/t1)(\varrho 2/\varrho 1)$

Where, $\eta 1$ = Viscosity of water, $\eta 2$ = Viscosity of mixture ,$\varrho 1$=Density of water, $\varrho 2$=Density of mixture, t_1=Time of flow of water, t_2=Time of flow of mixture.

THEORETICAL ASPECT

The following thermodynamic parameters were calculated from Jacobson's relation [**8–10]**.

Adiabatic Compressibility (β)

The adiabatic compressibility is the fractional decrease of volume per unit increase of pressure, when no heat flows in or out. It is calculated from the speed of sound (U) and the density (ϱ) of the medium by using the equation of Newton Laplace **[18]** as,

$\beta=1/U^2.\varrho$ .....(1)

Inter molecular free length (Lf):

The inter molecular free length is the distance between the surfaces of the neighboring molecules. It is calculated by using the relation [19],

$L_f=K_T\beta^{1/2}$ .....(2)

Where, K_T is the temperature dependent constant and 'β' is the a diabetic compressibility.

Free Volume (Vf):

Free volume in terms of ultrasonic velocity (U) and the viscosity (η) of liquid **[20]** is as follows

$V_f= (M_{eff}. U/K.\eta)^{3/2}$ ---------- (3)

Where 'M_{eff}' is the effective mass of the mixture,

'K' is a dimensionless constant independent of temperature and liquid. Its value is $4.281x10^9$ **[21]**.

Internal Pressure (πi)

The measurement of internal pressure is important in the study of the thermodynamic properties of liquids. The internal pressure is the cohesive force, which is are sultan of force of attraction and force of repulsion between the molecules. It is calculated by using the relation**[22]**,

$\pi_i=bRT(k\eta/U)^{1/2}(\varrho^{2/3}/M^{7/6})$ ----------(4)

Where, 'b' stands for cubic packing, which is assumed to be '2' for all liquids,

'k' is a dimension less constant in dependent of temperature and nature of liquids. Its value is 4.281x109.

'T' is the absolute temperature in Kelvin's is the effective molecular weight, 'R' is the Universal gas constant,

'η' is the viscosity of solution in $N.S.m^{-2}$, 'U' is the ultrasonic velocity in $m.s^{-1}$ and 'ϱ' is the density in $Kg.m^{-3}$ of solution.

Relaxation time(τ):

Relaxation time is the time taken for the excitation energy to appear as translational energy and it depends on temperature and impurities. The relaxation time can be calculated from the relation,

$\tau=4/3.(\beta.\eta)$ ---------- (5)

Where , 'β' is the a diabatic compressibility and 'η' is the viscosity of the mixture.

Acoustic impedance(Z)
The specific acoustic impedance is given by,

$Z=U.\varrho$ ---------- (6)

Where, 'U' and 'ϱ' are velocity and density of the mixture.

Gibb's free energy
The Gibb's free energy is calculated by using the relation

$\Delta G=kT.Ln(kT\tau/h)$ ---------- (7)

Where, 'τ' is the viscous relaxation time, '*T*' is the absolute temperature, 'k' is the Boltzmann's constant and '*h*' is the Planck's constant.

RESULTS AND DISCUSSION

The experimental data relating to density, viscosity and velocity at 298 K,308 K, 318 K and328 K for frequencies 2MHz for the mixtures are given in table-I. The calculated values of a diabatic compressibility (β), free length (Lf) and relaxation time (τ) are reported in table-2. Acoustic impedance (Z), Gibb's free energy (ΔG) and Internal pressure (πi) are reported in table-3. Surfacetenson (S), Rao's constant (R) and Wada's constant (W) are presented in table-4. Free volume (Vf), molar volume and available volume for the mixture are presented in table-5. The variation of different parameters with temperature are shown in fig.1-4.

Ultrasonic velocity increases with increase in mole-fraction of DMF. Also, velocity decreases with increase in temperature. This is due to the structural changes occurring in the mixtures resulting in increase of intermolecular forces. Intermolecular free length is the distance between the surfaces of the neighboring molecules in the mixture. Ultrasonic velocity in a solution depends on free length. As free length increases with temperature, ultrasonic velocity decreases with increase in temperature. Variation in free length indicates variation in molecular forces in the mixture which depends on the experimental density as well as temperature. It is found that free length decreases from s1 to s5 indicating increase in molecular interaction due to association in polar ends.

When the temperature is increased there is a reduction in molecular interaction as they move away from each other. This reduces the cohesive force. Thus, a decrease in internal pressure and an increase in free volume occurs with increases in temperature. In all the binary mixtures, internalpressure decreases with an increase in temperature indicating a weakening of interaction with higher temperature. Contraction in volume leads to a subsequent decrease in a diabetic compressibility as well as in intermolecular free length from s1 to s5 showing more cohesive forces as the concentration of n-but a no enhanced. The separameter increase with the increase in temperature for a particular concentration as high temperature decreases the inter molecular force resulting in an increase of volume.
Relaxation time increase with increase in mole fraction of DMF. Such situation suggests that, the molecules get rearranged due to co-operation process. When temperature increases relaxation time decreases indicating the reverse process. As temperature increases excitation energy increases and hence relaxation time decreases. Relaxation time is the time taken for the excitation energy to appear as translational energy. Further since kinetic energy of the molecules increases, longer time is taken for rearrangement of molecules. Molecular volume increases with rise in temperature. This is because thermal energy facilitates increase in molecular separation. Molar volume should increase with molecular weight, which is evident in our observation. Available volume changes in the same way as molar volume. Available volume is a direct measure of the compactness and strength of bonding between the molecules of the liquid mixture

Gibbs' free energy increases with increase in temperature. Increasing value of Gibbs function suggests that the closer approach of unlike molecule is due to hydrogen bonding **[18-19]**. The increase in Gibbs' free energy also suggests shorter time for rearrangement of the molecules in the mixtures. Decreasing trend of Gibbs free energy with increase in concentration of alcoholic group due to intramolecular hydrogen bonding and force of attraction between polar heads

CONCLUSION

Ultrasonic velocity studies on the system of binary mixture of DMF with n-Butanol shows that, when concentration of DMF increases, more rigid structure is formed due to bonding between the unlike molecules through dipole-dipole and dipole-induced dipole interaction. So acoustic parameters are highly affected at different temperatures due to dipole-dipole and dipole-induced dipole interaction between molecules. Dispersive forces along with intramolecular hydrogen bonding are also found to exist between the component soft the mixture.

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Table-1: Experimental vales of density, viscosity and ultrasonic velocity at different temperatures.

Solution	Density(Kg.m^{-3})				Viscosity(N.s.m^{-2})				Velocity(m.s^{-1})			
	298K	308K	318K	328K	298K	308K	318K	328K	298K	308K	318K	328K
S1	0.819	0.811	0.803	0.795	1.879	1.529	1.247	1.034	1266.4	1250.6	1239.8	1224.8
S2	0.8308	0.8225	0.8142	0.8058	1.546	1.276	1.065	0.901	1288.6	1276.4	1266.5	1251.4
S3	0.8438	0.8353	0.8267	0.8188	1.412	1.173	0.991	0.856	1322.5	1312.0	1306.6	1270.6
S4	0.8568	0.8482	0.8395	0.8307	1.256	1.059	0.903	0.784	1337.8	1315.9	1305.9	1279.7
S5	0.8739	0.8651	0.8562	0.8473	1.226	1.042	0.889	0.711	1351.5	1334.2	1313.0	1288.4

Table-2: Calculated values of adiabatic compressibility, free length and relaxation time at different temperatures.

Solution	Adiabaticcompressibilityx10^{-10}				Freelengthx10^{-10}				Relaxationtimex10^{-12}			
	298K	308K	318K	328K	298K	308K	318K	328K	298K	308K	318K	328K
S1	7.613	7.884	8.101	8.385	0.541	0.556	0.575	0.588	1.907	1.607	1.347	1.156
S2	7.249	7.463	7.657	7.925	0.528	0.541	0.559	0.572	1.494	1.270	1.087	0.952
S3	6.776	6.955	7.085	7.565	0.510	0.522	0.538	0.559	1.276	1.088	0.936	0.864
S4	6.521	6.809	6.985	7.351	0.501	0.517	0.534	0.551	1.092	0.962	0.841	0.769
S5	6.265	6.493	6.774	7.110	0.491	0.505	0.526	0.542	1.024	0.902	0.803	0.674

Table-3:Calculated values of acoustic impedance, Gibb's free energy and internal energy at different temperatures.

Solution	AcousticImpedancex10^{6}				Gibb'sfreeenergyx10^{-20}				Internalpressure			
	298K	308K	318K	328K	298K	308K	318K	328K	298K	308K	318K	328K
S1	1.037	1.014	0.996	0.974	1.196	1.231	1.267	1.303	3.123	2.914	2.714	2.550
S2	1.071	1.050	1.031	1.008	1.186	1.222	1.258	1.294	2.836	2.660	2.505	2.376
S3	1.116	1.096	1.080	1.040	1.180	1.215	1.251	1.290	2.703	2.542	2.403	2.324
S4	1.146	1.116	1.096	1.063	1.173	1.210	1.247	1.285	2.560	2.437	2.318	2.238
S5	1.181	1.154	1.124	1.092	1.171	1.208	1.245	1.279	2.550	2.432	2.323	2.151

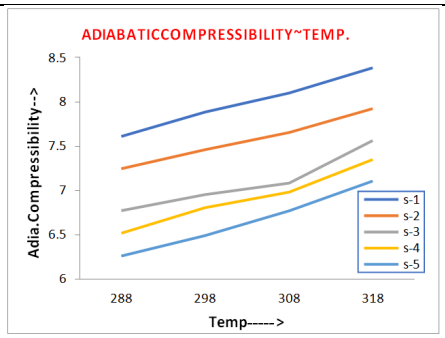

Fig-1: Variation of a diabatic compr. With temperature

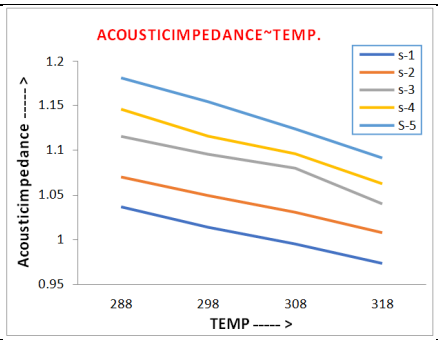

Fig-2:Variationofacou.impedancewithtemperature

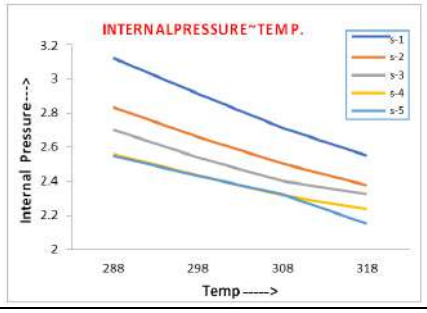

Fig-3: Variation of internal pressure with temperature

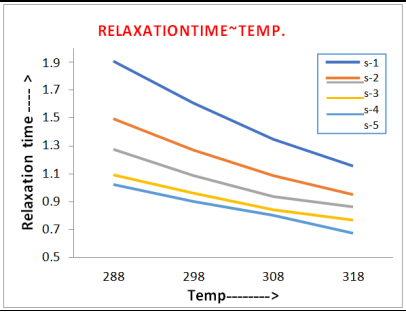

Fig-4: Variation of relaxation time with temperature

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RESEARCH ARTICLE

Analysis of Leaf Chlorophyll Content of Leguminous Plants Grown in Soil Media Containing Rhizobium and Organic Fertilizer.

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ABSTRACT

Chlorophyll is a green pigment in leaves that functions to absorb light energy for photosynthesis. The value of chlorophyll concentration in leaves indicates the health status of a plant. The aim of the present study was to determine the effect of Farm Yard Manure, vermicompost and rhizobium inoculation of different doses on concentration of chlorophyll in a leguminous plant. In the above investigation leguminous plants were given seven different treatments namely control (C),soil with rhizobium inoculated seed(S+R),soil with vermi compost application (S+V),soil with farmyard manure (S+FYM),soil and vermicompost along with rhizobium inoculation(S+V+R),soil with farmyard manure and vermicompost (S+FYM+V) and farm yard manure with vermicompost and with seed inoculation of rhizobium (S+FYM+V+R).Each treatment were taken in replicates. Concentration of chlorophyll a and b was calculated using Arnon method. The results showed that soil treated with seed inoculated with rhizobium along with farmyard manure and vermicompost (S+ FYM+V+R) gave high chlorophyll content .There was an increase in chlorophyll -b content which absorbs high frequency of blue light for photosynthesis.

Keywords: Chlorophyll a, Chlorophyll b, FYM, Vermicompost

INTRODUCTION

Chlorophylls is the main photo receptor for photo synthesis. They are a groups of tetra pyloric compounds. Chlorophyll is found with common structural elements and functions in all photo synthetic organisms including green plants cyanobacteria and algae. Chlorophyll and nitrogen components defines the health condition of plants and deficiency of the set weight cause lower or undesirable productions To prove this, various soil treatments were taken and chlorophyll content was estimated and quantified [1,11]. Legumes plants were chosen for the experiments as they are lifecycle are very short and easy to study different parameters. This work sheds light on the sustainable

use of vermicompost and organic fertilizer. Which has a great impact on ecological equilibrium and climate resilence.

MATERIALSANDMETHODS

Fresh leaves were plucked from the plant, washed with water and soaked by the filter paper immediately, so that it won't leave any moisture for weighing [2,6].The soaked leaf was weighed (in the weighing machine) for 0.5 g.0.5 g of leaf was taken and homogenised in the motor pestle with 80% acetone. Homogenates were centrifuged at 8,000 rpm for 10 min at 25□ for several times Supernatant was collected in a test tube and the remaining pellet was again mixed with acetone for another centrifuge, this process was repeated until the supernatant colour was straw yellowish. Collected supernatant was measured by the spectrophotometer and the absorbance value was recorded [3,4,8]

RESULT AND DISCUSSIONS

Based on the observation and calculation .The chlorophyll contentwas found. The chlorophyll acontent in replicas S+V+F- 3 was very much equal to control plants. The value of chlorophyll a content of p*lant*s was significantly less than chlorophyll b. The plants that were treated with S+V+R-3 have high chlorophyll a content. The value of chlorophyll b content of plants treated with S+F+V+R was the maximum. The total chlorophyll content was highest in S+F+V [9,10,11].

CONCLUSION

The results showed that soil treated with seedinoculated with rhizobiumalongwith farmyard manure and vermicompost (S+ FYM+V+R) gave high chlorophyllcontent .There was anincrease inchlorophyll -b content which absorbs highfrequencyofbluelightforphotosynthesis.

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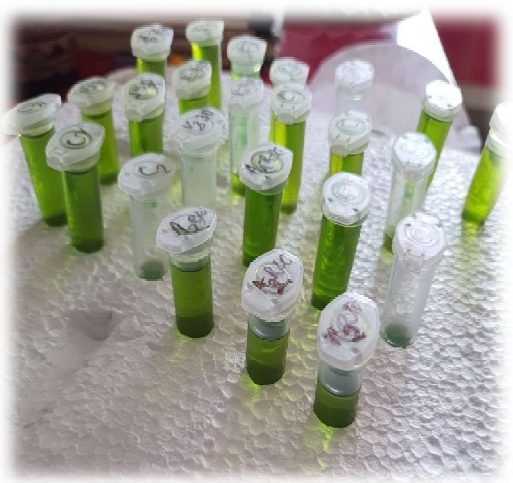
Table1: Showing Total Chlorophyll Content

Sl.No	Treatment	Chl-a	Chl-b	Total Chlorophyll Content (mg/gm)
1	C-1	0.565	0.618	1.118
2	C-2	0.543	0.623	1.216
3	C-3	0.498	0.598	1.164
4	S+V+R-1	0.501	0.516	1.106
5	S+V+R-2	0.491	0.536	1.027
6	S+V+R-3	0.614	0.751	1.365
7	S+R-1	0.602	0.86	1.463
8	S+R-2	0.609	0.984	1.593
9	S+R-3	0.614	0.868	1.605
10	S+V+F-1	0.583	0.701	1.284
11	S+V+F-2	0.566	0.686	1.288
12	S+V+F-3	0.565	0.665	1.274
13	S+FYM-1	0.55	0.753	1.303
14	S+FYM-2	0.583	0.784	1.367
15	S+FYM-3	0.583	0.859	1.443
16	S+V-1	0.599	0.878	1.478
17	S+V-2	0.611	0.975	1.574
18	S+V-3	0.601	0.895	1.585
19	S+F+V+R-1	0.572	0.807	1.379
20	S+F+V+R-2	0.589	0.987	1.575
21	S+F+V+R-3	0.612	1.066	1.679



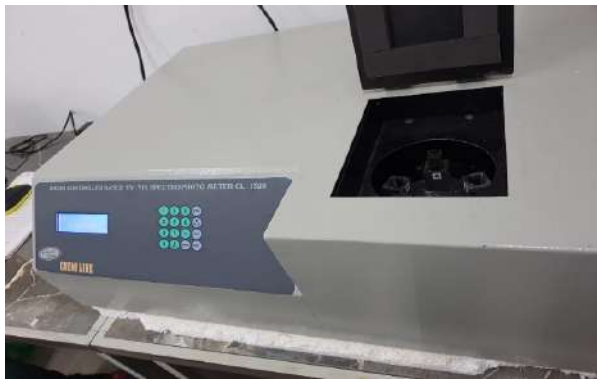
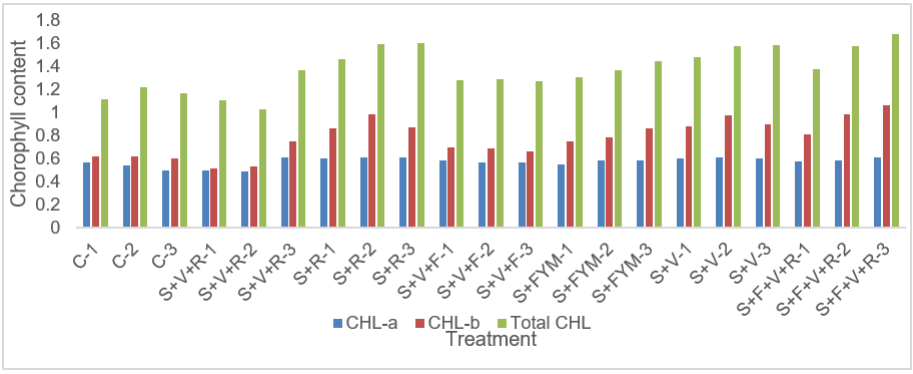


Plate-1 : Showing the figure of Chlorophyll estimation



Graph 1 : Depicting the chlorophyll content and Treatment

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RESEARCH ARTICLE

Improvement in Harris Hip Score (HHS) After Non-Cemented Total Hip Replacement; A Case Series of 60 Patients with Arthritis of the Hip Joint

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ABSTRACT

To determine the mean Harris Hip Score (HHS) improvement after a non-cemented total hip replacement (THR) in younger patients with arthritis of the hip joint. A case series of 60 patients (20-50 years of age) with arthritis of the hip joint was conducted at the Department of Orthopaedic Surgery Nishter Hospital, Multan. In all patients, total hip replacement was done by a consultant orthopedic surgeon. Postoperatively patients were evaluated for the outcome, i.e. Harris hip score at one month after surgery. The results showed that with the mean age of 36.60 ± 7.53 years, most females (53.33%) were between 36 to 50 years of age. Out of total 33.33%were male, and 66.67% were females with a male to female ratio of 1:2. The mean HHS was 48.32 ± 6.58 and 67.72 ± 6.12 at baseline and one month after surgery, respectively ($p < 0.01$). This study concluded that the mean change of HHS after non-cemented total hip replacement in comparative younger patients with hip joint arthritis is quite significant.

Keywords: Arthritis of the Hip Joint, Total Hip Replacement, Harris Hip Score.

INTRODUCTION

Arthritis of the hip is quite common in young adults that may have various etiological factors like avascular necrosis of the femoral head, post-traumatic arthritis, ankylosing spondylitis and juvenile rheumatoid arthritis that may lead to disabling arthritis of the hip [1]. The disability imposed by arthritis can compromise the activities of daily living of these young patients. This is the reason that orthopedic surgeons may come across frequent cases of end-stage hip arthritis in young patients with a needed surgical intervention[2].Earlier, for end-stage hip arthritis in young patients, resection arthroplasty or hip arthrodesis were used. However, lately, total hip arthroplasty (THA) materialized as the feasible alternative to the above surgical procedures [1,3].

Arthroplasty is simply the modification of a joint via surgery to resolve pain and restore movement. Total hip arthroplasty implicates replacement of acetabulum and femur (head and neck) [4]. It is the most re-compensating procedure in Orthopaedics done for patients distressed from advanced degeneration of hip [5]. The primary warning for total hip arthroplasty is always a debilitating pain in patients with precipitating osteoarthritis, especially in cases where conservative methods have proven futile in lessening pain and improving hip function [6,7].

There is a scarcity of literature available on this topic locally. However, the existing evidence elaborates that in young patients with advanced disease, the outcome of total hip replacement (THR) is mostly successful. Therefore, the rationale of this study was to determine the mean HHS after non-cemented total hip replacement in younger patients with arthritis of the hip joint.

MATERIAL AND METHODS

This case series was conducted at the Department of Orthopaedic Surgery in Nishter Hospital, Multan, from 9thApril 2018 to 8th January 2019. Total 60 patients of either gender aged 20 to 50 years presented with arthritis of the hip joint, disease duration of more than three months and baseline HHS < 70 were selected via non-probability consecutive sampling. While, patients with congenital joint deformity, earlier surgical intervention to the affected joint, septic arthritis, any chronic illness like a chronic renal failure (s/creatinine>1.5 mg/dl), chronic liver disease (s / bilirubin >2.0 mg/dl), and patients who lost to follow up were excluded from the study.

A pre-structured proforma was used to record the patient's data, including age, gender, body mass index (BMI), disease duration, the side affected, hypertension, diabetes mellitus, baseline and post-operative HHS (one month after surgery). Total hip replacement was done by a consultant orthopedic surgeon with at least three years of post-fellowship experience. Postoperatively patients were followed up for one month. Prior approval was attained from the institutional ethical committee. Informed consent was obtained from each patient after explaining the study objectives, ensuring confidentiality and no risk involved. The collected data was analyzed using SPSS version 25.0. Mean with standard deviation was calculated for age, duration of disease, baseline and postoperative Harris hip score. In addition, qualitative variables like gender, the side affected, hypertension and diabetes mellitus, frequencies and percentages were calculated. Paired sample T-test was used to compare the mean baseline and postoperative Harris hip score. Furthermore, Independent T-test was applied post-stratification to evaluate the effect of baseline characteristics on Harris hip score, and a p-value ≤ 0.05 was considered significant.

RESULTS

The baseline characteristics of the enrolled patients are given in table 1. Of the total, 20(33.3%) were male patients, and 40(66.6%) were females. The right side was involved in 34(57%) patients, while the rest had affected the left side. The most common mode of injury 51(85%) was road traffic accidents, while 15% of patients had a fracture after a history of falls from height. HHS was calculated for all patients at baseline and 1 month post-operatively. At baseline, the mean Harris hip score was 48.32 ± 6.58, which significantly improved post-operatively (after 1 month), i.e. 67.72 ± 6.12 ($p<0.01$). The changes in post-surgical mean Harris Hip Score regarding age, gender, BMI, and disease duration were assessed. It was found that there was a significant difference in the postoperative mean HHS among the patients with disease duration of < 6 months (65.77 ± 5.59) and > 6 months (73.06 ± 4.02) ($p<0.01$).

DISCUSSION

For the management of disabling end-stage osteoarthritis of the hip, THR has been accepted worldwide [8].The procedure is known to improve quality of life and functional disability significantly [9,10]. However, in the past ten

years, it has been witnessed that there is an increase in the number of THR surgeries globally [11 – 14]. Despite this worldwide increase and the fact that the first THR in Nigeria was done in 1974 [15], arthroplasty procedures had remained in their infancy until recently as a result of infrastructural decay in public institutions due to prolonged military rule [16]. Gogia *et al.* emphasized that an overall improvement of 56 % & 64% occurred in the third month and sixth months after surgery, respectively [17]. Also demonstrated in a study that most enrolled patients got outstanding outcomes post-THR surgery and follow-up physical therapy like reduction in joint pain and improved patient functioning.

The current study determined the mean change HHS after non-cemented total hip replacement in younger patients with a mean age of 36.60 ± 7.53 years. Our results revealed that out of these 60 patients, 33.33% were male, and 66.67% were females, with a male to female ratio of 1:2. At baseline, the mean Harris hip score was 48.32 ± 6.58, and at one month, the mean Harris hip score was 67.72 ± 6.12 with a p-value of 0.0001. Familiar to another study, where at baseline, the mean Harris hip score was 41.15 ± 5.12, at the second week it was 58.76 ± 4.57, while at one month, the mean Harris hip score was 68.13 ± 4.55 [15].

Many studies compared the preoperative Harris hip score with postoperative Harris hip score and changes in mean pain score. Almost all studies indicated enhancement in functional scores and pain relief. Literature also supported that uncemented stems have much decent integration without any signs of loosening, while cemented implants are responsible for high loosening rates. The current study proved that THA in a young patient is useful for better functional improvement and diminishing symptoms. While the more contemporary uncemented implant designs equipped with hard bearings can be related to improved implant survival [18].

In another study, with a male to female ratio of 1:2.1 patient, the most common cause was found to be primary osteoarthritis, while the least common was a vascular necrosis of the femur head occur in hemoglobinopathy [19]. In the same study, it was noted that means of HHS when compared between pre-op and post Op groups at one year was significantly improved with no comorbidity [19].

Joint Range of Movement (ROM) is one of the most vital factors for quality of life post hip replacement [20]. In younger patients, physical activity can be counted as an indicator of the quality of life andits role becoming popular [21]. HHS is a useful and variable system to assess hip joint function [22]. HHS may be increased after THA, especially subsequent to inflammatory arthritis [22,23], but the effect of THA on HHS is similar between young and old individuals [22]. In another study, HHS was obviously raised 18 months after the operation [24]. Patient satisfaction and quality of life were made better after THA in patients younger than 35 years. The ROM improvement obtained through this operation directly correlates with function and patient satisfaction, measured by HHS. It is difficult to achieve a good ROM, especially in young patients [24].

CONCLUSION

This study concluded that the non-cemented total hip replacement in younger patients with arthritis of the hip joint lead to a significant mean change in Harris Hip Score that was fairly extraordinary. Therefore, it can be recommended in young patients suffering from arthritis of hip joint is a preferred surgical approach to improve post-surgery quality of life in these patients.

CONFLICTS OF INTEREST

None.

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None.

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Table 1: Baseline Characteristics

Variables		n=60
Age (year)		36.60 ± 7.53
BMI (kg/m^2)		30.23 ± 3.41
Gender	Male	20(33.3)
	Female	40(66.6)
Co-morbidities	Diabetes Mellitus	34(57)
	Hypertension	25(42)
Side-Affected	Right	34(57)
	Left	26(43)
Mode of injury	Road Traffic Accident	51(85)
	Fall From Height	9(15)

*Values are given as mean±SD or n(%).

Table 2: Mean Harris Hip Score Before and After 1 Month of Non-Cemented THR

Harris Hip Score	**Baseline**	**Post-operative Follow-up (After 1 month)**	**p-value**
	48.32±6.58	67.72±6.12	< 0.01*

*p-value<0.05 is considered significant

Table 3: Harris-Hip Score with Respect to Age Groups

Variables		**HHS (Mean ± SD)**	**p-value**
Age Group	20 to 35 years	69.0±5.77	0.130
	36 to 50 years	66.59±6.29	
Gender	Male	68.10±SD	0.735
	Female	67.35±SD	
BMI	<30 kg/m^2	67.18±SD	??
	> 30 kg/m^2	68.19±SD	
Disease Duration	≤ 9 months	65.77±5.59	< 0.01*
	> 9 months	73.06±4.02	

*p-value<0.05 is considered significant