Recent Trends and Latest Innovation in life Science

Volume-1

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Global Academy

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Chapter 1

MYCOREMEDIATION OF XENOBIOTICS- BLUE PRINT FOR WASTE MANAGEMENT

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ABSTRACT

The roles of fungi and their non-specific extracellular enzymes - laccases, lignin peroxidises, manganese peroxidises, ligninase, oxidoreductase in the degradation of xenobiotic compounds are very important. Contamination of all moieties of environment like water, air, soil by various kinds of nocuous pollutants has become a global concern because of the destructive effects of xenobiotics on living beings and the environment destroying and disturbing the ecosystem and food chain. A variety of hazardous toxic pollutants inducing dyes, phenols, polycyclic aromatic hydrocarbons, chlorinated biphenyls, pharmaceuticals, heavy metals, acids/alkalis, insecticides, pesticides etc are being released into the aquatic bodies which have severely deteriorated the aquatic as well as soil ecosystem. Mycoremedial techniques has been effectively applied for the scavenging of environmental pollutants from soil and water. The different methodologies used in bioremediation process are cost-effective and ecologically sound. Fungi potentially utilize the xenobiotics as Carbon or Nitrogen sources to sustain their growth and metabolic activities. Diverse microbial populations live in harsh environments, exhibiting significance on biodegradation and transformation of pollutants. The applicability of fungi to the bioremediate the pollutants depends on the capacity of fungi to grow in the presence of such compounds as well as their ability to produce nadir enzymes required for degradation of individual and mixtures of xenobiotic compounds. Application of fungal technology for the cleanup of contaminants has shown promising results capable of metabolizing a number of important environmental pollutants.

Keywords: Mycoremediation, Fungi, extracellular enzymes, xenobiotics, harsh environments.

INTRODUCTION

The rapid development of several businesses over the last century has significantly increased the discharge of toxic waste effluents into surface and groundwater [1]. Environmental pollution brought on by the release of a wide variety of xenobiotic compounds from industries is disrupting the ecosystem [2], causing climatic changes, a decrease in water levels in the ground and oceans, melting of icecaps, global warming, ozone layer depletion due to photochemical oxidation, and many carcinogenic and mutagenic effects on living forms of life, among other things. This has caused more attention to be paid to the effects of pollution and its reduction.

VARIOUS SOURCES OF XENOBIOTICS

The direct and indirect sources of xenobiotics are wastewater and solid residual releases from the industries like chemical, textile, paper and pulp, pharmaceutical, plastics, pesticides, herbicides etc which contains hazardous compounds like Phenol, poly cyclic hydrocarbons, different dyes, paint effluents, Pesticides and Insecticides etc.

Dyes

Dye pollution has increased as a result of the widespread usage of dyes in many sectors. Due of its refractory, poisonous, carcinogenic, and mutagenic properties, synthetic dye pollution is currently the worst environmental problem.By reducing sunlight permeability, dye pollution has an adverse effect on aquatic life and can seriously harm the aquatic ecosystem. Wastewater containing dyes must therefore be treated. A safe and environmentally beneficial method of treating wastewater is bioremediation. Fungi have a huge potential for dye decolorization and can be utilised as a remedy. Numerous fungal species have been linked to the decolorization of dye in studies, making it important to understand how these fungal species will be used in the wastewater treatment process. This review concentrated on the use of fungus in the decolorization of dyes, the function of enzymes and proteins.Textile dyes and effluents from the dying processes has adverse impacts on the water quality in terms of total organic carbon (TOC), biological oxygen demand (BOD), chemical oxygen demand (COD), colour, pH and presence of recalcitrant synthetic compounds, such as azo-dyes and heavy metals[1,2]. The water polluted by the textile industry discharges has received an increased attention for several decades, to set up the strategies to solve the present problem[3]. The colouring operations in the textile and related industries use a variety of synthetic dyes and pigments. Dye pollution of soil and natural water bodies is caused by inefficient dyeing processes, careless handling of used effluent, and inadequate treatment of wastes from dyestuff manufacturers. Heavy metals like Cd, Cr, Co, Cu, Hg, Ni, Mg, Fe, and Mn that are highly poisonous, mutagenic, and carcinogenic may be present in significant amounts in untreated textile effluents.

It has been demonstrated through biodegradation studies on the degradation of dyes that fungi such as *Phanerochaetechrysosporium, Bjerkanderaadusta, Trametes versicolor, Phlebia radiata, and Pleurotus spp*. produce the enzyme laccase, which has been found to be closely related to the degradation of lignin and dyes.These fungi have been discovered to be quite effective at breaking down a wide range of dyes with various structural makeups. Due to the oxidative processes of fungi, it is feasible to prevent the production of dangerous anilines by bacteria and other microorganisms that result from the reductive cleavage of azo dyes [4]. The expression of several non-specific extracellular enzymes, such as the ligninolytic peroxidases, which have been linked to the degradation of synthetic dyes, is the primary reason for the interest in the fungal degradation/decolorization of textile dye[5].

These fungi have been discovered to be extremely effective at degrading a wide range of materials. White-rot fungi produce a number of enzymes that have been linked to their ability to degrade natural polymers such as lignin and cellulose, but they can also degrade a variety of synthetic chemicals that are typically resistant to biodegradation [5,6] The promising results obtained with this ligninolytic fungus have prompted researchers to

investigate the potential of other species of ligninolytic basidiomycetes. Fungi have been shown to be suitable and effective for dye degradation/decolorization and the removal of colourants from textile effluents in wastewater treatment. These fungi remove dyes and pigments in both living and dead forms via biosorption, biodegradation, bioaccumulation, and enzymatic mineralization using lignin peroxidase, manganese peroxidase, and manganese independent enzymes.The focus of study on the bio-treatment of wastewater constituents like metals, inorganic fertilisers, and organic compounds has switched to fungi.

Phenols

A wide range of organic compounds, including phenol and other substituted phenol, are present in the natural water sources from the effluents of various chemical and pharmaceutical industries, including coal refineries, phenol production, medicines, dying, petrochemical, pulp mill, etc. The simplest aromatic molecule, phenol, has a connected hydroxyl group to the benzene [6]. Due to its toxicity even at low concentrations and the generation of substituted compounds during the oxidation and disinfection processes, phenol is one of the most common chemical and pharmaceutical pollutants. Depletion of the ozone layer, changes to the earth's thermal balance, decreased visibility, and the addition of acidic air pollutants to the atmosphere are just a few of its direct environmental repercussions [7]. Prior to wastewater release, it is imperative to remove phenol from industrial wastewaters toin order to lessen each of these impacts. Because phenol is a carcinogenic substance, it must be biodegraded using a process that produces few secondary metabolites and safe by-products [8]. Numerous investigations and in-depth research into the biodegradation of phenol and its derivative chemicals have demonstrated that a range of pure cultures of bacteria may digest phenol aerobically.

Plastics

Because of the links and interactions between molecules, plastics are strong and disintegrate relatively slowly. Polystyrene, polyvinyl chloride, polyethylene, and its derivatives are the main ingredients of plastics. The natural biodegradation processes are very resistant to petroleum-derived (petro-)polymers like polyethylene (PE), polyethylene terephthalate (PET), polyurethane (PU), polystyrene (PS), polypropylene (PP), and polyvinyl chloride (PVC). Chemical structures, molecular weights, and levels of crystallinity are only a few of the variables that affect how quickly a polymer degrades. The latter gives polymers their flexibility. Polymers are big molecules possessing both regular crystals (crystalline region) and irregular groups (amorphous region). Polymers with high crystallinity, such as polyethylene (95%), are inflexible and have a poor ability to withstand impacts. The importance of microbial breakdown of plastics has increased recently, yet the fragmented chemicals generated by thesecould cause further environmental problems. Therefore, bioplastics, a type of plastic made from renewable biomass sources such vegetable fats and oils, corn starch, pea starch, or microbiota, were required in order for them to decompose quickly. Starch-based plastics, cellulose-based plastics, polylactic acid (PLA) polymers, and bio-derived polyethylene are examples of bioplastics.[9]

Polycyclic aromatic hydrocarbons (PAH)

One of the main pollutants that are discharged into the environment as a result of the incomplete combustion of organic materials like coal, wood, and petroleum is known as polycyclic aromatic hydrocarbons (PAH). Numerous natural or human activities might cause these hazardous chemicals to get into the air, water, and soil [10,11]. Pyrene, anthracene, chrysene, phenanthrene, 2-methyl naphthalene, and acenaphthene are examples of chemical compounds having fused benzene rings known as PAH. The three groups of these pervasive contaminants are biological, petrogenic, and pyrogenic [12]. These substances have the potential to impair immunity and result in skin, lungs, and stomach cancers. In addition, they can harm the kidneys and result in jaundice, inflammation, allergies, cataracts, and the lysis of red blood cells. These toxins will stay in the environment for a very long time and do significant harm to the ecology. Therefore, it is urgent to take action to remove these pervasive, persistent, and harmful compounds from polluted soil and water [13]. Numerous methods, including biodegradation, bioaccumulation, photodegradation, soil adsorption, leaching, and chemical oxidation, have been thoroughly investigated for the removal and degradation of PAH from polluted locations. Research on biodegradation, which employs microorganisms to break down resistant contaminants, is one of these techniques [14].

Paper and Pulp Effluents

Environmental pollution is also caused by the discharge of effluent from paper mill companies, which cannot be ignored. This is due to the fact that several chlorinated organic compounds are haphazardly created during pulp bleaching. If pulp mill effluents are discharged into oxygen-limited or oxygen-depleted (anaerobic) waterways, the issue is frequently made worse. Paper mills have been obliged to reduce the emission of adsorbable organic halides and to look for technology for cleaner productions as a result of greater public awareness of pollution and more stringent restrictions against polluting operations [11,13]. Certain anaerobic bacterial species have the ability to methylate chlorinated organic compounds, which increases the compound's toxicity and lipophilicity to higher animals [7,9]. Tetrachloroguaiacols, tetrachlorocatechols, di-, tri-, tetra-, and pentachlorophenols, as well as other hazardous substances, are found in the effluent from pulp and paper mills [15].

Pesticides and Insecticides

Numerous pesticides and insecticides, such as benzimidazoles, methyl parathion, morpholine, and organophosphorous chemicals, are widely utilised and have added to the pollution burden because of their slow breakdown [9]. Since these halogenated aromatic chemicals have a negative impact on the environment and ecosystem both directly and indirectly, microbial breakdown is seen as a benefit in this circumstance, despite their slowness. Pesticides have been widely criticised for their use since they have a large negative impact on the environment and cause serious health issues[16]. The necessity that a pesticide be degraded into non-toxic and environmentally acceptable compounds and the requirement for a sustained level of biological activity in the environment frequently conflict [17].Most of the time, the chemical composition and level of water solubility can be

used to explain persistence. Additionally, several of these pesticides have a propensity to accumulate at various trophic levels of the food chain species. One of the main classes of harmful chemicals that pollute the environment and pose a serious threat to human health are chlorinated organic pesticides [18].

Heavy Metals

Metals with a high density and high toxicity to living things are referred to as heavy metals. They fall into two categories: (1) essential elements, such as chromium (Cr), iron (Fe), and zinc (Zn), which are toxic when present in excess but necessary in small amounts for the physiological functions of organisms, and (2) non-essential elements, such as cadmium (Cd), lead (Pb), and mercury (Hg), which have unknown biological functions but negatively impact the organism. Natural sources of HMs in the environment include volcanic eruptions and the weathering of rocks containing metal. While human origins have contributed to the spread of HMs in soil, water, and air, the expansion in agricultural and industrial activities has greatly increased the environmental degradation caused by HMs [19]. Furthermore, HMs can disperse acrossvast distances in both gaseous and solid phase states, allowing for their quick agglomeration in some life systems as well as in soil and water. For instance, plants absorb and retain soils with high HM concentrations, which subsequently pass down the food chain to animals and people [20]. Plants, animals and humans as potential hosts can lead to a HM-polluted microenvironments where pathogens dynamically adjust to survive. Thus, soil and/or water pollution by HMs is a critical and complex-dynamic environmental problem.

HMs are among the most studied environmental contaminants, yet little is known about how they affect the patho biology of fungi and species that resemble fungus. Understanding the latter is critical and significant due to the potential that HMs may target pathogenicity-related processes and the fact that filamentous eukaryotic pathogens are the cause of many devastating diseases. In this review, we cover a variety of HMs toxicity issues as well as connections between HMs stress and microbial pathogenicity. As an illustration, HMs can interact with molecules like proteins and cause their deactivation [21,22]. According to research, essential HMs can cause significant growth suppression as well as morphological and physiological changes in non-pathogenic microorganisms that live in soil [23].

Additionally, metals have a negative impact on the soil microbial population and their activities that are linked to soil respiration rate at high concentrations, which may also result in a decrease in soil fertility [24]. Contrary to necessary HMs, non-essential HMs are mostly unknown and have poorly understood effects on both non-pathogenic and pathogenic microbes. However, given the rising environmental pollution, it is becoming a topic of research that is becoming more and more significant.

BUDDING FUNGI AND DIFFERENT DECAY TECHNIQUES

Mycoremediation can be a cost-efficient, environmentally responsible, and successful technique to address the ever-growing issue of soil and water pollution. Fungi are a prime candidate for the remediation of various pollutants due to their robust growth, extensive hyphal network, production of versatile extracellular ligninolytic enzymes, high surface

area to volume ratio, resistance to heavy metals, adaptability to changing pH and temperature, and presence of metal-binding proteins [5, 6,7,8].

Mycoremediation is the practise of employing fungi to bioremediate polluted wastes.

The decomposition of several harmful compounds, including petroleum hydrocarbons, polychlorinated biphenyls, heavy metals (via biosorption), phenolic derivatives, persistent pesticides, etc., is greatly aided by mycoremediation. Some of these harmful substances are used as a source of nutrition by fungi, who then transform them into more straightforward fragmentary forms. Microalgae may one day serve as a commercial-scale substrate for the production of bioenergy.

There are various mycoremediation techniques, including:

Biosorption

Certain biomass naturally engages in biosorption, a physiochemical process that enables it to passively concentrate and bind pollutants onto its cellular structure [25]. The advantage of biosorption over bioaccumulation is that deposited metal or waste can be easily removed using straightforward physical techniques without endangering the structural integrity of the biosorbent. The most promising adsorbent is fungus, whose cell walls and constituent parts play a significant role in biosorption. Even in the absence of physiological activity, it has been observed that fungal biomass can absorb sizeable amounts of organic contaminants from aqueous solution by adsorption or a similar process. There are many different types of fungi, including Neurospora crossa Botrytis cinerea, Phanerochaetechrysosporium, Mucor sp., Aspergillus carbonaruius, Aspergillus niger, Rhizopus sp., Saccharomyces cerevisia and Lentinus sajor-caju been thoroughly investigated for the biosorption of heavy metals [26]. The effective biosorberbant was determined to be Saccharomyces cerevisiae.

Lignin Degrading Enzymes

Generally speaking, there are two main categories of lignin-degrading enzymes: lignin-degrading auxiliary enzymes and lignin-modifying enzymes. Lignin-degrading auxiliary enzymes require cooperation from other enzymes in order to completely digest lignin; otherwise, they are unable to do so [27]. By coordinating the sequential actions of many proteins, including potentially oxidative H_2O_2, lignin-degrading auxiliary enzymes facilitate the process of lignin degradation [27]. Cellobiose dehydrogenase, aryl alcohol oxidases, glyoxal oxidase, glucose oxidase, and pyranose 2-oxidase are members of this group [27]. These include lignin (LiP), manganese (MnP), versatile peroxidase (VP), and feruloyl esterase, which the lignin modifying enzymes produced by diverse microorganisms that are categorised as laccase and heme-containing peroxidase [28,29].

These lignin-modifying enzymes are also known as ligninolytic enzymes as a group. These enzymes have attracted a lot of interest from biological agents for the breakdown of substances found in lignocellulosic waste as well as other organic contaminants. Additionally, it has been claimed that ligninolytic enzymes are efficient at treating xenobiotics and industrial waste through the biodegradation and decolorization process [30]. Laccase (EC 1.10.3.2), Lignin peroxidase (EC 1.11.1.14), Manganese peroxidase (EC

1.11.1.13), and Versatile peroxidase are the most prevalent enzymes that break down lignocellulosic waste (EC 1.11.1.16). Researchers recently discovered that a number of other enzymes, including feruloyl esterase (EC 3.1.1.73), aryl-alcohol oxidase (EC 1.1.3.7), quinone reductases (EC 1.6.5.5), lipases (EC 3.1.1.3), xylanase (EC 3.2.1.8), and catechol 2, 3-dioxygenase (EC 1.13.11.2), indirectly support the ligninolytic [28,31,32].Laccase enzyme functions as a mediator for hydroxycinnamic acid, which is changed by feruloyl esterase during the breakdown of lignin [28]. Different bacteria and fungi participate in the breakdown of lignin by producing aryl-alcohol oxidase and quinone reductases [31]. It was suggested that it operate on quinones' reduction so that ligninolytic enzymes may utilise them or use them to enhance a peroxidase activity [32]. Similar to this, lipase enzymes can act as excellent biocatalysts for in-situ peracid synthesis in non-aqueous conditions, starting with carboxylic acids with dilute hydrogen peroxide. Dimethyl carbonate was employed for lipase-mediated oxidation both as a solvent and as an acyl-donor reagent for lignocellulosic delignification in a non-aqueous solvent. Furthermore, immobilised lipase was successfully used in this approach.

Not much lignin was released by xylanase and catechol 2, 3-dioxygenase, but the enzyme made it easier to remove the lignin fraction by dissolving the monocyclic aromatic connecting between xylan and lignin [33,34]. The amino acid sequence and co-factor makeup of the ligninolytic enzymes determine their varied molecular weights.

Laccases

A copper-containing extracellular enzyme called laccase (EC 1.10.3.2) is made up of monomeric, dimeric, and tetrameric glycoproteins. This is primarily seen in bacteria, fungus, and actinomycetes, which are microorganisms [35,36]. Several researchers have observed that various isoenzymes range in molecular weight from 50 to 300 kD [37]. About 500 amino acid residues, three successive domains, and a Greek key–barrel topology are found in the laccase enzyme's molecular structure, which is cycled as a single molecule (Matera et al., 2008). Initial 150 amino acids are present in the first domain, between 150 and 300 residues are present in the second domain, and between 300 and 500 amino acids are present in the third domain [37]. Typically, two disulfide bridge bonds located between domains I and II stabilise the structure [37,38,39]. Even so, there is also some laccase in the three disulfide bridge bonds. In domain I, between domain I and domain III, and between domain II and domain III, Melanocarpusalbomyces possesses disulfide bridges [40].

Three different types of copper atoms are found in laccase and are connected together to coordinate with one another and keep the amino acids' active site intact. Similar to other multicopper oxidases, the first domain (T1 Cu), also known as the substrate reducing site, has a varied triangular planar coordination [41]. They showed that the active region contains an amino acid sequence known as the equatorial ligands, which includes two histidine’s and one cysteine. As opposed to this, other multicopper oxidases enzymes incorporate a second axial ligand that contains methionine [38, 39,40,42]. Another example of coordination between T2 Cu and two His amino acids and a water molecule. T3 Cu, however, the two. to share an oxygen molecule that reduced into a water molecule and split away, two Cu molecules with six His are present in two groups of three active sites

[38,39,40]. Due to its ability to oxidise a wide range of compounds using O2, laccase is regarded as a perfect "green catalyst," with H2O being the only byproduct [43,44].

Details on bacterial species strains and laccase-like proteins are mentioned, along with their functions. This enzyme facilitates communication and aids in the breakdown of lignin polysaccharide complexes [28]. The laccase enzyme activity decrease as the substrate size increases, although this substrate accessibility can be overcome by using the appropriate laccase mediators. Through the use of laccase and regulated reaction kinetics, mediators are oxidised for unstable intermediates in the first phase of the reaction. The oxidised mediator diffuses away from the location where the enzyme is active, and due to its tiny size, it can enter the pores in the cell walls of plants to reach the desired substrate. On the other hand, a wide variety of substrates can be oxidised through laccase and the process can be sped up.Sometimes the mediating agent is a highly reactive unstable cationic radical that can oxidise a more complicated substrate before reverting to its initial form.

For the purpose of detoxification and degradation, laccase can work on lignocellulosic material that contain phenolic and non-phenolic compounds as well as extremely residual compounds. They believed it to be a useful tool for bioremediation. In order to produce phenoxy radicals via coupling with polymerization, laccase removes one electron from the hydroxyl groups of substances that contain phenolic lignin, such as vanillyl glycol, 4,6-di (t-butyl) guaiacol, and syringaldehyde [45]. Phenoxy radicals (1-) are produced during the breakdown of phenolic compounds like the lignin model (1-(3,5-dirnethoxy-4-hydroxyphenyl)-2 (3,5-dimethoxy-4-ethoxyphenyl)propane-1,3-diol) (3,5-dirnethoxy-4-hydroxyphenyl) 2,6-dimethoxy-p-benzoquinone, 2,6-dimethoxy-p-hydroquinone, and -2 (3,5-dimethoxy-4-ethoxyphenyl)-3-hydroxypropanone(3,5-dimethoxy-4-ethoxyphenyl)-3hydroxy-propanal), which causes C-oxidation, C-C cleavage, alkyl-aryl cleavage, and aromatic ring cleavage [45,46].In the presence of a mediator, the enzyme laccase is essential for the depolymerization of a number of substances, including lignin and its derivatives for the delignification of oxidised -O-4 lignin dimers [47].

Lignin Peroxidases

Lignin peroxidases (EC 1.11.1.14) are an oxidoreductase family member that breakdown lignin and its by-products when H2O2 is present [48]. These are heme-containing enzymes that breakdown the polymer through an oxidative mechanism, and they are mostly released by higher fungi and some bacteria [49]. Additionally, some insects, including Reticulitermes flavipes and eastern subterranean termites, have employed this enzyme to decompose higher woody waste. Lignin peroxidases (LiPs) are monomeric glycosylated enzymes with a molecular weight of (40-68 kDa), two calcium ions, three forty-three amino acid residues, four carbohydrates, and a heme group [50]. However, LiP is helicoidal in form, with two anti-parallel beta-sheets, main and minor eight helixes, and two domains on either side of the heminic group, two domains. The heme, which has 40 residues, forms hydrogen bridges with the protein. The protein is supplemented by this group, which also possesses two tiny solvent accessibility channels [50].Additionally, the high redox potential of the enzyme and the heme iron linked to the His amino acid. The distance between each heme group and the His amino acid raises the enzyme's redox potential, which results in an electronic deficit in

the iron's porphyrin ring [50,51]. Additionally, Phlebia radiata, a fungus that produces lignin peroxidase, has a molecular structure with a molecular weight of 38439.0, 361 amino acids, a theoretical isoelectric point of 4.29, the formula C1692H2604N456O535S17, negatively charged residues (Asp + Glu) of 48, positively charged residues (Arg + Lys) of 19, an index of computed instability [51].

Various organic compounds have been oxidised using the lignin peroxidase enzyme with the use of co-substrate (H_2O_2) as a mediator. These enzymes are essential for the conversion of many non-phenolic lignin derivatives and lignin-containing compounds with -O-4 links to homologous ketones or aldehydes. Additionally, they participate in the hydroxylation of aromatic ring cleavages' benzylic methylene groups [52,53]. In contrast to non-phenolic substances, it preferentially and considerably more quickly catalyses the oxidation of phenolic compounds like vanillyl alcohol, catechol, acetosyringone, syringic acid, and guaiacol. LiP is a crucial catalyst for the enzymes needed to break down materials containing lignocellulosic material.

Manganese Peroxidise

The heme-containing enzyme manganese peroxidase (MnP), which is a member of the oxidoreductases family [54]. In their microenvironments, ligninolytic bacteria release the MnP enzyme in both solid and liquid form [55]. After coding and regulating different genes, it has been reported that numerous bacteria, basidiomycetous fungi, and algae produce MnP isozymes with an average molecular mass of 40–50 kDa[56]. MnP has frequently been noted as essential enzymes for the breakdown of lignin. Two Ca2+ ions and five disulfide-bridging components found in the molecular structure of the MnP enzyme are in charge of preserving the enzyme's active site structure [57,58].

The proximal histidine ligand (His), which is H-bonded to an aspartic acid residue (Asp), and the distal side peroxidase-binding pocket, which contains catalytic His and arginine (Arg) residues, are among the amino acids that make up the MnP enzyme active site. The mutations of the MnP enzyme show that there is only one Mn2+ binding site, which is composed of two water molecules, three acidic ligands, and a heme propionate. MnP enzyme is the crystal structure of the substrate-binding site [59,60]. In a multistep process, ligninolytic microorganisms such basidiomycetes, white-rot fungi, and bacteria converted Mn2+ to Mn3+. The MnP enzymes' activities and synthesis of the substrate are accelerated and triggered by Mn2+.

The Mn3+, which was produced by the MnP enzyme, then serves as a mediator in the oxidation of a number of phenolic and non-phenolic substances. The oxalate that the Mn3+ chelates is too tiny to permeate into the enzyme's active site. Certain lignin structures that are similar in some cases, such as stubborn substances buried deep in the soil, are not always incompatible with enzymes [61]. Additionally, the native MnP enzyme's hydrogen peroxidase equivalent creates the electronic absorption spectrum. phenolic and nonphenolic chemicals found in lignocellulose were oxidised by the enzyme manganese peroxidase.Through the oxidation of phenolic substances such phenol-containing pigments, amines, and lignin derivatives, MnP enzymes produced Mn (III). In addition to acting as a diffusible oxidant and producing intermediate phenoxy radicals, it also causes bond

cleavage and rearrangement, non-enzymatic degradation, and other processes that result in a variety of products. In the presence of the second mediator, the reaction was catalysed by the oxidation of various non-phenolic lignin derivative chemicals via Mn (III).

Versatile Peroxidise

The oxidoreductase family includes versatile peroxidase (VP), also referred to as hybrid peroxidase (manganese-lignin peroxidase), which incorporates glycoproteins. Different fungus species, including *Bjerkandera, Lipista, Pleurotus,* and even bacterial species, have been found to produce peroxidase [62,63,64,65] Fungal genomes have two families of enzymes, such as the LiP and MnP genes, which are both in a "hybrid peroxidase," according to genetic studies [66]. With a dual oxidative capacity, low to high redox potential, substituted phenol dyes, and $Mn^{2+,}$ VP are a desirable wild-type enzyme [67]. These classes of enzymes can oxidise phenolic, non-phenolic, and lignin compounds. In the absence of manganese, these sets of enzymes can oxidise phenolic, non-phenolic, and lignin derivatives. They may oxidise substances without the need for a mediator.Dye-decolorizing peroxidases, which include LiP, MnP, and VP, are a novel family of heme peroxidases that are phylogenetically unrelated to the traditional LME peroxidases [68]. Two domains with - helices and anti-parallel -sheets are shown in the structure of DyP-type peroxidases, and the heme cofactor is found in the cavity between the two domains [69]. The observed similarities of the catalytic site (heme pocket) must be viewed as a convergent form of evolution to offer similar reactivity of these enzymes given the little evolutionary relationship between DyPs and the standard LMP family [70]. In a culture of the fungus B. adusta (formerly known as *Geotrichum candidum)*, the DyP-type peroxidases were first identified. They were given their name because of their capacity toto discolour a variety of dyes [71,70]. Other fungi, including *Termitomyces albuminosus, Auricularia auricula-judae, Irpex lacteus,* and the bacteria *Rhodococcus josti*, *Thermobifida fusca* [72], and *Pseudomonas fluorescens*, have also been found to exhibit ligninolytic ability [73].

FUNGI'S INVOLVEMENT IN BIOREMEDIATION

WRF- White Rot Fungi

In nature, white-rot fungi play a key role in the biodegradation of ligninous materials, which helps to recycle carbon globally. With regard to their breakdown by white-rot fungi, endocrine disrupting chemicals (EDCs) and toxic organic compounds (TOCs), such as pharmaceuticals and personal care products (PPCPs), have attracted a lot of attention. These substances can have negative effects on human health as well as bioaccumulation, acute and chronic toxicity to aquatic organisms, and possible bioaccumulation. The majority of research have shown that white-rot fungi like *Phanerochaete chysosporium*, *Trametes versicolor*, *Bjerkandera adjusta,* and *Pleurotus* sp., which produce various ligninolytic enzymes such laccases and peroxidases, are capable of bioremediation. [74]. By encouraging microbial activity with the use of a bio purification system (BPS), the ligninolytic enzymes from white-rot fungi have been used to convert a variety of organic contaminants, including pesticides, from contaminated wastewaters [75]. Pressure refining was used to separate the fibres of lignocellulosic materials because lignin granules that are accumulated on the surface of the fibres prevent ligninolytic enzymes from accessing them. This method improved the

availability of ligninolytic enzymes from *Ceriporiopsissub vermispora*, a white-rot fungus that demonstrated better delignification from pressure-refined miscanthus than from milled miscanthus [76]. In the case of the decolorization of Direct Blue 14 by several extracellular ligninolytic enzymes, white-rot fungi were shown to be the dominant factor in the area of dye degradation or decolorization.

Coriolus versicolor, Hirschioporusl arincinus, Inonotushis pidus, *Phanerochaete chrysosporium,* and *Phlebia tremellosa* are just a few of the diverse fungal groups that have been reported to decolorize dye effluent [14], while 38 species of white-rot fungi have been shown to reduce total phenolics (>60%) and colour (70%) from olive-mill Similar to this, two strains of white-rot fungi—*T. versicolor* and *Lentinus tigrinus*—have been used to remediate cresolate-contaminated soil. [77]. After a biopiling treatment, the cresolate-polluted soil was still contaminated with high molecular weight PAH fraction and refractory petroleum hydrocarbons. By biostimulation with lignocellulosic substrate and bioaugmentation of fungi, the residues might be significantly degraded. But there was always a chance that this kind of treatment may encourage the development of nearby microorganisms, which might then take control of the enhanced creature, highlighting the necessity of verifying such experiments on a small scale before field usage. Other properties, like laccases, have also been used by white-rot fungus for breakdown of substituted organic compounds at increased removal efficiencies in addition to the ligninolytic enzyme applications mentioned above for bioremediation of a variety of chemicals [78].

Given the importance of these characteristics in bioremediation, efforts have been made to increase the laccase production in *T. versicolor* and *P. ostreatus*, two white-rot fungi, through solid state fermentation on orange peels, followed by further testing of the ability of the organisms to bioremediate PAHs like phenanthrene and pyrene [79]. Though *P. ostreatus* generated 2700 U/L laccase and T. versicolor cultures produced 3000 U/L laccase, P. ostreatus demonstrated superior elimination of phenanthrene and pyrene. It is necessary to investigate these fungi at the genome level in order to fully comprehend and utilise their bioremediation potential. productivity [80].

Basidiomycetes

White rot, brown rot, and leaf litter fungus are only a few examples of the species, which are thought to be a particularly intriguing group of fungi and natural lignocellulose destroyers. Laccases, an enzyme with copper discovered in these basidiomycetes, breakdown polycyclic aromatic hydrocarbons from natural oil deposits [81]. PVC is broken down by white-rot fungi in an aerobic environment by secreting extracellular enzymes that interact with the polymers.

*Pleurotus pulmona*rius, an edible rot fungus, is renowned for its capacity to break down crude oil [82]. The ability of ligninolytic fungi to break down organ contaminants, such as synthetic colours, is higher. Due to their benefits, which include a long biomass retention time in the system, simplicity of use in a continuous reactor, and ability to scale up, immobilised fungal cultures are now used for efficient biodegradation of textile dyes in semisolid state-, trickling-bed-, and rotating disc reactors [83]. Mascoma proved that *Saccharomyces cerevisiae* can produce ethanol from paper sludge at a rate of 85% without the

need of industrial enzymes. Cellulolytic enzymes produced by the well-known fungicide *Trichoderma harzianum* are widely utilised in the paper and textile sectors to break down cellulose.[84]

Marine Fungi

Marine fungi have been shown to have the ability to produce novel enzymes, biosurfactants, polysaccharides, and polyunsaturated fatty acids in addition to their use in the bioremediation of heavy metals and hydrocarbons [85]. These fungi have a biological advantage over terrestrial fungi because of their capacity to adapt to very alkaline and acidic environments. The effectiveness of marine microbes in the removal of metal ions suggests the potential of extremophilic organisms in both bioremediation and nanotechnology. [86] reviewed the role of marine fungi from mangrove areas with the various potential applications in mind, paying particular attention to their diversity, enormous ecological role, and biotechnological potential as a source of new medications, enzymes, biodiesel, biopesticides, and bioremediation.

Recent research by [87] has demonstrated the importance of marine-derived fungal enzymes and their biotechnological applicability. Even high concentrations of heavy metals like lead and copper have been discovered to be tolerated by marine fungi [88], and their interaction with metal ions in marine ecosystems can be exploited to synthesise metal nanoparticles with desired characteristics. Fungi have the capacity to generate nanoparticles both extracellularly and intracellularly, which is employed for a variety of purposes in industries like the textile industry, food preservation, pharmaceuticals, and clinical microbiology, among others [89]

Extremophillic Fungi

Due to their extremophilic enzymes' particular properties, such as thermotolerance, pH resistance, and tolerance to other severe circumstances, fungi from extreme habitats are very valuable from an industrial standpoint [90]. Due to their exposure to high levels of pollutants from industrial effluents, effluent treatment plants represent one of the potentially lucrative niches that might be targeted by fungi capable of a variety of bioremediation applications.

The aforesaid characteristics make them the best candidates for processing and bio-conversion of raw materials that are both affordable and environmentally beneficial, such as in the food industry, leather processing, textile manufacturing, animal feed preparation, and bio-remediation [91]. revealed the potential uses of metallophilic bacteria in bioremediation of troublesome heavy metals from the environment and achieved nanoparticle synthesis with their use. *Cryptococcus sp.*, a psychrophilic fungus isolated from deep-sea sediments, demonstrated tolerance and proliferation in the presence of high concentrations of heavy metals (up to 100 mg/L) $ZnSO_4$, $CuSO_4$, $Pb(CH_3COO_2)$, and CdC_{l2} [92], which may shed light on their manner of adaptation in such circumstances. Numerous hydrolytic enzymes that are known to be active in extremophilic environments have beeninvolved in cleanup procedures in situations with excessive salinity and contamination from extra-heavy crude oil (ECHO) drilling debris from oil belts [93].

When wheat bran was present, it was found that extreme acting laccases were in charge of the bioremediation activity in *Pestalotiopsis palmarum*, while lignin peroxidases were generated when extra heavy crude oil served as the sole source of carbon and energy [94]. Because they can affect the chitin exoskeleton of insects, other enzymes like chitinases made by the psychrophilic fungus *Lecanicilliummus carium* could be used to increase the activity of pesticides [95]. The isolation of the extremophilic fungi from harsh environments, such as the deep biosphere habitat represented by fumarolic ice caves on Mount Erebus in Antarctica, can be used to identify particular fungi capable of using energy sources other than photosynthesis in addition to providing information about bioremediation studies.

SYMBIOTIC FUNGI WITH PLANTS AND BACTERIA

Fungi are known to form tight relationships with plants and bacteria in order to get over the obstacle of their growth being constrained by various environmental factors. The most typical symbiotic relationship between fungi and plants is represented by arbuscular mycorrhizal fungi (AMF), in which the microbial partner facilitates pollutant removal by supplying a larger surface area for absorption of pollutants through its hyphae and spores by mobilising the pollutants and binding to the root. Root samples from plants employed for phytoremediation of groundwater contaminated with various contaminants in a built wetland showed signs of AMF colonisation [96]. A. *nidulans, Bjerkandera adusta, Trametes hirsuta, T. viride, Funaliatrogii, Irpexlacteus,* and *P. ostreatus* are a few plant-associated fungi that might survive and decolorize textile industry effluents [97].

High levels of tolerance to PAHs, especially anthracene, were caused by similar colonisation of the AM fungus *Rhizophagus custos* under root-organ cultures, which also resulted in decreased synthesis of the hazardous by-product anthraquinone [98]. It has also been demonstrated that increased 137Cs uptake by quinoa plants on loamy soil following inoculation with a commercial AM product is related to the mycorrhizal effect as a result of root colonisation [99]. *Suillusbovinus* and *Rhizopogonroseolus,* two ectomycorrhizal fungi, have recently been demonstrated to be beneficial for removing cadmium from Pinus, albeit this effect was also influenced by other environmental conditions as the type of nutrients and pH [100]. By co-cultivating microalgae and fungi for the production of algal biofuels and photosynthetic biorefineries, these fungi have also been used in other applicationsfrom a medium for fermentation. This led to higher yields of biomass, lipids, and bioproducts as well as their extraction and collection by straightforward filtration [101]. Despite the advantages of co-culture research for bioremediation, their applications are challenging and call for a greater understanding of how a variety of metabolic pathways from various organisms interact.

EFFICACIES OF FUNGI IN BIOREMEDIATION

Numerous pollutants, including POPs, textile colours, petroleum hydrocarbons, pulp and paper industry effluents, leather tanning effluents, PAHs, pesticides, and PPCPs, have been found to be bioremediated by fungi. For their capacity to tolerate metals, filamentous fungus like *Aspergillus, Curvularia, Acrimonium, and Pithium* have been investigated [102]. According to reports, Basidiomycota species like *T. versicolor* and the white-rot fungus *Pleurotus ostreatus* breakdown model PAHs in solid-state fermentation (SSF) when they

grow on agricultural wastes like orange peels [103]. *Aspergillus, Penicillium*, and alkalophilic white-rot fungi have all been documented to bioremediate or decolorize coloured effluents from the sugar industry, textile dye, bleached kraft pulp mill, and leather tanning effluents, demonstrating a variety of substrate preferences.

Coffee pulp could be decaffeinated when fungi like *Aspergillus restrictus, Chrysosporium keratinophilum, Fusarium solani, Gliocladiumroseum, Penicillium*, and *Stemphylium* were present under controlled conditions with additional nutrients for applications in animal feed preparation or for the production of bioethanol [104]. Short incubation times for bioremediation in the presence of the fungus *A. niger* and *P. chrysosporium* resulted in significant removal of petroleum hydrocarbons from soil contaminated with gasoline and diesel [105]. The removal of chloropyriphos and its metabolite 3,5,6-trichloro-2-pyridinol (TCP) from polluted soils by the fungal strain *A. niger* JAS1 was examined by Silambarasan and Abraham [106] even in the absence of additional nutrients with complete removal of both metabolites. TCP degradation induced by chlorpyrifos-induced Chloropyriphos and its metabolite 3,5,6-trichloro-2-pyridinol (TCP) were completely removed from polluted soils by the fungal strain *A. niger* JAS1 even in the absence of additional nutrients[107]. Given the antibacterial properties and catabolite suppression property displayed by TCP, the degradation of TCP by chlorpyrifos-degrading strain was a remarkable discovery. fungus demonstrating different substrate choice of these fungi [108,109,110].

Table 1. Fungal Enzymes and their Role in Bioremediation

Pollutants	Fungi	Mechanism	References
Polycyclic Aromatic Hydrocarbon	*Dentipellis sp. (KUC8613), Phanerochaete chrysosporium, Trametes versicolor, Pleurotus ostreatus, Pleurotus eryngii, Cochliobolus lunatus*	Ligninolytic enzymes, cytochrome P-450 monooxygenase, dioxygenase, dehydrogenases, FAD dependent monooxygenases, glutathione transferase and epoxide hydrolases mediated degradation	[14,15,16,23,25]
Heavy Metals	*Aspergillus species, Rhizomucor species, Fusarium* species, *Emericella species, Funneliformis geosporum, Pleurotus ostreatus, Trichoderma harzianum, Trichoderma ghanense, Penicillium rubens*	Ligninolytic enzymes in the degradation of heavy metals, and antioxidants enzymes in tolerating damage due to oxidative stress	[6,24,37,39,40]
Dyes	*Aspergillus flavus,* Marasmius cladophyllus, Phlebia acerina, Bjerkandera adusta	laccase, manganese peroxidase and lignin peroxidase in degradation of dyes	[8,89,90,91,92]

Pesticide and Herbicide	*Botryosphaeria laricin*a, *Aspergillus glaucus, Trametes pavonia, Penicillium spiculisporus, Penicillium verruculosum,*	Ligninolytic enzymes, esterification, dioxygenation, dehydrogenation, dechloriantion, demethylation mediated degradation	[42,43,45,46,47,48]
Antibiotics	*Pleurotus ostreatus, Leptospaherulina sp, Irpex lacteus, Lentinula edodes*	versatile peroxidase, laccase, manganese peroxidase, cytochrome 450 system	[71,72,73,74,76,77]
Pharmaceuticals	*Mucor hiemalis, Trametes versicolor, Phanerochaete chrysosporium, Lentinula edodes,*	ligninolytic enzymes and cytochrome 450	[62,63,64,65,66,68]

CONCLUSION

Based on the studies reviewed here, it can be concluded that mycoremediation can be a cost-efficient and successful strategy to degrade a variety of recalcitrant, persistent, and toxic pollutants, including detergents, heavy metals, plastic, herbicides, insecticides, herbicides, herbicides, and antibiotics. The majority of research demonstrate how these pollutants are degraded by cytochrome 450 and a variety of extracellular ligninolytic enzymes. However, the fundamental process of these dangerous chemicals' mycoremediation is typically obscure and requires additional study. Another area that should be investigated to comprehend the mechanism of mycoremediation might be functional or comprehensive proteome investigations.

Overall, using enzymes for pollutant bioremediation seems to be a cost-effective, efficient, and practical approach. Although there are still many ways to go, further studies and experiments on enzyme activity and mechanism of action and isolating new enzymes would be a promising way to reduce pollutants and make a healthier environment for humans and all other species.

These investigations may shed light on different genes and proteins involved in the mycoremediation procedure. The knowledge will be used to model genetically enhanced fungus that can remove pollutants from the environment more quickly and effectively. Additionally, the fungi and their enzymes can be grown in bioreactors to remove the contaminants on a big scale. Studies that concentrate on enhancing the conditions inside the bioreactors for the efficient mycoremediation process are necessary. As they are adapted to the high concentration of different toxins in hard environmental conditions, the native fungi growing on polluted locations should be taken into consideration for further investigations. However, there is promising evidence that mycoremediation can remove environmental toxins and turn this planet into a safe place to live.

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Chapter
2

WASTEWATER TREATMENT AND MANAGEMENT

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ABSTRACT

Water is an essential component for human beings. Wastewater recycling is a promising area of interest in water management. The wastewater is discharged without proper treatment it causes various environmental as well as climate-associated problems. It the important to decrease the influence occurring through the wastewater with different treatment techniques including treated water is reused for several applications. The wastewater treatment techniques are divided into preliminary, primary, secondary, including tertiary or advanced wastewater treatment. Wastewater management is an important approach that protects the environment of secure public health and social addition to economic stability. Promoting the use of safe, inexpensive including appropriately accessible wastewater treatment methods is a new approach to sustainable wastewater management.

Keywords: Wastewater, Wastewater treatment, wastewater Reuse

INTRODUCTION

Water is the most essential component of human life [1]. Water contamination is one of the major issues faced by the whole world today [2]. Wastewater formed through industrial, domestic, as well as commercial sources is expanded due to population as well as urbanization [3]. Recently, the various water resources are mainly contaminated due to anthropogenic activity like household as well as agricultural waste along with industrial activities [4]. The wastewater treatment techniques are used to eliminate pollutants from the wastewater like halogenated hydrocarbon substances, dyes, heavy metals, pesticides, as well as herbicides, these are major contaminants in the wastewater [5]. wastewater treatment techniques are divided into preliminary, primary, secondary, including tertiary or advanced wastewater treatment [6]. The wastewater is described based on physical, chemical in addition to biological characteristics. Wastewater recycling is a growing area of interest in water management, promising conservation of the freshwater including large quality extent, and decreasing contaminants in an environment with total supply costs [7]. The latest development in technology with changes of approach the authorities as well as the public to reuse water proposed that a probable development in the management of wastewater as well as treatment [8]. Wastewater reuse needs treatment as well as the use of proper wastewater treatments technique. Newly, growing research is mainly carried out on wastewater treatment with the help of low-cost, simple-to-use techniques in developing

countries [9]. Around 80% of water provide flows return to the ecosystem as wastewater without treatment. It is a critical environmental as well as health risk that is not treated appropriately but well management can be useful for the water managers to meet the city's water needs. The use of appropriate wastewater treatment including discarding is crucial for protecting the public health of wastewater treatment, in addition to immunization plans. The wastewater is transmitted diseases along with polluting the sources of drinking water [10]. The wastewater is treated appropriately to avoid the water-borne as well as vector-borne diseases caused by the deadliest pathogen or micro-organism. Wastewater reuse is a new approach to the sustainability of the increasing population. Wastewater Reuse for several purposes like agriculture irrigation, [11] aquifer recharge, toilet flushing, industrial activities, and various other urban uses [12].

WASTEWATER CHARACTERISTICS

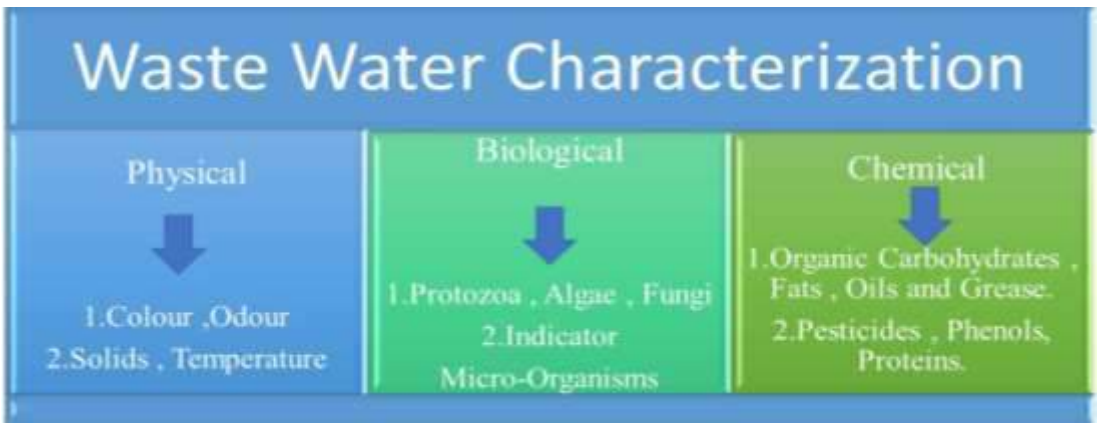

Fig.1. Waste Water Charachterization[26]

A . Physical Characteristics

Physical characteristics consist of color, odor, as well as turbidity. The color of the water is generally regarded as water quality due to several reasons. The Color of water shows a found of organic compounds, like algae or humic substances. Recently, color is used for quantitative evaluation of founding the harmful or toxic organic compounds in the water. Odor is generated by gas formation because of decomposition of the organic material or through compounds added to the wastewater. turbidity is a measure to obtain water clarity. Turbidity is the measurement of light-transmitting characteristics of the water with constituted of suspended as well as colloidal substances.

B. Chemical Characteristics

The chemical characteristics include pH as well as oxygen demand. pH is an important parameter of water quality. This is the negative logarithm of the hydrogen ion concentration. The Chemical oxygen demand (COD) measures the concentration of organic compounds in wastewater depending on the oxygen needed to oxidize it. Nitrogen is measured in various modes like nitrite, nitrate, ammonia, as well as organic nitrogen.

Phosphorus is commonly measured in the mineral including organic, and total phosphorus. Alkalinity in wastewater occurred due to the foundation of hydroxides, carbonates in addition to bicarbonates of elements like such as calcium along with magnesium.

C. Biological characteristics

The biological properties of the wastewater include the occurrence of a bacterium as well as living microbes, such as fungi, algae, and protozoa. Wastewater treatment is mainly useful to protect the environment as well as health. Several types of opportunistic pathogens like ***Escherichia coli***, ***Enterobacter cloacae***, ***Klebsiella pneumonia***, ***Enterococcus faecalis***, ***Proteus Vulgaris in addition to Pseudomonas aeruginosa*** are found in wastewater, these are causes various kinds of systemic infections, particularly in those people that have weakened immunity. The pathogens of ***Salmonella*** including ***Shigella*** genera as well as enteropathogenic strains of the ***E.coli*** mainly caused salmonellosis, shigellosis including gastroenteritis, that are present in the wastewater [13].

LEVELS OF WASTEWATER TREATMENT

Preliminary treatment: The wastewater is entered for treatment activity, which generally goes through preliminary treatment. The treatment mainly includes screening that eliminates large floating materials, like cans, rags, bottles as well as sticks it can block pumps, and small pipes, including downstream methods. The screens are mainly set in a chamber as well as a channel inclined to wastewater flow. That inclined screen permit debris it captured on the upstream surface of a screen, providing a way for manual as well as mechanical cleaning. The other plants have used devices called comminutors or terminators that united a role of the screen including a grinder. These devices capture including cut with shred a heavy solid in addition to floating objects. In the process in which pulverized substances remain in a flow of wastewater smaller fragments are eliminated after the primary settling tank.

Primary treatment: This treatment is useful for separating suspended solids as well as grease in the wastewater. The other treatment plants, primary including secondary levels can be joined in one fundamental action. The several wastewater treatment activities, influent undergo preliminary treatment before primary and secondary treatments started. The screening is finished and grit is eliminated, wastewater consists of dissolved organic in addition to inorganic components including suspended solids. A suspended solid includes tiny fragments of the substances it may be eliminated from wastewater of other treatments like chemical coagulation, sedimentation, and gravity settling, including filtration. The contaminants are dissolved in very minute including the remaining suspended matter in wastewater is not eliminated efficiently with gravity settling. Wastewater enters the sedimentation tank, that sink with suspended solids constantly settling down in the bottom, like primary sludge it can later be removed from a tank through several techniques.

Secondary treatment: It is a biological treatment method that eliminates dissolved organic substances in wastewater. The ninety percent of organic substances in wastewater can be removed with the help of this treatment. The Sewage microbes are cultivated with added to the wastewater. The microbes absorb organic substances from sewage like its

food supply of activity removing the organic substances from the circulation. There are three main conventional techniques used to carry out secondary treatment like attached growth activity, suspended growth activity as well as lagoon systems. The attached growth processes consist of microbial growth occurring on surfaces like a stone as well as plastic media. The suspended growth process eliminates biodegradable organic matter as well as organic nitrogen-containing substances with convert ammonia nitrogen into nitrate. The wastewater lagoon and treatment pond is a scientifically generated pond, with depths are 3 to 5 feet, it permits sunlight, algae, and bacteria including oxygen to interact. Biological including physical treatments are carried out in lagoons to increase the water quality [14].

Tertiary treatment or advanced treatment: This treatment occurs when particular wastewater components are not removed through the secondary treatment. The Advance treatment eliminates a notable quantity of nitrogen, biodegradable organics, phosphorus, heavy metals, bacteria as well as viruses. The two techniques may be used efficiently the sand filter along with membrane filtrations. The other filters are greatly improved, the filters, as well as membranes, are also removed from the helminths. A new technique is disk filtration which used large disks of the cloth media jointed with rotating drums of the filtration. This step in which disinfection with an injection of Chlorine, Ozone as well as Ultra Violet (UV) radiation may be completed to prepare water to acquire present international standards of the agricultural as well as urban re-use [15].

MODERN WASTEWATER TREATMENT TECHNOLOGIES

The eco-friendly as well as cost-efficient of the anaerobic including aerobic methods that are useful for organic wastewater treatment. The first step is which select the appropriate treatment method to determine wastewater attributes; So, which are essential to describe water to find important characteristics of wastewater, like volatile solids, chemical oxygen demand, salt content, and total solids.

1. Nanofiltration (NF)

The Membrane filtration technique like nanofiltration is identified as efficient because supplying a safe as well as a good source of water through reuse of the drinking water in addition to non-drinking water uses. Membrane filtration is advantageous and is differentiated as compared to other conventional method: very rapid reaction kinetics, low-energy needs, as well as great selectivity of the separations. The predicted flexibility of the formation as well as the wide range of the raw materials of NF formation that expanded with spread their importance in distinct methods. NF is distinguished by eliminating the calcium including magnesium ions due to that water softening, with the addition of the sodium ions in filtration as compared to the ion exchange process. The NF does not need other chemical treatments that decrease hardness. The NF does not need heating as well as cooling of the feed as distillation decrease the value of separation efficiently. Including, the mechanical stirring is not needed it is managed moderate molecular separation. The NF is an essential advantage of handling the large volume of the feed constantly with a steady flow rate allowed.

2. Use of Algae in Wastewater Treatment

The biological wastewater treatment process using microalgae is greatly a new aspect, generally believed it the algal wastewater treatment method is useful as conventional treatment methods. Due to their properties, algal wastewater treatment methods are become viable low-priced options of more elegant with costly treatment, mainly for municipal wastewater. The Algae retrieved from treatment ponds is generally used in nitrogen as well as phosphorus additive in agriculture, further it can also be fermented to form energy for methane. The algae can remove harmful substances like arsenic, and selenium including zinc from the aquatic environment. The various algae are absorbed with accumulate several radioactive minerals in the cells if their amount in the water is high. Like, spirogyra accelerates radio-phosphorus. The capability of the algae is it purifies wastewater of several kinds, The algal technology is very useful in the wastewater treatment process it is expected that more famous in the future.

3. Biosorption

Biosorption is the Physico-chemical method carried out naturally in some biomass that permits passively concentration with attached contaminants onto the cellular structure. It is described as a capability of the biological substances to accelerate heavy metals of the wastewater by metabolically moderated and Physio-chemical process of consumption. That does not need energy, including various pollutants in the solvent may eliminate based on the kinetic equilibrium with the constitution of the cellular sorbent surface. Pollutants are adsorbed on cellular structures. Furthermore, the concept of biosorption is generally new and used for various applications for a long period. That greatly called to used in the Activated Carbon Filter. It may filter air including water by letting contaminants attached to porous along with large surface area structure. The consist of the use of microbes, agriculture including industrial wastewater, plant-derived substances, and biopolymer as the biosorbent. This is the reversible fast technique included in the attached biosorbent in the aqueous solution with signifies several interactions instead of oxidation by aerobic and anaerobic metabolism. The benefits consist of simple action, great efficiency, no more nutrient needs, low amount of sludge, no rise of COD in water as well as regeneration of the biosorbent.

4. Advanced oxidation

The Advanced oxidation processes (AOPs) refer to a set of the chemical treatment process that is removed the organic as well as inorganic substances in the wastewater with the oxidation by reactions to the hydroxyl radical (OH). Its role is very important because several of the organic composites occurred in industrial water that is resistant to conventional treatment. AOP process is used in cleaning biological harmful and non-degradable compounds like pesticides, aromatics, and petroleum compounds, as well as volatile organic constituents, which occurred in the wastewater. Alternatively, accumulating and transferring pollutants to another phase may effectively eliminate organic composites in the aqueous phase. Because of the reactivity of the OH, that reacts to several aqueous components. The AOPs are used in a condition where several organic pollutants are mainly eliminated at a similar time. A Disinfection is achievable through certain AOP

designs, from these AOPs a unified solution to certain water quality problems. This technique does not form any dangerous material in water, the reason for byproduct produced through reducing OH is the H2O [16].

SUSTAINABLE WASTEWATER MANAGEMENT

The aim of wastewater management is a sustainable development of the water resources, such as protecting public health including the environment. Sustainable development is described as meeting the requirements of society without adjustment in the future. Circumstances of water quality and sustainable development are the proper management of natural resources thus present as well as future importance of the resource are not reduced. According, to the main objectives of water use, treatment, reclamation, as well as reuse are compatible with the aim [17]. Wastewater recycling is a growing need of water management, that promises conservation of the freshwater including great quality amount, in addition to decreasing contaminants in an environment with complete provide costs. The latest development in the technology including developing the approach of authorities as well as the public to reuse the water proposed its capability to development in wastewater management as well as treatment [18]. Generally, water resource management is greatly based on the wastewater treatment that confirmed water quality is managed [19]. The wastewater treatment is not mainly concentrated on one pollutant. They're mostly a stability competing components it integrates sufficient disinfection that protects public health, reducing disinfection by-product (DBP) generation, reducing greenhouse gas (GHG) mark along with decreasing influence. That also needs a precise decision method it involved a clear difficulty explanation, transparent as well as broad sustainability evaluation technique including clear further assessable standards to evaluate sustainability. In addition, a plan of the wastewater management process that is well unified in the greater community requirements is regarded. The awareness of sustainable wastewater management needs a greatly stabilized strategy in assessing specific management designs of sustainability for the most sustainable development [20].

APPLICATION ON REUSE OF WASTEWATER

Wastewater reuse is a growing perspective all over the world and is an essential component of water resources management [21]. Concurrently, economical thought is becoming essential between the introduction of the market-formed system in the environment including water management. The reclaimed wastewater of municipalities, as well as industries, are used as the added water source that supplies in various regions of the world, mainly in the region where water resources lack with the population as well as economic development is fast. The reclaimed wastewater is useful for several aspects, such as irrigation for agriculture, toilet flushing, urban lawn watering, groundwater recharge, car washing, recreational facilities as well as cleaning of roads. Reclaimed wastewater is also useful in public garden irrigation that is greatly used in various regions [22]. Recently, wastewater reuse play an important role in global water scarcity The wastewater reuse is useful in various applications, such as industrial activities, wetland formation, firefighting, domestic use, aquaculture as well as aquifer recharge [23]. The main importance of reclaimed wastewater is used in agriculture irrigation. The treated water is used in irrigation for agriculture and is mainly useful in water scarcity areas. The

water reuse in irrigation for agriculture is generally differentiated into restricted as well as unrestricted applications. The former importance includes the use of poor quality water in particular agricultural situations, with involves irrigation for crops and processes such as fodder, seed crops, nurseries, fiber, pastures, turfgrass as well as aquaculture. The wastewater is used for several urban purposes like play-grounds, park irrigation, schoolyards, vehicle washing, confinement, fire protection, as well as ornamental fountains. They are also useful for in-building purposes such as air conditioning in addition to toilet flushing. One of the most important applications of reclaimed water is reused indirectly in the heat source. The reclaimed municipal wastewater is mainly used in various industrial activities like pulp as well as paper, textiles, chemicals, steel making, petroleum as well as coal products, including the building projects for concrete construction, boiler feedwater, and dust control, cooling towers addition to cleansing [24]. Water is the basic element of the textile industry. They are mainly useful in cleaning raw materials as well as several levels of textile dyeing [25].

Figure 2: The Applications on Reuse of Wastewater.

CONCLUSION

Wastewater is essential for human beings. Wastewater is mainly treated to provide a safe environment including public health. Wastewater recycling is a growing area of interest in water management. An NF technique is used for treating wastewater that presents fewer

pollutants. They also, soften water as well as purify water. Algae used in the treatment of wastewater is an interesting method that is greatly economical. Biosorption is also a growing method that is effective in eliminating harmful ions as well as their working is easy. Advanced oxidation is a chemical treatment technique, it is greatly effective in removing organic substances.

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Chapter 3

STUDY OF LENGTH-WEIGHT RELATIONSHIP OF *NIPPONOCYPRIS TEMMINCKII* (TEMMINCK & SCHLEGEL, 1846)

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ABSTRACT

length-weight relationship (LWR) is a essential factor in fishery management studies. It helps to understand information astir fish growth, their fitness in their natural environment and their overall well-being. In present study, the length-weight relationship of freshwater fish *Nipponocypris temminckii* **(Temminck & Schlegel, 1846)** (dark gorse) from Ujani Dam, Bhigwan Pune was studied. To understand the relationship, 97 specimens of *Nipponocypris temminckii***(Temminck & Schlegel, 1846)** with a total length from 50.29 mm to 85.60 mm and a total weight from 1.00 g to 6.46 g were calculated. Cubic law was employed which computed to be (n= 3.41), which shows that the maturation of *Nipponocypris temminckii* **(Temminck & Schlegel, 1846)** exhibits positively allometric. The value of the coefficient of determination (r^2) was calculated to be 0.898. The result shows that *Nipponocypris temminckii* **(Temminck & Schlegel, 1846)** from Ujani Dam shows fish health in its natural habitat and this may be due to less pollutants being added to the river.

INTRODUCTION

India plays an important role in world fish production. India represent third larger creator of fishes and stands second as the bigger producer of aquaculture globally. Fishes show great diversity in size, species and biology and habitat. India has 2 hotspots, the Western Ghats and the Eastern Himalayas, with a wide variety of flora and fauna. Fish fauna shows abundance of diversity in fresh water habitat. This study examines the longitudinal relationship of *Nipponocypris temminckii* (Temminck & Schlegel, 1846). It belongs to the Cyprinidae family and the Actinopterygii class. The maximum length till date is 17.4 and is called (Dark chub). This study helps determine expected weight loss in a specific length group, which in turn indicates fatness, general prosperity, gonad development, and suitability for our fish's environment. (Le Cren, E.D.1951) is more mutualistic on size of the individual than the age. Accordingly, the variation in size has essential significance for various aspects of fishery sciences (Froese, R., & Pauly, D. (eds). (2021)) and may require time in the field (Demirel, N., and Murat Dalkara, E. (2012). The widely used fishery information analysis is long association (Diaz, L. S., et al., (2000). their growth, population and biomass (Abdel-Hakim,et al., 2010; Le-Cren, 1951).. LWR has implications for fish ecology, biology, conservation physiology and fisheries assessment (Froese, R.2006). In this

study, LWRs *Nipponocypris temminckii* (Temminck & Schlegel, 1846) are used to determine the status of fish in Ujani Dam, which may be useful for fisheries management and future research on LWRs of this species. pa economic activities that involve catching wild fish or any aquatic life or breeding them in closed conditions (fish farming/farming).

Fig. :1 *Nipponocypris Temminckii* (Temminck & Schlegel, 1846)

MATERIALS AND METHODOLOGY

Study area

Bhigwan is located in the Pune district of Maharashtra. Bhigwan at latitude 18.1590577 and longitude 74.9659447 (Figure:2). Bhigwan is located in Pune on the border of Ahmednagar. This village is located near the Ujani dam. It is dominated by an abundance of aquatic grass and plants, as well as home to many small and large fish. In summer and winter, the water flow is slightly reduced, but in the monsoon season, it increases and sometimes floods.

Fig.: 2 Satellite View of Collection Site.

SAMPLING

A random collection of *Nipponocypris temminckii* (Temminck & Schlegel, 1846) was obtained from a local market near Kumbhargaon. For the study, 97 samples were collected regardless of gender and age. Fishing is carried out by local fishermen using various tools such as

fishing lines, ropes, nets, hand nets and some local fishing tools. Fishing gear was left in the river overnight and retrieved in the morning. The collected samples were analyzed in detail after being fixed in formalin.

METHODOLOGY

A study of *Nipponocypris temminckii* (Temminck & Schlegel, 1846) was conducted to understand the standard length of fishes. Samples stored in ice packs were collected from the market and taken to the laboratory for further analysis. Each fish is washed with distilled water, excess water is cleared using a paper towel, and then weighed using a measuring scale. The corresponding weight of individual fish was determined to the nearest 0.1 g with the help of a digital weighing balance.

INSTRUMENTS

Digital Vernier Dial: brand: SKADIOO Material: Carbon fiber (Figure : 3)

The Digital Vernier Calliper is an updated version of the Analog Vernier Calliper, a widely used linear measuring instrument that is more accurate than the Analog, measuring 0.01 mm.

Nice Lcd Screen: High-quality digital dialer, large and easy-to-read LCD display helps to obtain accurate solution, digital panel automatically twist on when the rail is moved and automatically turns off after 5 minutes. Battery operated.

4 Development Modules: The digital dialer can be utilized to obtain internal and external diameter, it is made up of depth along with pitch with 2 sets of jaws along with probes. This is produced from best quality, long-wearing plastic carbon fiber composite.

Receipte: Scale Range: 0 - 6" / 0 - 150mm; Resolution: 0.01" / 0.1mm; Accuracy: ±0.2mm / 0.01". It is one of the handy and perfect measurement tool for laboratory / DIY measurements etc.

Two Unit Conversion and Zero Setting Function: A single button quickly switches within two measurement status; inches and millimeters. Cagey design permits to set zero and begin with a new activity at any element on the scale. It is essential for differential measurements, with a simple touch of button.

Fig.: 3 Vernier Calliper

Weighing Machine

This scientific weighing scale is called a balance scale. It consists of a horizontal lever with a weight suspended from an arm of equal length. The object to be weighed is placed in one weighing container, and the other is placed in another until the known mass weight reaches equilibrium with the balance of the beam. (Figure:4)

Fig.: 4 Electronic Balance (Source : Bio-Rad Laboratories, Oct 16, 2012)

Analysis of Length-Weight

The statistical relation between the length(l) and weight (w) of *Nipponocypris temminckii* (Temminck & Schlegel, 1846) was stated with the equation given by Le Cren (1951) as follows:

$W = aL^b$,

Where, W is the total wight of fish (gms), L is the exact total length (cm), a is the intercept of regression and b denotes the regression coefficient (growth rate).

"a" and "b" values were acquired from a linear regression of the length and weight of the fish metric after transforming above equation as follows:

$\log W = \log a + b \log L$

The value of b denotes the data on the pattern of the growth in fish.

RESULT

For better understanding and for computing purpose we have created two groups of the fishes with respect to their length. first group is from 50 gm to 65 gm and the second group is from 65 gm to 85gm. The following table 2, represent the mean value and the coefficient of correlation of 97 fishes under the present study.

Table 1: Length Weight Relationship of *Nipponocypris Temminckii* (Temminck & Schlegel, 1846)

Mean TL	61.60
Mean w	2.52
a	0.0032
B	3.416
R^2	0.898

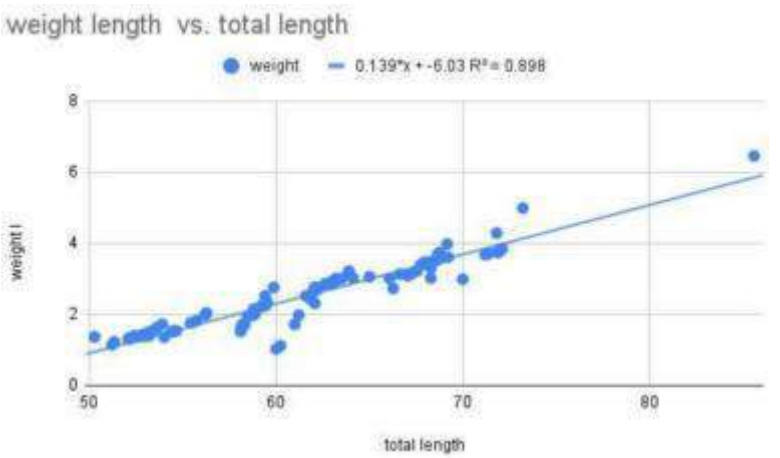

Fig. 5: Graphical Representation of Total Length and Weight of Nipponocypris Temminckii (Temminck & Schlegel, 1846)

At the end of experiment, all the measurements i.e the total length along with weight were measured, mean obtained result of length-weight relationship are presented in table no. 2 The present study collected that length weight of 97 specimens of *N. temminickii* which was collected from Bhigwan stated in table 1. Statistical factor like, mean length and weight of the fishes, maximum obtained length, regression parameters of a and b for studying the length weight relation, correlation of determination (r^2) are for good understanding. The computed minimum and maximum weight and total length obtained were 6.46 gm and 1.03 gm, 85.60 mm, and 50.29cm, respectively table 1. The 'b' value was recorded 3.41, which indicates that growth of this fish was in positive allometric table 2. The coefficient of determination (r^2) value was obtained to be 0.898 respectively (Figure 4).

DISCUSSION

The correlation coefficient (r^2) value of *Nipponocypris temminckii* (Temminck & Schlegel, 1846) with length in Bhigwan is close to 1 and the value of b is near to 3, indicating the isometric growth of the *Nipponocypris temminckii* (Temminck & Schlegel, 1846). The measure of the exponent in the equation W = aLb is generally between 2.5 and 3.5. The 'b' value recorded in the monsoon season in the present work shows the same trend as other studies such as (Sujansingani, K.H 1957; Froese R., Thorson J. T. & Reyes Jr R. B 2014). The value of b for fish investigated in this study is generally consistent with previous results. In addition, it is noted that the regression function "b" value is directly related to body type and weight, can be influenced by environmental factors such as temperature, food supply, lactation and another factors namely age of the fishes, sex and also the harvesting time and habitat (Ricker, 1973). The estimated value of b for the fish ranged between 2.5 to 3.5 (Froese, 2006). Small variations in "B" value are due to habitat of the fish, seasonal variations, sex of the fishes, maturity, along with several environmental and biological factors (Hassan HU et al., 2020; Lee S et al., 2015). In the present studies height, weight were considered in the uncontrolled population, and therefore we advocate future studies that provide a

standardized sampling methodology that includes all factors. This relationship is often used to calculate stocked biomass (Smith MKH, 1996). Growth rate is an important part of the life of all organism (Baird JW, Stevenson SC 1983).

CONCLUSIONS

Length and weight value is essential standard outputs from sampling programs. The present study of N. temminckii shows positive allometric growth and healthy population in Bhigwan. Knowing the stock assessment of any species is a important for sustainable fisheries management. The information obtained by studying the longitudinal relationship and status of *Nipponocypris temminckii* (Temminck & Schlegel, 1846) in Bhigwan will be useful for fisheries management.

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Chapter
4

THE EFFECTS OF COVID-19 ON HUMAN HEALTH A REVIEW

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ABSTRACT

COVID-19 has a different impact depending on age and gender. The biological characteristics of age and gender differences in Indian COVID -19 cases: The likelihood of contracting SARS - CoV-2 varies according to age and gender. A retrospective data analysis included information on 73,797 (65.39%) male and 39,063 (34.61%) female COVID -19 patients. The majority of COVID-19 cases (37.48 percent) were found in people aged 18 to 35. . The 18-35 year age group had the highest proportion of infected male (37.21 percent) and female (37.99 percent) patients, while the 0 to 4 year age group had the lowest proportion of male (1.28 percent) and female (2.19 percent) patients. Females of lower age categories (35years) had a higher chance of being infected with COVID-19, which decreases with age. Females had significantly higher recovery odds than males. With increasing age, the chances of recovery decrease, and the variation could be significant.

Keywords: COVID-19, impact, health , age and gender.

INTRODUCTION

With the emergence of coronavirus disease 2019 (COVID-19) as the latest pandemic affecting human health and the global economy, Nobel Laureate Joshua Lederberg1's prophetic warning that "the microbe that felled one child in a distant continent can reach yours today and seed a global pandemic tomorrow" has once again proven its relevance. SARS-CoV-2 is a positive sense, single-stranded RNA virus with a genome of about 30 kb. The virus is primarily spread through close contact between two people, most notably through small droplets produced by coughing, sneezing, and talking. It is most contagious during the first three days after symptoms appear, but it can spread before symptoms appear and from people who do not show symptoms. The infected patient had symptoms ranging from a dry cough, fever, and a sore throat to septic shock, pulmonary edoema, multiple organ failure, pneumonia, and ARDS (acute respiratory distress syndrome).COVID19 has been linked to the persistence of other symptoms such as sore throat, diarrhea, tiredness, and severe vomiting in addition to breathing difficulties, fever, and cough B.W. Lee & et al 1996., S.L. Klein 2016.

Viruses are highly aggressive biological entities. Entity can refer to either a living or non-living unit. In fact, viruses are classified as a cellular because they require a compatible host to survive; they are biological because they are composed of bio-molecules. Despite the

fact that the novel corona virus is a new virus, corona viruses are a group of viruses associated with mammals and birds. It has been linked to mild to fatal respiratory tract infections in humans. Placid symptoms in humans include the common cold, while severe cases can result in multiple organ failure. In humans, the degree of severity is determined by their medical history. The global health system and medical science are being tested by the COVID 19 pandemic. The world is experiencing an increase in COVID-19 cases. As a result, the purpose of this study is to describe the impact of the COVID -19 pandemic on human health depending on age and gender. K.T. Lulbadda *et al* 20020, K.P. Wasdani & A. Prasad., 2020.

METHODOLOGY

For this systematic review and meta-analysis, data was extracted from a well-known web-based portal of published studies. The search was restricted to manuscripts written in English and published within a specific time period (till july12, 2021). The WHO, CDC, and major journals' websites were also searched. It includes studies that reported the epidemiological and clinical characteristics of COVID-19. The data was gathered primarily from government websites and newspapers.

RESULT & DISCUSSION

COVID-19 has a different impact depending on age and gender. The biological characteristics of age 4,5and gender 6 differences in Indian COVID -19 cases: Hoffmann M and *et,al* 2018,. Sungnak W and *et,al* 2020. The likelihood of contracting SARS - CoV-2 varies according to age and gender. The immune system plays a crucial role in the prevention from various microorganisms, including viruses. The normal human immune system adapts during the fetal to infant stage, matures during adolescent to the adult stage with variability during pregnancy and decreases as the senescence approaches., Klok FA and *et,al* 2020.

Since many clinical and epidemiological studies have been published, much emphasis has been placed on the elderly or those with pre-existing health conditions such as obesity, hypertension, and diabetes as being at risk of dying from viruses; however, men are more likely to die from viruses in every country that provides sex disaggregation data. A.K. Simon 2015.

The Effects of Covid-19 on Human Health

SARS-CoV-2 targets cells such as nasal and bronchial epithelial cells and pneumocytes early in infection via the viral structural spike (S) protein, which binds to the angiotensin converting enzyme 2, (ACE2) receptor. The host cell's type 2 trans membrane serine protease (TMPRSS 2) promotes viral uptake by cleaving ACE2 and activating the SARS CoV-2 (S) protein, which mediates coronavirus entry into the host cell. ACE 2 and TMPRSS 2 are expressed in target cells of the host, specifically alveolar epithelia cells of type 2 In humans, the pathogenesis of SARS-COV-2 infection manifests itself as mild symptoms to severe respiratory failure. After binding to epithelial cells in the respiratory tract, SARS-COV-2 begins replicating and migrating down to the airways, where it enters alveolar epithelial cells in the lungs. This rapid replication could result in a strong immune response.

Cytokine storm syndrome cause acute respiratory failure which is considered the main cause death in patients with COVID-19. Patients of older age (>60 years) and with serious pre-existing diseases have a greater risk of developing acute respiratory distress syndrome and death. Multiple organ failure has been reported in some covid -19. (fig.1) In later stages of infection of Cavid-19, when there is rapid viral replication, epithelial - endothelial barrier integrity is compromised. SARS - CoV-2 also infect pulmonary capillary endothelial cells, accentuating inflammatory response. And also triggering, on influx of Monocytes and neutrophils. Autopsy studies have shown of diffuse thickening alveolar wall with mononuclear cells and macrophages infiltrating airspaces with hyaline membrane formation, Follows, compatible with early phase acute respiratory distress syndrome (ARDS)Collectively endothelial barrier disruptions, dysfunctional, alveolar – capillary oxygen transmission, and impaired oxygen diffusion capacity are characteristics features of COVID-19. Most persons experience fever (83-99%),cough(59-82%)fatigue(44-70%),anorexia(40-84%),shortness of breath (31-40%).0ther nonspecific symptoms such as sore throat ,nasal congestion, headache, diarrhoea ,nausea, vomiting, have been reported. Loss of smell, loss of taste preceding onset of respiratory symptoms has also been reported. (COVID-19 clinical management, WHO)

Non communicable diseases like diabetes, hypertension, cardiac disease, chronic lung disease, cerebrovascular diseases, Dementia, mental disorders, chronic kidney disease, immunosuppression, obesity have been associated with higher mortality . H. Fan.,et al 2014. M.F. Hannah *et al* 2008.Many infections, in particular in children and young adult people with Co- morbidities are at higher risk of severe disease, respiratory failure and death. The incubation period is~5 days. Severe disease usually developed ~8 days after symptoms onset and critical diseases and death occur at ~16 days) Self reposted of factory and taste disorders were also reported by patients. . (fig1)

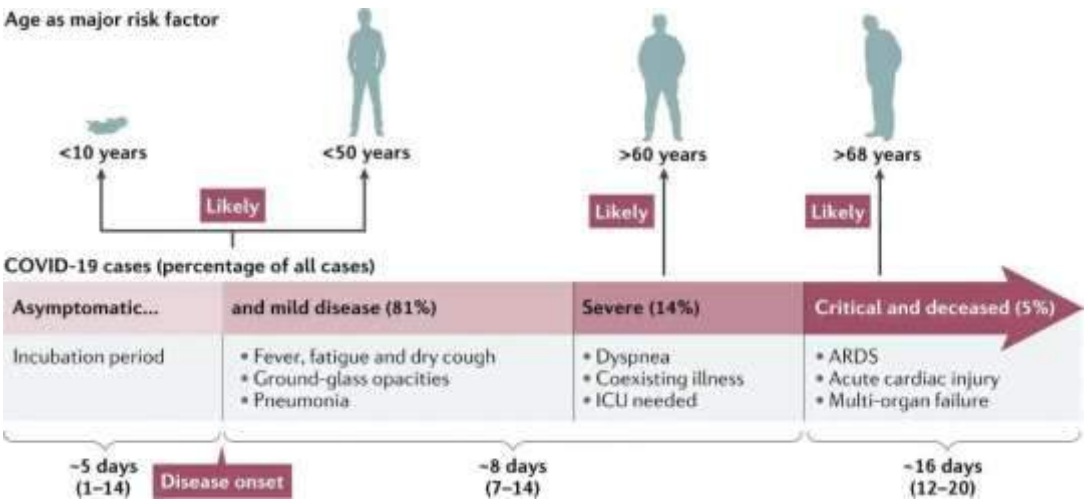
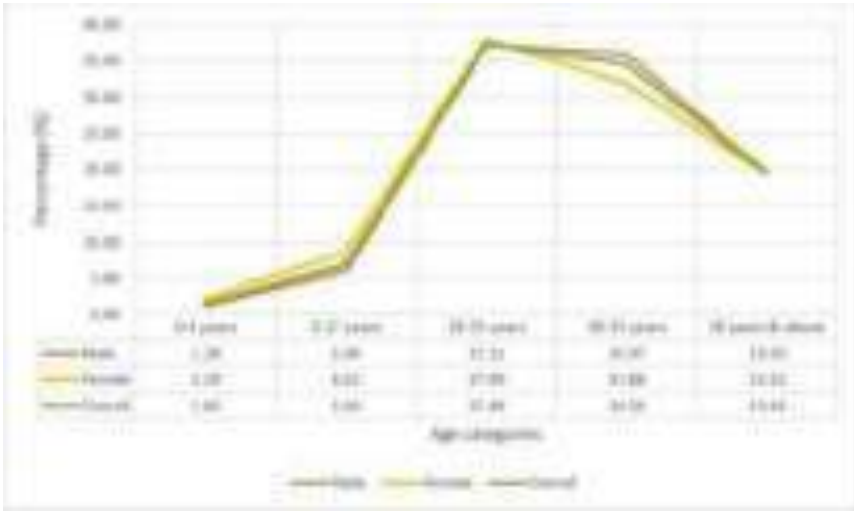


Fig.1 - Age as a Major Risk Factor

A retrospective data analysis included information on 73,797 (65.39%) male and 39,063 (34.61%) female COVID -19 patients. The majority of COVID-19 cases (37.48 percent) were found in people aged 18 to 35. (Fig. 2). The 18-35 year age group had the highest proportion of infected male (37.21 percent) and female (37.99 percent) patients, while the 0 to 4 year age group had the lowest proportion of male (1.28 percent) and female (2.19 percent) patients (fig. 2). Females of lower age categories (35years) had a higher chance of being infected with COVID-19, which decreases with age. Females had significantly higher recovery odds than males. With increasing age, the chances of recovery decrease, and the variation could be significant.

Fig. 2- Trends of COVID 19 Cases among Male and Female Across Different Age Categories.



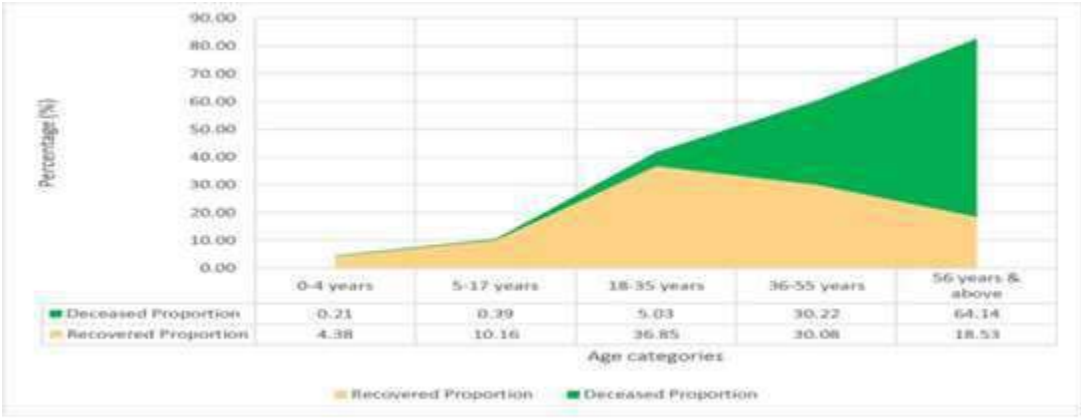


Fig.3- Trends of COVID 19 Patients Status Across Different Age Categories.

Most of people with COVID-19 develop only mild or modrate (80%) disease, approximately 15%developed severe disease that requires oxygen support and 5% have critical disease with complications such as respiratory failure, acute respiratory distress syndrome, septic shock, multiorgan failure, including acute kidney injury and cardiac injury. A. Sarkar *et al* 2020., A.K. Simon *et al* 2015. C.P. Nelson 2020.

CONCLUSION

The majority of COVID-19 patients have mild or moderate disease (80%), 15% have severe disease that requires oxygen support, and 5% have critical disease with complications such as respiratory failure, acute respiratory distress syndrome, septic shock, multiorgan failure, including acute kidney injury and cardiac injury. Age, as well as underlying long-term conditions like diabetes, hypertension, cardiac disease, chronic lung disease, and cancer, have been identified as risk factors for severe disease and death. Male sex and growing old are both known risk factors for death Male sex and growing old are both known risk factors for death. Following COVID-19 infection, children experience mild illness with a minor inflammatory response. In many cases, it has been discovered that even after the virus is eliminated from the body and the infected person is no longer positive, there are long-term effects on various organs. COVID-19 also weakens the immune system, preventing the body from effectively fighting infection. Individuals recovering from COVID-19 are therefore at risk for mucormycosis. The SARS-CoV-2 virus evolves over time. As a result, the newly formed variants affect virus properties such as transmission and severity

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Chapter 5

NOVEL CARBON NANODOTS AS ECO-FRIENDLY CORROSION INHIBITOR FOR MILD STEEL IN 1.0 M HCl

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ABSTRACT

Carbon nanodots attracts more attention by researchers because of its various applications such as bioimaging, photocatalytic activity, sensing ability, drug delivery, opto-electronic devices and corrosion inhibition (Fig. 1a). This chapter describes about the biosynthesis of carbon nanodots via microwave assisted synthesis using *Guettarda speciosa* leaves extract (Fig. 1) and characterizing the CNDs using UV-Visible studies and analysing the corrosion application of the CNDs. The mitigation efficiency was measured by conventional weight loss measurement and polarization studies. The addition of different strengths of CNDs in the acid solution, the mitigation efficiency values were increased and reached the maximum value 92.90%. The Electro chemical polarization studies acted as the further evidence for mitigation of corrosion. The Scanning electron microscopy technique revealed the topography of the inhibited mild steel surface. From the results the CNDs derived from *Guettarda speciosa* leaves extract represented as an excellent ecological inhibitor.

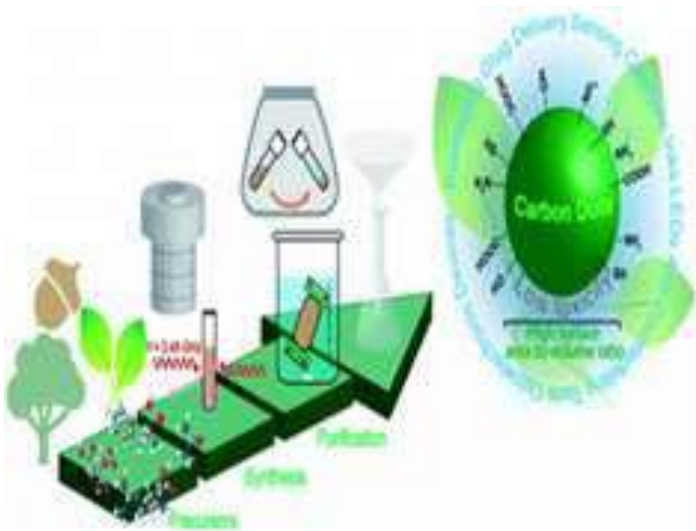

Fig. 1: Graphical Abstract

Fig. 1a: Applications of CNDs.

INTRODUCTION

The metals possess properties like hardness, conductivity, tensile strength and malleability. Because of these properties, metals are used as the raw materials in many industries [1-2]. When the materials are exposed in an environment, the properties of the metals deteriorate called the process corrosion. By applying different techniques and methods, the researchers are trying to prevent the corrosion of metals. In recent times usage of corrosion inhibitors is considered as an excellent scheme to reduce the decomposition rate of metals in different aggressive media. The organic, inorganic and natural products which are have hetero atoms, aromatic rings and π- electron systems are used as the corrosion inhibitors [3-5]. In recent studies the organic corrosion inhibitors excellently replaced by green carbon nanodots (CNDs).

Carbon nanodots (CNDs) or Carbon quantum dots (CQDs) are less than 10 nm small particles of carbon with an excellent features and latent applications. CNDs are luminous constituents and have exclusive characteristics such as biocompatibility, stability towards photochemical change, less toxic, supportable, and biodegradable [6-9]. CNDs can be produced at very affordable through numerous justifiable approaches that hire low-priced renewable resources as preparatory constituents. Carbon nanodots are captivating carbon-based constituents that have established great consideration by researchers for their significant applications in varied fields. CNDs have a vast impression on both well-being and conservational applications because of their latent to assist as non-hazardous substitutions to traditional heavy metal-based quantum dots [10]. The preparation of CNDs can be commonly carried out by two tactics, which are top-down and bottom-up approaches using chemical, electro-chemical or physical performances. The top-down method comprises procedures such as arc discharge method, laser ablation and electrochemical techniques, whereas the bottom-up method encompasses techniques like

plasma behaviour, chemical treatment, hydro-thermal treatment, solvothermal treatment and microwave synthesis [11]. Among the aforesaid synthesis practices, microwave-assisted synthesis is gained more consideration since it is well-thought-out as an eco-friendly and cost-effective approach which offers fast heating and calm to raise starved of suffering thermal gradient properties [12]. Numerous research papers on the effective synthesis of CNDs using microwave-supported synthesis have been testified [13]. For occurrence, with citric acid, urea, and thiourea as the resources, CNDs with the ability in sensing mercury and iodide compounds in aqueous solution have been efficaciously invented through microwave-assisted method [14-15]. In another case, eggshell membrane vestiges which were renewed to CNDs purportedly owning photocatalytic deprivation capability in dropping the methylene blue [16]. Natarajan Architha *et al*. 2021 synthesized the fluorescent carbon nano dots by microwave assisted synthesis from Mexican Mint extract and detected Fe^{3+} and used in bio-imaging. In addition to this, plant wilds such as pomelo skin, willow bark, watermelon bark, and waste carbon paper biomaterials such as carbohydrates (starch, glucose, and sucrose) have also been used as carbon predecessors for the synthesis of carbon nanodots [17-18]. The greener and natural precursors were considered as an alternative for toxic and expensive precursors for the synthesis of biodegradable and latent fluorescent carbon dots.

In this section, the ecological CNDs were prepared from *Guettarda speciosa* leaves extract and characterization carried out for synthesized carbon nanodots with UV-Fluorescence studies and applied as the corrosion inhibitor for mild steel in 1.0 M HCl solution. The inhibited solution suppressed the corrosion rate and protects the mild steel from corrosion. The effect of inhibition was measured by non-electrochemical and electrochemical methods. The geomorphology of the mild steel specimens evaluated by scanning electron microscopy.

EXPERIMENTAL METHODS

Guettarda Speciosa

The *Guettarda speciosa* plant image is given below in Fig. 2.

Fig. 2: Guettarda Speciosa Plant.

Botanical Name - *Guettarda speciosa*; Tamil Name - Paneer Pushpam; Kingdom: Plantae; Order: Gentianales; Family: Rubiaceae; Genus: *Guettarda L.*; Species: *Guettarda speciosa*.

Traditional therapeutic plant in Asia for the handling of various inflammatory conditions, together with cough, fever and maternal postpartum infection. Preliminary phytochemical screening of the leaves extract shows the existence of steroids, triterpenoids, flavonoids, saponins, essential oils and coumarin compounds [19].

Guettarda speciosa leaves were collected from Sri Koothaipar nagar, Thiruverumbur, Trichy district. The leaves were valid and recognized by Dr. John Britto, The Rapient Herbarium and Centre for Moduler Systematics, St. Joseph's college, Tiruchirappallli, Tamilnadu, India.

Work Plan

The working procedure is schematically signified in Fig. 3.

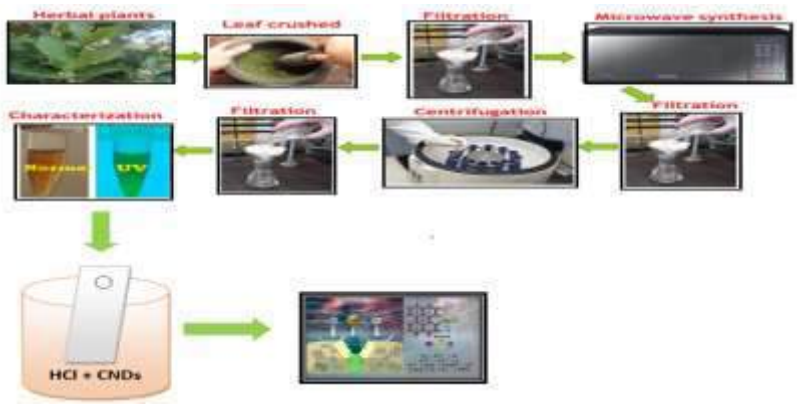

Fig. 3: Schematic Illustration of Working Procedure

Chemicals and Equipment's

Acids

Using Analar grade HCl, 1.0 M HCl was made up with double distilled water.

Preparation of Leaves Extract

Guettarda speciosa fresh leaves have been collected and three times cleaned up with distilled water. The leaves were dehydrated in shadow and grinded to progress the surface area of the particles. The aqueous extract of *Guettarda speciosa* leaves were prepared in an ultrasonic bath at optimum temperature for 5 h with ultra-pure water at the strength of 12.5 g leaves/100 mL. On the last phase of the extraction technique, extract was centrifugated at 6000 rpm for 15 min to eliminate dense portions and pure extract was set aside at + 4◦C [20].

Microwave Oven-Aided Synthesis of Cnds

For the synthesis of CNDs *via* domestic, a kitchenette type microwave oven with 800 W output power was utilized. Aqueous extract of *Guettarda speciosa* was used as carbon source

for CNDs preparation, discretely. For the synthesis of CNDs using *Guettarda speciosa* aqueous extract as the carbon basis, 1 mL ultra-pure water was taken in the ceramic container. For the CNDs synthesis *through* MWO, earthenware containers holding reaction medium was located at MWO with 800 W output power for 15 mins. After the heating process, the residue is scratched from the container, and liquified in ultra-pure water and centrifugated for removing the dense particles. The solvent was vanished at 80°C to acquire extremely fluorescent CN-dots as black fine dust [21].

Mild Steel Composition

The elemental configuration of the mild steel used in the studies is pictorially epitomized below in Fig. 4.

Fig. 4: Composition of Mild Steel

The mild steel has 1x4x0.1 cm dimension and the coupons were mechanically refined to mirror finished and strains are removed with acetone and utilized for the weight loss method.

For electrochemical measurements, rectangle mild steel strip entrenched in Teflon with an unprotected area of 1cm^2 was used. The working electrodes were refined with abrasive paper papers of 0/0, 2/0, 3/0, and 4/0 grades and degreased with acetone, desiccated and utilized [22].

Weight Loss Method

Weight loss studies have been carried out for pre-weighed mild steel strips by dipping in blank HCl and HCl with the different concentrations CNDs at an optimum temperature for about 2 hrs. Using the subsequent expressions, the erosion rate, exterior coverage and mitigation efficacy were measured [23] (1-3),

Corrosion rate (P) (mpy) = $(87.6\times\Delta W)/(D\times A\times T)$ ---------- (1)

ΔW= Weightiness loss of mild steel strips in mg, D=Thickness in gm/cm^3, A= Area of mild steel strips in cm^2, T= Immersion period in hrs.

I.E (%) = $(W_{blank}-W_{CNDs}/W_{blank}) \times 100$ ---------- (2)

Where, W_{blank} = Weight loss in plain acid

W_{CNDs} = Weight loss in acid + CNDs

Surface coverage (Θ) = (I.E.)/100 --------- (3)

Electro-Chemical Polarization

Potentiodynamic polarization studies were done for mild steel strips in the plain acid and acid with CNDs. This study was executed to compute the decomposition current, corrosion

potential and Tafel slopes $b_{cathode}$ and b_{anode}. The polarization cells contain a three-electrode assembly [23].

$$(\%\ I.E.) = ((I_{corr})_{blank}-(I_{corr})_{CNDs}/(I_{corr})_{blank})\times 100 \text{ ----------(4)}$$

$(I_{corr})_{blank}$ = Corrosion current in plain acid

$(I_{corr})_{CNDs}$ = Corrosion current in acid + CNDs

RESULTS AND DISCUSSION

Uv-Visible Absorption and Fluorescence Spectrum

The aqueous solution of CNDs shows in the Figs. (4, 5a & 5b). The UV-Visible spectrum of the peak 245 nm exhibited to π- π* shift for C=C bonds. The peak with the wavelength 279 nm clearly depicts the n-π* transition of C=O bonds show the presence of carboxyl group on the C-dots exteriors. The maximum emission spectra at 518 nm in photoluminescence spectra of CNDs is exhibited in Fig. 5b. The higher intensity in the spectra compared with citrate-based CNDs described prior [20]. The cause of this strong emission is maybe owing to the existence of some functional groups on the superficial that act as emissive snares for the electronic transition [24].

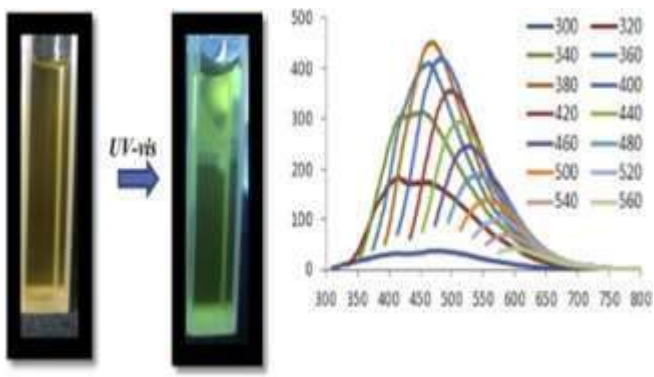

Fig. 4: Carbon Nanodots in UV-light.

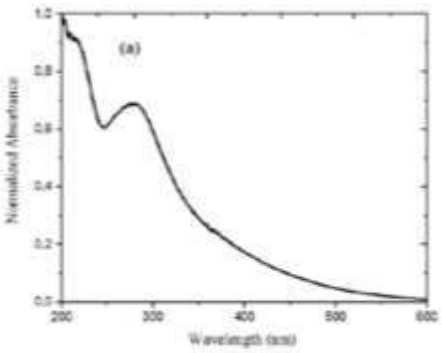

Fig. 5a: UV-Visible Spectrum of CNDs.

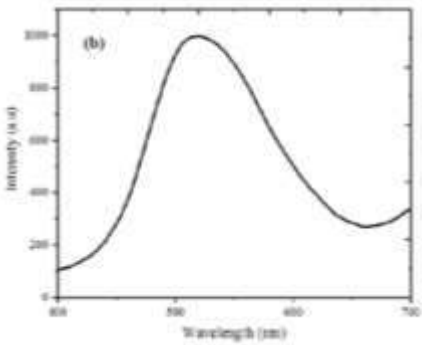

Fig. 5b: Fluorescence Emission of CND Spectrum Nanodots.

CORROSION INHIBITION STUDIES

Weight Loss Studies at Different Concentrations

The anti-corrosive effect of CNDs in HCl medium at various concentrations was followed using conventional mass loss method [22-23]. The results obtained from this study are tabulated in Table-1. The obtained data clearly predicts the mitigation efficacy rises with the increase of strengths of CNDs. The inhibition efficacy values reach maximum 92.90 % at 800 ppm of CNDs at 303 K. Comparing the results, the corrosion rate value predominantly decrease from blank solution to high concentration of inhibitor solution. It is because of the establishment of covalent bond between CNDs and mild steel [25]. The distinction of corrosion rate, inhibition efficacy with respect to the concentration of CNDs is given in Fig. 6.

Table 1. Inhibition Efficacy Data on Mild Steel Corrosion in HCl and HCl + CNDs.

[CNDs], (ppm)	Rate of corrosion, (mpy)	Inhibition Efficiency (%)
Blank	0.702	-
200	0.351	59.74
400	0.314	70.10
600	0.276	87.56
800	0.208	92.90

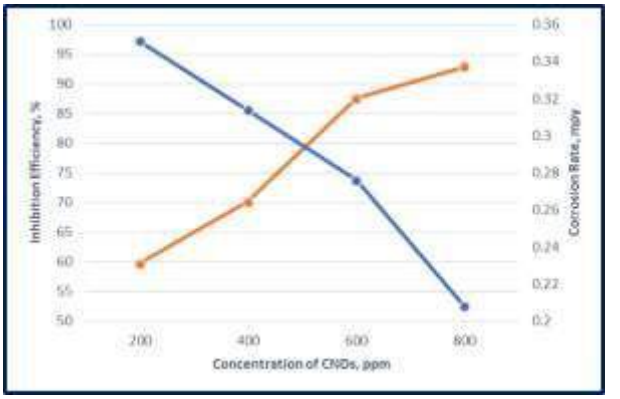

Fig. 6: Rate of Corrosion and Inhibition Efficacies for Mild Steel in Different Strengths of CNDs in 1.0 M HCl.

Potentiodynamic Polarization Studies

Potentiodynamic polarization studies data for blank HCl solution and the solution containing 200 ppm to 800 ppm of CNDs were tabulated in Table-2. Cathodic and anodic tafel slopes are given in Fig. 7. The corrosion current values (($I_{corr.}$) were found to decrease from blank to higher concentration of CNDs [24]. The $E_{corr.}$ values replicate that both the current densities were reduced with the addition of CNDs. It shows that the CNDs stifled both the anodic and cathodic reactions. The changes observed in the tafel cathodic slopes and anodic slopes preferred the CNDs were of mixed type inhibitors [26]. The attack of chloride ions was prohibited by the formation of barrier between solution and the mild steel exterior [24].

Table 2. Data of Potentio-Dynamic Polarization Method for the Mild Steel Corrosion in HCl and HCl + CNDs.

[CNDs] ppm	$I_{corr.}$, mV	$-E_{corr.}$, mV	$b_{anode.}$, mV dec^{-1}	$b_{cathode.}$, mV dec^{-1}	Inhibition Efficacy (%)
Blank	0.113	-93.544	154	179	-
200	0.066	-195.96	136	146	41.59
400	0.034	-237.89	146	163	69.91
600	0.021	-193.27	139	174	81.41
800	0.011	-247.22	134	179	90.26

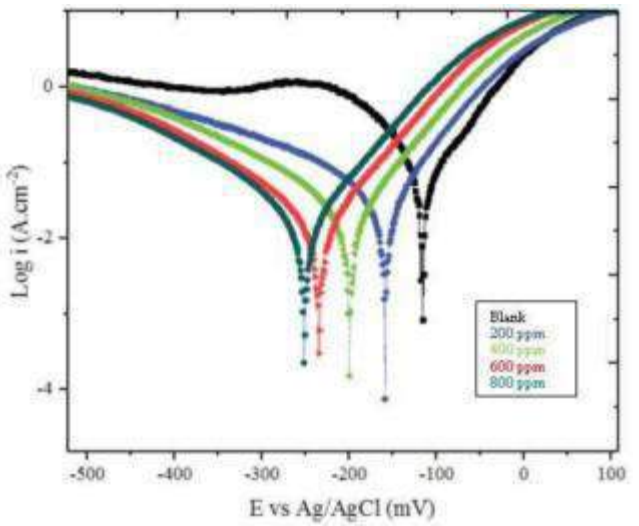

Fig. 7: Tafel Curvatures of Mild Steel Corrosion in HCl and HCl + CNDs.

TOPOGRAPHY STUDIES

Scanning Electron Microscopy (Sem) Technique

The SEM images for refined steel, metal strip dipped in blank acid solution and metal strip dipped in the solution containing 800 ppm of CNDs were exposed in (Figs. 8a,8b & 8c). The surface of mild steel is smoother in polished mild steel (Fig. 8a). Comparing the (Figs. 8b & 8c) images more pits and cavities were observed in (Fig. 8b). The surface of the mild steel became more smoother in the (Fig. 8c) compared with the (Fig. 8b). From these images the formation of insoluble film by the adherence of CNDs was confirmed [27].

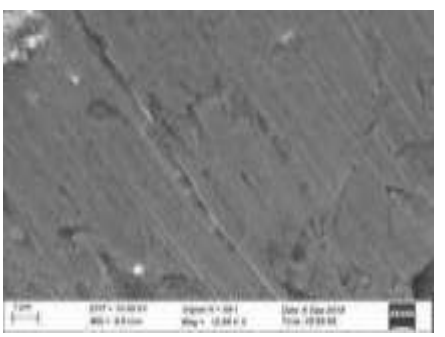

Fig. 8a: SEM Micrograph for Refined Mild Steel

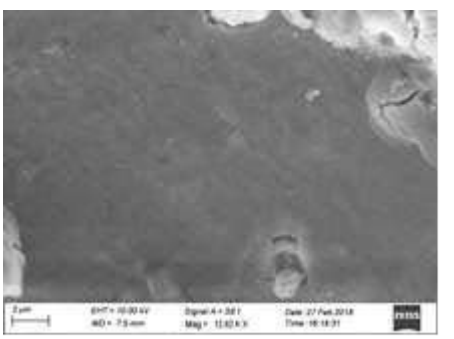

Fig. 8b: SEM Micrograph for Mild Steel Dipped in 1.0 M HCl

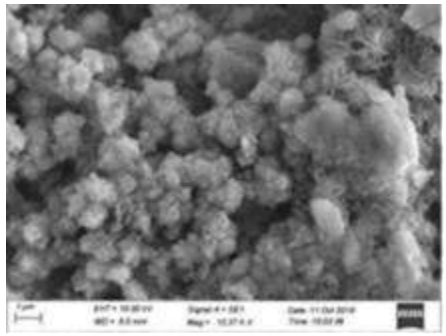

Fig. 8c: SEM Micrograph for Mild Steel Dipped in 1.0 M HCl/800 ppm of CNDs

CONCLUSION

In this chapter, luminous carbon nanodots (CNDs) have effectively synthesized from *Guettarda speciosa* leaves extract and it act as a recyclable corrosion inhibitor of mild steel in aggressive atmosphere. The corrosion inhibition effect of CNDs on mild steel was examined by weight loss and potentiodynamic polarization approaches and SEM measurement. Outcomes point to that CNDs displays good inhibition efficacy and can be used as a latent inhibitor. The conclusion of potentiodynamic polarization exhibited CNDs denote a mixed-type inhibitor for mild steel in 1.0 M HCl solution.

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Chapter 6

EXTRINSIC FACTORS AFFECTING MICROBIAL GROWTH AND SURVIVAL IN FOOD

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INTRODUCTION

The growth of microorganisms in food can be affected by several factors present inside the food (intrinsic factors) or and outside environment (extrinsic factors) where food is kept. These factors play an important role in understanding the growth of microorganisms in food, and by these factors, we may know how to keep our food safe for consumption, such information's are also helpful in designing a better condition for preserving food products for a longer period with maintaining their nutritional value. In the previous module, various intrinsic factors affecting microbial growth and survival in food were discussed in detail.

In general, extrinsic factors are factors in the surroundings and external to the food that affects both the microorganisms as well as the food itself during, processing handling, and storage.

EXTRINSIC FACTORS

1. Storage Temperature

Diverse microorganisms grow over a wide range of temperatures, For example, some microorganisms prefer to grow in the cold (i.e. low temperature), a few at room temperature, and others to grow at high temperature. While the growth rate increases with rising temperature, the growth rate tends to decline rapidly after that, until the temperature maximum is achieved. Both low and high temperatures may affect the rate of microbial growth: At low temperatures, microbial growth ceases because of slower reaction rates for the individual enzymes, and at low temperature, there is a decrease in the fluidity of the cytoplasmic membrane which affects its transport mechanisms. At high temperatures, there is denaturing of structural cell components as well as inactivation of heat-sensitive enzymes may occur. Such type of knowledge of storage temperatures is very important from the food safety point of view, for example, if we have the information of the temperature growth ranges for pathogenic microorganisms, which would help us to select the appropriate temperature for storing food that would restrict microbial growth.

In general, microbial growth is possible in between temperatures from -18°C to 70°C. Though, it has been reported that few microorganisms can grow at -34°C (as the lowest

temperature) and the highest is somewhere in a surplus of 100°C. Normally, all microorganisms have a defined temperature range in which they grow, with a minimum, optimum, and maximum. Based on temperature requirements for microbial growth, microorganisms may be placed into three groups, as presented in below Table 1.

Besides bacteria, interestingly, yeast and molds can grow over a wide range of pH, osmotic pressure, and nutrient content. Likewise, also able to grow over wide ranges of temperature.

Although yeasts can grow over the psychotropic and mesophilic temperature ranges but usually not within the thermophilic range Numerous molds can grow at refrigerator temperature, especially some strains of Aspergillus, Cladosporium, and Thamnidium which may be found growing on eggs, sides of beef, and fruits stored at low temperature.

It suggested that the quality of the food product must also be taken into care while selecting a storage temperature, as it would seem desirable to store all food at refrigerator temperatures or below, but this is not always best for the keeping quality of some food.

Table 1: Division of Microorganisms and their Physiological Functions at Different Temperature Ranges

MICROBIAL GROUPS	PHYSIOLOGICAL PROPERTIES
Psychrophiles	1. Those organisms that grow well at or below 7°C and have their optimum between 20°C and 30°C. 2. These organisms grow well at refrigerator temperatures and are responsible for spoilage of meats, fish, poultry, eggs, and many other foods normally stored at this temperature. For example The genera Pseudomonas and Enterococcus (most common) and others such as Alcaligenes, Shewanella, Corynebacterium, Lactobacillus, Pseudomonas, Psychrobacter, Enterococcus, etc.
Mesophiles	1. Those that grow well between 20°C and 45°C with optimal between 30°C and 40°C. These types of microbes may be found in food stored at refrigerator temperatures. 2. In fact, they do not grow at this temperature but do grow at temperatures that fall in the mesophilic range, depending on other suitable conditions. It has been observed that Enterococcus faecalis can grow over a range from 0°C and 30°C or above.
Thermophiles	1. Able to grow at and above 45°C with an optimum temperature range between 55°C and 65°C. For example Bacillus and Clostridium, the general belonging to this group are of great interest to the food microbiologist and dairy food technologist in the canning industry.

It is better to keep vegetables, potatoes, celery, cabbage, etc. at 10°C. The best storage temperature for bananas is 5-7°C rather than at 13-17°C. However, the maintenance of proper storage temperature depends on several other environmental parameters such as relative humidity of the surrounding environment, the presence or absence, and

concentrations of gases like CO_2. Hence, the temperature of storage is the most important parameter that affects the growth of the microorganism and their survival in food.

Relative humidity

Microbial growth at the food surfaces is also affected by the humidity of the storage environment; If we store food in a dry atmosphere (less humidity), microorganisms are less able to grow than if the food is stored in a moist (high humidity) environment, that is why dry conditions are considered better for storing food than moist conditions. In general, there is a great interaction between the water activity (a) of food and the relative humidity of the storage environment. It is important to note that, if the aw of food is set at 0.65, it must be stored under conditions of relative humidity that do not allow the food to pick up moisture from the air and thereby increase its surface and subsurface to a point where microbial growth may occur. There is always an equilibrium between food and the relative humidity of the environment. For example, if food with low values is kept in environments of high relative humidity, in such conditions, the food picks up moisture until equilibrium has been established. Similarly, food with high loose moisture when placed in an environment of low relative humidity. Temperature is also affecting the relative humidity of the environment, so we should be careful while selecting proper storage environments for food if higher the temperature is higher then relative humidity will be lower and vice versa.

It has been noted that the food stored at low relative humidity is less susceptible to undergo surface spoilage from holds, yeasts, and certain bacteria. Food that requires certain water activity for safety or shelf-life consideration will need to store in such a way that the environment does not markedly alter their characteristics, as such type of food eventually come to moisture equilibrium with the environment. Therefore, manufacturers and distributors need to provide appropriate storage conditions to account for this fact which is why packaging plays a major role in the susceptibility of the food to the influence of relative humidity. Improperly, wrapped meat suffer much surface spoilage in the refrigerator before deep spoilage occurs due to the high relative humidity of the refrigerator and aerobic environment that supports the growth of meat-spoilage microorganisms Sometimes even within a sealed container, the spoilage microorganisms were able to grow particularly pathogenic organisms, because of at a low water activity (a) can be subject to moisture condensing on the surface thanks to wide environmental temperature shifts. Hence, environmental conditions of relative humidity must be taken into consideration while storage of food.

Gases: Presence and Concentration

Aerobic microorganisms require oxygen for their growth. For example, E. coli is a fecal bacterium that grows readily on many foods. If food is stored in a reduced oxygen environment, then aerobic bacteria would not grow and reproduce. In contrast, few microorganisms can grow in the absence of oxygen, named anaerobic microorganisms, Clostridium botulinum causing botulism.

The antimicrobial effect of some of the gases on microorganisms present in food at ambient pressures is demonstrated in various scientific studies. Microbial growth is affected by gases with two mechanisms, described below in Table 2.

Table 2: Antimicrobial Effect of Gases on Microorganisms.

TYPE	MECHANISM
Direct effect	Some gases such as Carbon dioxide (CO), ozone (O3), and oxygen (O2) are directly toxic to certain microorganisms that can inhibit growth and proliferation. Interaction of gas with the aqueous and lipid phases of the food, chemical, and physical properties of the gas; determines the potential of gas as an antimicrobial agent. As oxidizing radicals generated by Oy and Ox are highly toxic to anaerobic and aerobic bacteria depending on their concentration. For example, CO_2 effective against obligate aerobes and at high levels can prevent the growth of other microorganisms.
Indirect effect	Such types of effects are exerted by altering the ecology of the microbial environment, in which gas composition is modified. For example, replacement of O by N. As soon as the surrounding atmosphere is changed, the competitive environment is also converted. Thus, atmospheres that harm the growth of one particular microorganism may promote the growth of another (positive effect). This effect may have positive or negative consequences depending upon the native pathogenic microflora and the type and nature of the substrate

Several newer technologies are in practice to inhibit the growth of microorganisms, and most of these are based on temperature to enhance the inhibitory effects. It has been noted that controlled atmosphere and modified atmosphere packaging of certain food which can significantly enhance their shelf-life. Normally, the inhibitory effects of CO: increase with decreasing temperature due to the increased solubility of CO: at a lower temperature. The pH of food becomes lower after the dissolution of CO, In general, N. (being an inert gas) mainly wont to displace oxygen in food packages either alone or together with other gases (.e., CO_2), hence showing an indirect inhibitory effect on the growth of aerobic microbes.

Activities of other microorganisms

Some microorganisms produce secondary metabolites, i.e., antibiotics, bacteriocins, hydrogen peroxide, and organic acids which are either inhibitory or lethal to other microorganisms.

Nowadays, the "cidal" or killing effect of some food microflora on others is well known. Substances produced by one organism either kill or inhibit the other organisms is an example of "microbial interference or microbial antagonism". Many scientists study microbial interferences;

Sir Howard Florey, gave some examples of interference back to Pasteur and Joubert in 1877. Before the 1960s, such type of work was done by clinical researchers, Later on, in the same 1960s, some food microbiologist showed their interest in this work.

Dack and Lippitz, noted that the natural Rora of frozen pot pies kills inoculated cells of S. aureus, E. coli, and S. typhimurium.

SUMMARY

The potential of microbial growth in food is determined by the food environment and the environment where food is stored. Intrinsic factors are the parameters related to the food itself such as nutrients, water activity, pH, redox potential, and oxygen, while extrinsic factors are the environmental conditions where food is kept such as storage temperature, relative humidity, gaseous environment, and activities of other nearby microorganisms, plays a significant role in the multiplication of microbial cells.

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Chapter
7

ROLE OF GREEN NANOMATERIALS AND CARBON QUANTUM DOTS WITH VERSATILE APPLICATIONS IN PHOTOCATALYTIC DYE DEGRADATION

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ABSTRACT

Phytonanotechnology has the huge potential in regulating the targeted delivery of biomolecules, controlled release of agrochemicals and revolutionizing the product yield. Application of nanotechnology in plant science is a rapidly growing area towards attaining sustainable and safe food technology. This chapter comprises the role of plant extracts in nanotechnology and development of an eco-friendly nanocatalyst for dye degradation, including green carbon dots. In addition, the role of ZnO nanoparticles as photocatalysts for the photocatalytic degradation of phenolic red upon UV-light irradiation is discussed. Major focus is given to the chemical and green method of ZnO synthesis using $ZnSO_4$ precursor. A Comparative study is made on the observed catalytic degradation efficiency, and the catalytic effectiveness was greater for green synthesized ZnO nanoparticle. The effectiveness was confirmed by protein estimation test as well.

Keywords: Nano particles, carbon quantum dots, ZnO nanoparticle, green method, photocatalytic degradation, UV -Irradiation.

INTRODUCTION

Nanotechnology and Carbon Quantum Dots

Nanotechnology is an interdisciplinary field deals with the separation, invention and handling materials of size between 1- 100 nm (Kumar et al. **2013**) .These nanoscale materials exhibit enormous applications in organic dye degradation, dye sensitized solar cells, nano robotics, and biomedical field. Due to the exceptional antibacterial and antimicrobial properties of nanomaterials, nano antibiotics are introduced into the pharma industry and considered as a most relevant development in the field of bio nanomaterial research (Zhang et al.**2015**) .The unique surface volume ratio, shape and size of the Zn, Ti, Au, Ag , Pt and Pd nanoparticles make them a significant changes in physical and chemical properties and these are intended to apply in aerospace devices ,chemical industries and optical devices(Piccinno et al.**2012**).

Now a days carbon quantum dots exhibit a special area of interest due to its surface passivation and of appreciably small size. Carbon quantum dots derived from a green route

have received a great attention due its biocompatibility, optical properties, low toxicity and high antimicrobial and anticancer properties .citric acid, ammonium citrate, ethylene glycol, thiourea etc are some of the chemical precursors used to synthesize carbon quantum dots. In order to minimize the usage this chemical synthetic route, we have to develop green precursors to derive *Green C dots* (Keller et al.**2013**). Various attempts a have been done to develop green precursors from animal and plant sources, of these human hair, a waste keratinous material, because of its availability, low toxicity and high carbon content can be considered as a green precursor for the development of highly efficient carbon quantum dots. Carbon quantum dots because of it's outshine properties resulted a number of applications in various fields (Keller et al.**2013**).

Some research institutes in India has been conducted synthesis and applications in advanced level like nanosensors, multiflouresent particles etc. in various research centers such as Indian Institute of Technology (IITs),Indian Institute of Sciences (IISc) and other universities. National level contribution towards nanomaterials is listed below. Vinay Sharma, *et.al* (**2018**) studied full colour emitting fluorescent carbon materials as reversible PH sensor with multicolor live cell imaging. Gopinath, *et.al* (**2015**) reported green synthesis of multifunctional carbon dots from coriander leaves and their potential applications as antioxidants, sensors and bioimaging agents. MingYuan *et.al* (**2013**) has been studies room temperature and solvothermal green synthesis of self-passivated carbon quantum dots from agricultural straw waste and its applications in sensing and photocatalysis. Pradeep Kumar, *et.al* (**2018**) reported green synthesis of fluorescent carbon dots from *Azadirachata Indica* leaves and their peroxidase-mietic activity for the detectox of H_2O_2 and ascorbic acid in common fresh fruits. Vadivel Ramanan *et.al* (**2016**) studied green synthesis of fluorescent carbon dots from Eutrophic algal bloom and it's in vitro imaging.

Waste Human Hair Derived Carbon Quantum Dots

Human hair is often considered as waste material even though it is biodegradable. Due to the burning of hair in tanneries release large amount of residue containing COD, BOD, and TDS leads to severe environmental issues (Kessler et al.**2011**) Human Hair (HH), consist of 99% keratin and 1% other elements, mainly a source of carbon, nitrogen, oxygen and sulpher. Carbon based nanoparticles can also act as good platform for the attachment of several drugs.Due to the presence of strong S-S bonds between cysteine molecules, keratine in hair fiber considered as very strong and insoluble and may stabilize in metal nanoparticles synthesis (Iosub et al.2017) Reported ball milling method can be used for preparing fine human hair powder and unwanted organic substances can be removed by simple extraction techniques and resultant fine powder can be used for the synthesis of carbon quantum dots

This waste keratinous material dumped into lakes and rivers may lead to many environmental problems (Hull et al.**2015**) Utilization of this solid waste is still a crucial issue for researchers only because of its strong disuphide linkage. So conversion of this type keratinous protein into useful products may lead to developments in many research areas. Recently development of biological fibers became an efficient and alternative for fiber reinforcement for researchers and engineers (Wang et al.**2011**). Due to its high mechanical

strength and ecofriendly nature can replace commonly used engineered fibers like carbon, glass etc. Many biological fibers are available in our environment, by considering availability, efficacy and low degradable nature waste human hair can consider as an effective biological fiber in this era. Environmental degradation and the energy crisis are recently noticeable issues all over the world (Xie Y et al. **2011**). So the generation of energy storage devices with high reliability, promising energy density, and safety are of important concern. Due to high tensile strength of human hair fiber, it can be used as an excellent reinforcing material in many polymers for the development of polymer nanocomposites. It can give resulting composites with high tensile strength and tensile modulus.

Applications in Photocatalytic Dye Degradation

Extensive use of organic synthetic dyes due to the development of various industries all over the world causes huge amount of environmental pollution (Muthulingam et al.**2021**). Many techniques are also available for the removal of such industrial effluents, however those discharged into lakes, rivers or ground water during dyeing process need complicated removal strategies and cause many health hazards. The extensive releases of the dye into the environment are often toxic as most of them are mutagens and carcinogens and take long time to degrade(Muthulingam et al**.2020**) The main three methods of dye removal i.e. physical, biological and chemical treatments have only definite results. Therefore, it is necessary to look for an effective treatment where hazardous substance can be left as residue (Muthulingam et al.**2021**) Recent research on photo catalytic effect shows it as the most effective in degrading organic dyes. Semiconducting materials, such as TiO_2, ZnO_2,Fe_2O_3, CdS and ZnS are excellent photocatalysts in this regard. Among these materials, Zinc Oxide (ZnO) nanoparticles are widely accepted due to the comparatively simple methods of synthesis and wide applications. Their large surface to volume ratio and <100 nm diameter makes them applicable in many optical and electrical devices. This is characterized by the high band gap of 3.37 eV at room temperature (Periyayya Uthirakumar et al.**2013**)ZnO nanoparticles are mostly used in sunscreens and act as an alternative for the degradation of atmospheric pollutants. This is because of its large absorption ability of UV light (Muthulingam et al **2015**). A few modes of preparations such as sol-gel synthesis, homogeneous precipitation and hydrothermal synthesis have some disadvantages like expensive equipment, obtained large particle size and poor dispersion (Periyayya Uthirakumar et al.**2015**)

Nearly 20% of the industrial developments cause discharge of various dye effluents into water bodies (Ozgur U et al.2005) This is mainly due to the incomplete combustion of organic waste from textile industries. These impurities not only affect water bodies, it affects the entire web and change ecosystem entirely (Milles et al.**1993**). Most of these dyes are carcinogenic and pose a serious health issues in human beings.Various azo dyes are used in many industries, among these phenol red is widely used in microbiological and analytical laboratories for cell biology studies and water quality analysis respectively . These dyes are water-soluble, red crystal and stable in air and belong to the category of triphenylmethane dyes.Major toxic effect of Phenol dyes includes irritation of dyes, respiratory problems, and skin allergy. Recently, in addition to these toxic effects, epithelial cell growth inhibition and mutagenic variations also reported(Robinson et al.**2001**)

In this chapter, we have reported application of green synthesized ZnO for dye degradation. Here nanoaprticles ZnO nanoparticles were synthesized by co-precipitation method using $ZnSO_4$ as acid precursor and NaOH & *psidium guajava* leaf extract as base precursor. The synthesized nanoparticles were used to study Photocatalytic degradation of phenol red under UV light.

2. EXPERIMENTAL METHODS

Green synthesized Zinc Oxide Nanoparticles

Fig.1.Green Route Synthesis of ZnO NPs

Guava leaf is dried in sunlight for 24 h, and then 1g of the crushed leaf is mortar grinded with 20ml distilled water and transferred into a conical flask. This was shaken for 30 min-1 h under 34.8 ^oC temperature and filtered. Similar to the chemical synthesis, 1mM of $ZnSO_4.7H_2O$ was prepared equal amounts of leaf extract and $ZnSO_4$ were magnetically stirred for 1 h.

Preparation of phenol red dye

The stock solution of phenol red was prepared by dissolving 0.1 g of commercially available phenol red dye in 100 of double distilled water to obtain a stock concentration of 100 mg\ml. Experimental dye solutions of desired concentrations were prepared by appropriate dilution of stock solution.

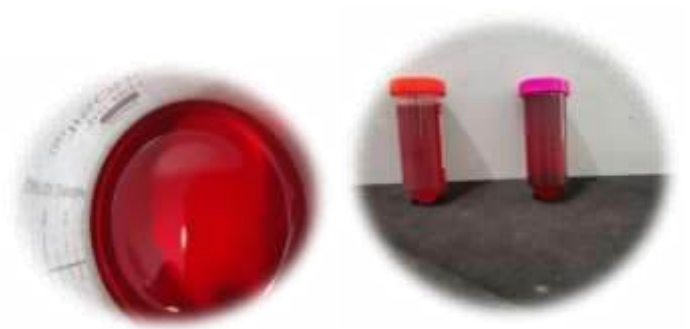

Fig. 2.Phenol Red Dye

Photocatalytic Degradation Experiment:

The photocatalytic activities of the synthesized ZnO photo catalysts were studied for degradation of commercial phenol red dye (PR).The experiment was carried under ultraviolet illumination (source-sunlight). About 10 ml of the stock solution was taken in 3 different beakers, with one left as control and to the other two 2.5 ml and 5 ml of the chemically precipitated ZnO nanoparticles were added. These beakers were exposed to the UV light for 3 h, and the experiment was repeated in the same way with green synthesized ZnO nanoparticles.

The figure 3 and 4 show the degradation of phenol red solution by the photocatalyst under UV light after complete 3 h.

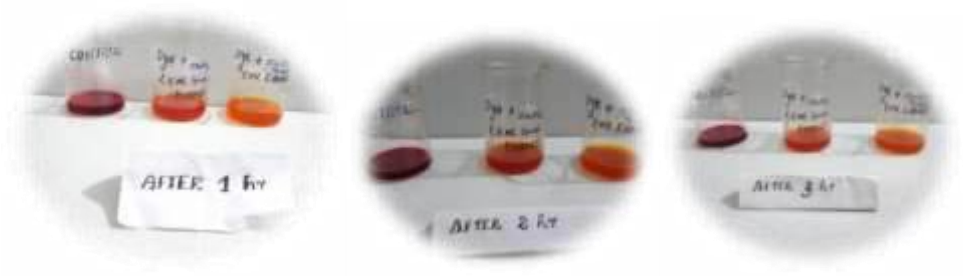

Fig.: 3 Green Synthesized ZnO and Phenol Red Dye

The degradation efficiency calculation

For each 1hour, the degradation efficiency of phenol red dye was checked by UV spectrophotometer at 650 nm and percentage degradation was calculated. It was found that after 3 hours of study green synthesized nanoparticle can able to degrade 88.4% of phenol red dye. The same analysis on the chemically synthesized gave result of 58% of phenol dye degradation

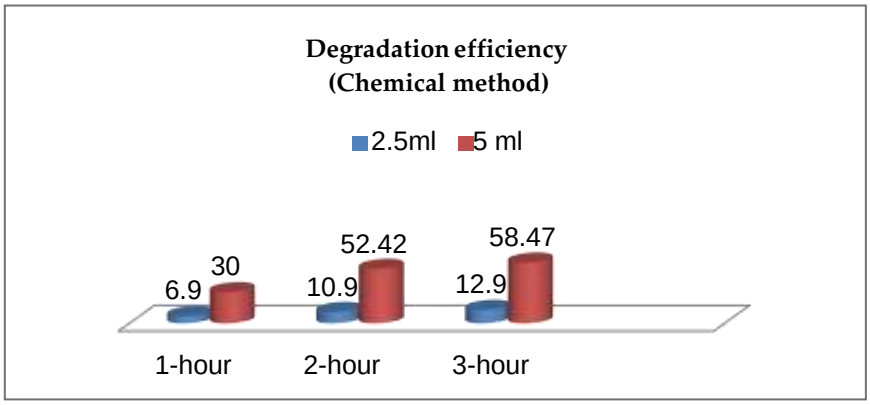

Fig. 4: Degradation Efficiency of Chemically Synthesized ZnO NPs.

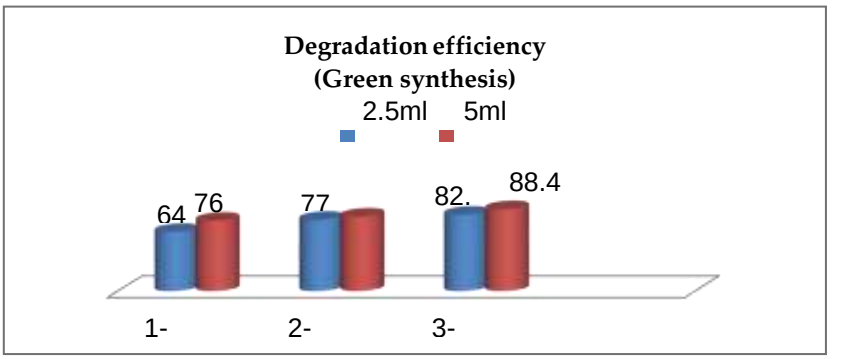

Fig. 5: Degradation Efficiency of Green Synthesized ZnO NPs

CONCLUSION

Functionalized, charged, biocompatible and stable NPs and green carbon dots play a vital role in the worldwide research and development of nano medicine. In this chapter we reviewed introduction about nanoparticles and development of human hair derived green carbon dots. Proposed methods require only hair extract as a substrate and free from other environmental hazardous chemicals. This further asserts that there are no harmful byproducts during synthesis. These performances will enforce firm limitations on the use of synthetic chemicals used for the synthesis of metal nanoparticles. Due to the exceptional properties of human hair like chemical composition, tensile strength, degradation rate, thermal insulation etc, it will be a cost effective nano catalyst. The results will confirm excellent physicochemical properties of synthesized carbon quantum dots. Experimental method confirmed that the green synthesized ZnO nanoparticles have greater efficiency of dye degradation, which enlightens the application of green synthesized ZnO nanoparticle in nano catalyst. Now this treated water may also find application in cosmetic industries, agricultural irrigation purposes and so on when properly treated.

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Chapter 8

SOLVENT FREE SYNTHESIS OF SUBSTITUTED 4-PHENYLPYRIMIDINE-SHIFFS BASE-5-CARBOXYLATE AND BIOLOGICAL ACTIVITIES

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ABSTRACT

Simple, efficient, green, solvent free and cost effective synthesis of Ethyl-2-(1H) One-1, 4-dihydro-6-methyl-4-phenylpyrimidine-shiffs Base-5-Carboxylate by condensation of 1, 3-dicarboxyl compound , substituted aldehydes and urea /thio-urea. The reaction is carried under observation that mixture of 1, 3-dicarboxyl, different aldehydes and urea / thio-urea without any acid catalyst within ½ hour indicates the advantages of solvent less reaction. The newly synthesized compounds 5(a-i) are screen for IR, NMR, Mass & CHN an analysis for structure elucidation.

Keywords: Solvent free, Schiff base, phenyl pyridine, Di-hydro derivative, etc.

INTRODUCTION

The green chemistry[1, 2] is to provide a path that reduces or eliminates the use of such hazardous toxic solvents, eco-friendly reagents and catalysts, selected medium such as water, supercritical fluids, ionic liquids or solvent-free reactions, non-classical modes of activation such as ultrasounds or microwaves. Synthetic chemical transformation reactions involve the use of different organic solvents. Toxic solvents[3-7] are used in chemical laboratory, industry and have been considered a very serious problem for the health, safety of workers and environmental damage through pollution, large numbers of reactions occur in solid state without the solvent. Green chemistry, also called sustainable chemistry due to very rapid reactions, frequently a few minutes, brought about by high and homogeneous temperatures and combined with pressure effects, higher degree of purity achieved due to short residence time at high temperatures, yields often better, obtained within shorter times and with purer products.

Microwaves consist in an electromagnetic wave within the range 1 cm^{-1m} in the electromagnetic spectrum useful frequency devoted to industrial, medicinal, domestic or any scientific purposes is imposed by international legislation to 2450 MHz, i.e. to a wave length of 12.2 cm. According to the Planck law, the energy involved in MW–materials interactions is 0.3 cal mol^{-1} and therefore is largely non-sufficient for molecule excitation results in essentially material–wave interactions of electromagnetic nature, consequently with specificity for polar systems. It is also noticeable that, in order to have a good compatibility with wavelength, the penetration depth of MW into materials is in the order

of magnitude of the decimeter and heating of products submitted to microwave exposure can only result from material–wave interactions. Simple, efficient, solvent free & multi-component reactions (MCR) as synthetic protocols that join together tree or more substrates in a highly region and stereo selective manner to deliver structurally complex organic molecules, have applications in all fields of organic synthesis.MCR are powerful tools for the efficient creation of organic molecules in an one-pot fashion. Green chemistry is the development of environmentally friendly chemical protocols and technologies. Therefore, the development of new MCR towards biomedical and industrial is inevitable at the present time.

RESULT AND DISCURSION

To Prepare Ethyl-2-(1H) One-1, 4-dihydro-6-methyl-4- phenylpyrimidine- 5- Carboxylate and Ethyl-2-(1H) One-1, 4-dihydro-6-methynl-4-phenylpyrimidine-shiffs Base-5-Carboxylate by MCR one step synthesis.

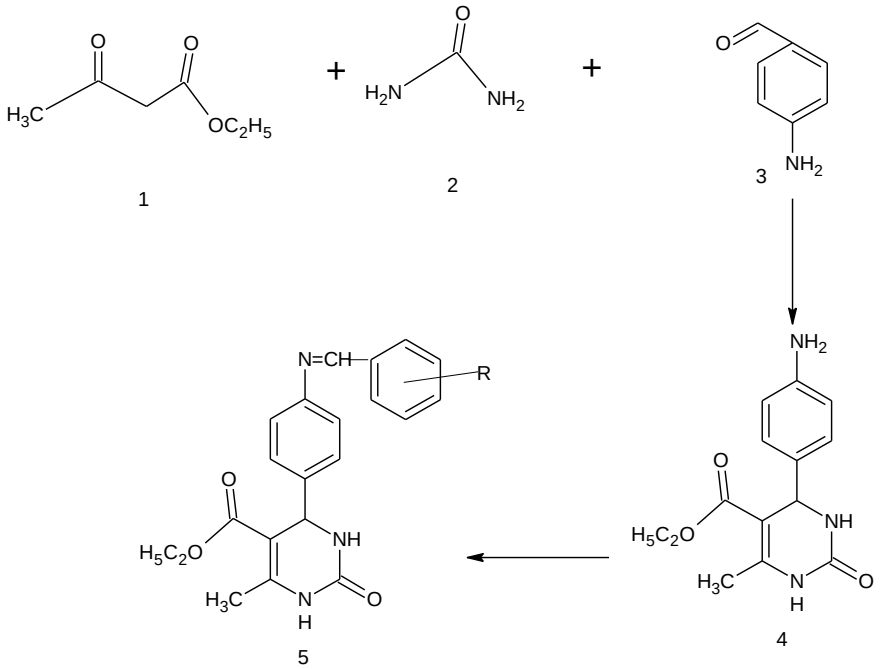
Biological activities

The synthesized Ethyl-2-(1H) One-1, 4-dihydro-6-methyl-4-phenylpyrimidine-shiffs Base-5-Carboxylate were tested for their antimicrobial activity in vitro against gram positive bacterium *S. aureus* and gram negative bacterium *E. Coli*. using ciprofloxacin as standard, Nutrient Agar was prepared separately and divided into two equal parts in two 250ml of conical flasks and sterilized by autoclaving. To a sterilized petriplates first basal layer of nutrient agar was seeded with bacterial cultures (*E. coli & S. aureus*) & allowed to set. After solidification, a hole in the center of plate was bored with sterile bases and filled with heterocyclic compounds under studies and observed for zone of inhibition. Synthesized Ethyl-2-(1H) One-1, 4-dihydro-6-methyl-4-phenylpyrimidine-shiffs Base-5-Carboxylate 5a, 5e, 5f, 5h show good antibacterial activity against *S. aureus.* The synthesized compounds were tested at 100g/ml **Table –I**.

Table – I – Data for in Vitro Antibacterial and Anti Fungal Activities (in mm)
(NA=Not Active, --=No Inhibition of Growth)

Comp.	Minimum Inhibitory Concentration's g/ml					
	E. *Coli*	**S. *aurous***	**Ps. *aeruginoa***	**P. *Vulgaris***	**A.*niger***	**C. *albicans***
5a	15	17	16	16	12	18
5b	16	9	10	12	22	12
5c	17	10	11	13	19	NA
5d	13	9	10	11	17	NA
5e	17	15	13	-	14	22
5f	15	16	-	12	-	21
5g	NA	-	7	10	-	12

5h	17	15	15	18	16	21
5i	12	4	NA	10	18	NA
5j	13	6	12	14	12	-



	R
1	H
2	2-OH
3	3-OH
4	4-OH
5	2-Cl
6	4-Cl
7	2-NO_2
8	4-NO_2
9	2-OCH_3
10	4-OCH_3

Scheme-I

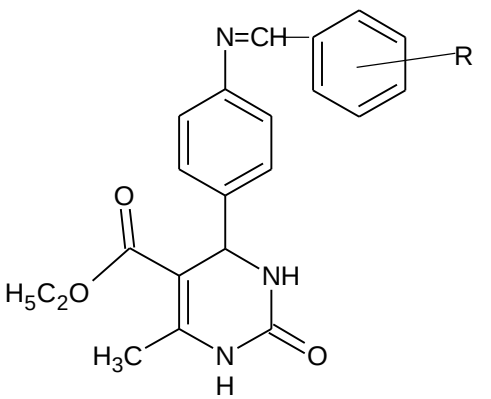
Synthesis of dihydropyrimidine-2(1H) one

A mixture of substituted aldehydes (1mole) ethyl acetoacetate (1mole) and urea/thiourea (1mole) was taken in a 250ml RB with magnetic stirring. The reaction mixture was heated in sand bath for 1hours at 110^0 to 120^0c temperature. First reaction mixture was cooled at room temperature and poured in ice cold water. The solid separated out was filtered and wash several time with water and recrystallized from ethanol.

Synthesis of ethyl-2-(1H) one-1, 4-dihydro-6-methyl-4-phenylpyrimidine schiffs base-5-carboxylate

Mixture of Dihydroaminopyrimidine-2(1H) one (1mole), substituted aldehydes and one or two drops of H_2SO_4 was taken in 250ml RB flask. The reaction mixtures was heated for 1hours, then cool at room temperature and poured over ice cold water. The solid was separated and filtered washed with water and recrystallized form ethanol to give the product.

Table III-Characterization Data of Newly Synthesized Ethyl-2-(1H) one-1, 4-Dihydro-6-Methyl-4-Phenylpyrimidine Schiffs Base-5-Carboxylate (5a-j)



5

Comp	R	Mol Formula	M. P.(°C)	Yield (%)	C	H	N
5a	-H	$C_{21}H_{21}O_3N_3$	145	71	69.45	5.8	11.5
					(69.3)	(5.7)	(11.4)
5b	2-OH	$C_{21}H_{20}O_3N_3$	137	67	69.45	5.8	11.5
					(69.3)	(5.7)	(11.4)
5c	3-OH	$C_{21}H_{20}O_3N_3$	131	65	69.45	5.8	11.5
					(69.3)	(5.7)	(11.4)
5d	4-OH	$C_{21}H_{20}O_3N_3$	130	58	69.45	5.8	11.5
					(69.3)	(5.7)	(11.4)

5e	2-NO_2	$C_{21}H_{20}O_5N_4$	148	68	69.45 (69.3)	5.8 (5.7)	11.5 (11.4)
5f	3-NO_2	$C_{21}H_{20}O_5N_4$	144	64	69.45 (69.3)	5.8 (5.7)	11.5 (11.4)
5g	4-NO_2	$C_{21}H_{20}O_5N_4$	147	81	69.45 (69.3)	5.8 (5.7)	11.5 (11.4)
5h	2-Cl	$C_{21}H_{20}O_3N_3Cl$	153	66	69.45 (69.3)	5.8 (5.7)	11.5 (11.4)
5i	4-Cl	$C_{21}H_{20}O_3N_3Cl$	157	77	69.45 (69.3)	5.8 (5.7)	11.5 (11.4)
5j	2-OCH3	$C_{22}H_{23}O_4N_3$	158	66	69.45 (69.3)	5.8 (5.7)	11.5 (11.4)

CONCLUSION

In present manuscript procedure of the synthesis of one step MCR for the formation ethyl 2-(1H) one -1, 4-dihydro -6- methy l-4-pheny l pyrimidine - 5- carboxylate in solvent free and catalyst free condensation. This solvent free and multi component reaction avoid use of volatile and hazardous solvent and toxic catalyst and give new diversion in organic synthesis.

ACKNOWLEDGEMENT

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Chapter
9

PHARMACOLOGICAL ACTIVITIES OF HETERO-FUSED ANALOGUES

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ABSTRACT

A wide range of biological properties are possessed by nitrogen-containing heterocycles in nature. In the treatment of osteolytic breast cancer metastases, brain tumors, kidney sarcoma, and myeloblastic leukemia, indole alkaloids display promising results. Several types of cancer are highly sensitive to substituted indoles, which also have limited toxic side effects and no hematological toxicity.

Keywords—Carbazoles, Hetero-fused indole alkaloids

INTRODUCTION

Nitrogen-containing heterocycles are widespread in nature and possess a broad spectrum of interesting biological properties. Among the nitrogen heterocycles, carbazole alkaloids and its derivatives are growing class of natural compounds. The initial discovery of carbazole in the anthracene fraction of coal tar followed by the first isolation of the antimicrobial murrayanine from the plant *Murraya koenigii* Spreng., started the enormous development of carbazole chemistry. Since then, there has been a strong interest in this area by chemists and biologists due to the intriguing structural features and promising biological activities associated with many carbazole alkaloids. The progress in the chemistry of carbazole alkaloids is emphasized by the publication of several reviews and book chapters covering the field. [1-10]

A large number of carbazole alkaloids have been isolated from higher plants of the genera *Murraya, Glycosmis*, and *Clausena*, all belonging to the family *Rutaceae* (subtribe Clauseninae, tribe Clauseneae, subfamily *Aurantioideae*). The occurrence of carbazole alkaloids in these three genera of the *Rutaceae* is of chemotaxonomic importance and justifies their classification as an independent subtribe. Carbazoles have also been reported from other genera, such as *Micromelum* of the family *Rutaceae* (subtribe Micromelinae), *Ekebergia* of the Meliaceae, and *Cimicifuga* of the Ranunculaceae. The genus *Murraya*, especially the species *Murraya euchrestifolia* Hayata, represents the richest source of carbazole alkaloids among all terrestrial plants. Various monomeric and also bis-carbazole alkaloids, formed by the combination of two of the monomeric units, have been reported from the genus *Murraya*. It is noteworthy that, while *Murraya koenigii* grown in Indian soil did not afford any bis-carbazole alkaloids, the same species grown in a green house in Japan from seeds collected in Taiwan generated bis-carbazole alkaloids. Depending on the

seasonal and geographical variation, the genus *Murraya* is known to provide different alkaloids. Moreover, carbazole alkaloids have been isolated from several different *Streptomyces* species. Further natural sources for carbazole alkaloids are for example the blue-green alga *Hyella caespitosa*, species of the genera Aspergillus, *Actinomadura, Didemnum*, and *Iotrochota*, and the human pathogenic yeast *Malassezia furfur*.

Since then a broad range of structurally interesting indole alkaloids with useful biological activities has been isolated from diverse natural sources. The pharmacological potential of these natural products initiated the development of novel synthetic methods for efficient routes to carbazoles. Ellipticine was the first isolated pyrido[4,3-*b*]carbazole alkaloids and more recent studies have also indicated activity against HIV[11] and tumor cells.[12-16] Since then, pyridocarbazoles and related ring systems have made a tremendous development, both in the synthesis and in their biological evaluation.[17-18] The carbazomycins were an important class of antibiotics with a carbazole nucleus.[19] Its two parent compounds namely, carbazomycins-A and carbazomycins-B were found to inhibit the growth of phytopathogenic fungi and have anti-bacterial and anti-yeast activities. Franzblau *et al*. reported the *in-vitro* anti-TB activity of various carbazole derivatives such as 3-formylcarbazole, methyl carbazole-3-carboxylate, lansine, 3-formyl-6-methoxycarbazole and micromeline.[20] In addition to these carbazole alkaloids, isomers of glycozoline and girinimbine were tested against various microbes and found to be active against *S. aureus*.[21] Some aminoacyl carbazoles were found to be active against *B. subtilis* (ICC-Strain) and *B. cereus* (NRRL-B-569).[22]

Anti-tumor active Carbazoles

Cancer and related diseases represent one of the major causes of death for humankind. The etiology of cancer is multiple, but great progress has been made in recent times toward the understanding of these diseases with the discovery of oncogenes. Various natural products of plant and animal origin constitute the major sources for compounds affecting such oncogenes. With the passage of time, a wide range of synthetic analogs based on natural products emerged as therapeutically useful anti-tumor agents. Among these natural products, the carbazole alkaloids constitute one of the important classes of natural products. Within the carbazole alkaloids, natural and synthetic congeners of the pyrido[4,3-*b*]carbazole and the indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole alkaloids comprise a large group of therapeutically useful anti-tumor agents, either in current clinical use, or in the various stages of clinical development. [20,23-31]

Anti-Biotic Carbazoles

Among the various carbazole derivatives, murrayanine (3-formyl-1-methoxycarbazole) was the first carbazole alkaloid isolated from a natural source and it showed antimicrobial properties.[32] Various carbazole derivatives showed antibacterial, antifungal and anti-tuberculosis activities and some are given below.

Anti-Viral Carbazoles

The tubingensins A and B showed activity against the widespread crop pest *Heliothis zea*, and display *in vitro* anti-viral activity against herpes simplex virus type 1 with IC50 values

of 8 and 9 mg/mL, respectively.[33a] Some basic ethers of carbazoles are anti-viral. In 2000, Boyd *et al* reported for the first time an anti-HIV active carbazole alkaloid, siamenol[33b] and some more active carbazole derivatives are given below.

Anti-Inflammatory Carbazoles

The anti-inflammatory properties of several carbazole derivatives have attracted widespread attention. Some acidic tetrahydrocarbazoles have been shown to posses anti-inflammatory activity.[34] Among these derivatives, 1-ethyl-8-n-propyl-1,2,3,4-tetrahydrocarbazole-1-acetic acid was found to be a novel anti-inflammatory agent[35], and 6-chloro-1,2,3,4-tetrahydro carbazole-2-carboxylic acid was clinically active in the treatment of acute gout.[36]

Anti-Malarial Carbazoles

In 1998, Bringmann *et al* reported the anti-plasmodial activity of a series of mono and bis-natural and structurally modified carbazoles and found that the synthetic compound 1,4-diacetoxy-3-methylcarbazole[37] showed higher activity against *Plasmodium falciparum* than natural 1-hydroxy-3-methylcarbazole.[38] In 2000, Yenjai *et al* reported the anti-plasmodial activity of 2-oxygenated carbazole alkaloids against *P. falciparum*. In their studies, clausine H (clauszoline-C) and heptaphylline showed good activity.[39] Prior to these studies, a report on the anti-plasmodial activity of 3- and 4-carbazole dialkylaminocarbinols had appeared.[40]

Diverse Pharmacologically Active Carbazoles

N-Alkylamino carbazoles possess significant anti-convulsant and diuretic activity.[41] Rimcazoles is a novel anti-pyretic and neuroleptic agent. It was found to be a specific competitive antagonist of s-sites in the brain. It reverses psychotic conditions induced in humans by phencyclidine and/or s-opiod antagonists, probably by binding to receptors in the brain.[42-44] Ramatroban functions as a novel, dual antagonist of the thromboxane A2 (TXA2) receptor and chemoattractant receptor-homologous molecule expressed on Th2 cells (CRTh2), a newly identified prostaglandin D2 (PGD2) receptor.[45-46]

Based on the emerging importance of the carbazole derivatives as indicated above, it was felt worthwhile to pay some attention on the synthesis of heteroannulated carbazoles and their biological aspects along with the crystallographic studies of some carbazole derivatives. Thus the introductory chapter deals with the literature survey pertinent to the various synthetic routes available for the carbazole derivatives for the past decades followed by the objective of the present work.

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Chapter
10

MEDICINALLY ACTIVE CARBAZOLES AND CYCLOHEPTA[*B*]INDOLES

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ABSTRACT

A wide range of biological properties are possessed by nitrogen-containing heterocycles in nature. In the treatment of osteolytic breast cancer metastases, brain tumors, kidney sarcoma, and myeloblastic leukemia, indole alkaloids display promising results. Several types of cancer are highly sensitive to substituted indoles, which also have limited toxic side effects and no hematological toxicity. It is believed that their high DNA binding affinity contributes in part to these pharmacological properties since they are DNA intercalating molecules.

Keywords—Heterocyles, Carbazoles, pyridocarbazole, cyclo hepta[*b*]indoles.

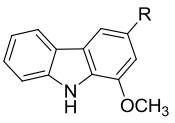
INTRODUCTION

The prevalence and diversity of aromatic nitrogen-containing heterocycles found in natural products and used in medicinal chemistry continue to stimulate the development of new methods and strategies for their syntheses.[1-3] Indole ring systems are the core structural elements in natural and synthetic organic compounds possessing a wide diversity of important biological activities.[3-6] Substituted indoles are capable of binding to many receptors with high affinity.[7] Therefore, the synthesis and selective functionalization of indoles have been the focus of active research over the years. Numerous methods have been developed for the synthesis of indoles due to the importance of compounds that incorporate the indole subunit.[8-12] However, the search for new methods for the simple and efficient construction of the fused indole ring system continues to be an important synthetic goal. Numerous indole alkaloids have been reported, namely bis-indoles, carbazoles, indoloquinolines, carbolines, etc. So, our particular interest will be in the methods for the synthesis of polycyclic indoles, such as newly growing field of cyclohepta[*b*]indoles and carbazoles.

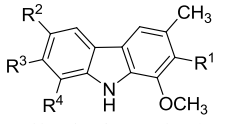
Carbazole and its derivatives are an important type of nitrogen containing aromatic heterocyclic compounds. Many condensed heterocyclic compounds containing a carbazole nucleus have been reported to develop a broad range of potent biological activities, such as anti-microbial, anti-tumor, anti-viral, anti-inflammatory, anti-malarial, anti-diarrhoeal and other biological properties such as immunosuppression, neuroprotection and pancreatic

lipase inhibition.[13-15] Among these, natural or synthetic pyridocarbazoles, indolocarbazoles, pyranocarbazoles, pyrrolocarbazoles, benzocarbazoles or simply tricyclic carbazoles have been reported. Since then there has been a strong interest in this area by chemists and biologists due to the intriguing structural features and promising biological activities exhibited by many carbazole alkaloids. The explosive growth of carbazole chemistry is emphasized by the large number of monographs, accounts, and reviews.[16-25]

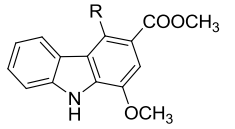
A large number of carbazole alkaloids have been isolated from higher plants of the genera *Murraya, Glycosmis*, and *Clausena*, all belonging to the family *Rutaceae* (subtribe Clauseninae, tribe Clauseneae, subfamily *Aurantioideae*).[25] The occurrence of carbazole alkaloids in these three genera of the *Rutaceae* is of chemotaxonomic importance and justifies their classification as an independent sub tribe. Carbazoles have also been reported from other genera, such as *Micromelum* of the family *Rutaceae* (subtribe Micromelinae), *Ekebergia* of the Meliaceae, and *Cimicifuga* of the Ranunculaceae. The genus *Murraya*, especially the species *Murraya euchrestifolia* Hayata, represents the richest source of carbazole alkaloids among all terrestrial plants. Some of the naturally occurring carbazole alkaloids are listed below.



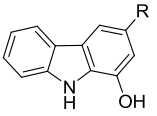
Murrayafoline A[26] (R=CH_3)
Koenoline[27] (R=CH_2OH)
Murrayanine[28] (R=CHO)
Mukoeic acid[29] (R=COOH)
Mukonone[19] (R=$COOCH_3$)



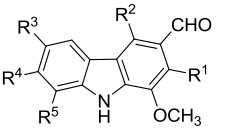
Murrastine[30] (R^1, R^2 =H, R^3, R^4=OCH_3)
Clausenapin[31] (R^1=prenyl, R^2, R^3, R^4=H)
Clausenine [32] (R^1, R^3, R^4=H, R^2=OCH_3)



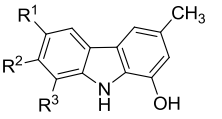
Clausamine D[33] (R=prenyl)
Clausamine E[33] (R=HC=CHC(OH)Me_2)
Clausamine G[33] (R=HC=CHC(OOH)Me_2)



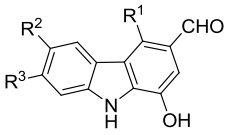
1-Hydroxy-3-methylcarbazole[34] (R=CH_3)
O-Demethylmurrayanine[35] (R=CHO)
Clausine E[36] (Clauszoline I) (R=$COOCH_3$)



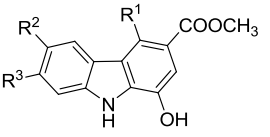
6-Methoxymurrayanine[37] (R=R^1,R^2,R^4,R^5=H, R^3=OCH_3)
Indizoline[38] (R^1=prenyl, R^2,R^3,R^4,R^5=H)
Ekeberginine[39] (R^2=prenyl, R^1,R^3,R^4,R^5=H)
Clausenal[40] (R=R^1,R^2,R^3,R^4=H, R^5=OCH_3)
Clausine Q[41] (R=R^1,R^2,R^3,R^5=H, R^4=OH)



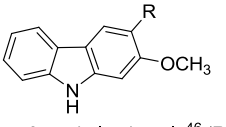
6,7-Dimethoxy-1-hydroxy-3-Methylcarbazole[42] (R^1,R^2=OCH_3, R^3=H)
Murrayafoline B[26] (R^1=H, R^2=OCH_3, R^3=prenyl)
Clausenol[32] (R^1=OCH_3, R^2,R^3=H)



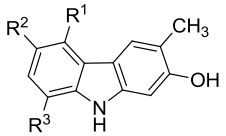
Clausine D[43] (R^1=prenul, R^2,R^3=H)
Clausine I[36] (R^1=R^3=H, R^2=OCH_3)
Clausine J[44] (R^1=H, R^2=OCH_3, R^3=OH)
Clausine Z[45] (R^1,R^3=H, R^2=OH)



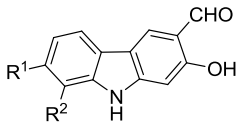
Clausine F[43] (R^1=prenul, R^2,R^3=H)
Clausine G[44] (R^1=R^3=H, R^2=OCH_3)
Clausine R[41] (R^1,R^2=H, R^3=OH)
Clausamine F[33] (R^1= HC=CHC(OH)Me_2. R^2,R^3 = H)



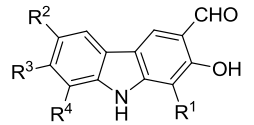
2-Methoxy-3-methylcarbazole[46] (R=CH_3)
Glycosinine[47] (R= CHO)
Clausine L[48] (R = $COOCH_3$)



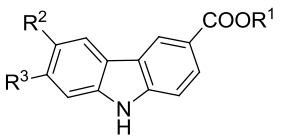
Carbalexin A[49] (R^1=OCH_3, R^2=R^3=H)
Carbalexin B[49] (R^1,R^2=H, R^3=OCH_3)
Carbalexin C[49] (R^1,R^3=H, R^2=OCH_3)
Glybomine B[50]
(R^1=prenyl, R^2=OCH_3, R^3=H)
Glybomine C[50]
(R^1=prenyl, R^2=OH, R^3=H)



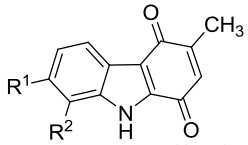
Clausine A[44] (R^1=H, R^2=OCH_3)
Clausine O[41] (R^1=OH, R^2=H)
Clauszoline-M[51] (R^1=H, R^2=OH)
Murrayaline-C[52] (R^1=OCH_3, R^2=CHO)
Murrayaline-D[52]
(R^1=OCH_3, R^2=geranyl)



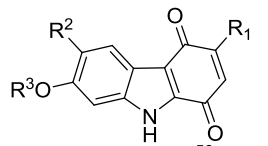
Heptaphylline[53]
(R^1=prenyl, R^2,R^3,R^4=H)
Heptazoline[54]
(R^1=prenyl, R^2,R^3=H, R^4=OH)
Clausine B[36]
(R^1,R^3=H, R^2,R^4=OCH_3)
Clausine S[41]
(R^1=$CH_2CH(OH)C(Me)=CH_2$,
R^2,R^3,R^4=H)



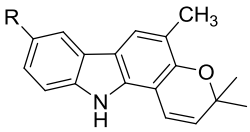
Clausine C[44]
(R^1=CH_3, R^2=H, R^3=OCH_3)
Clausine M[41]
(R^1=CH_3, R^2=H, R^3=OH)
Clausine N[41]
(R^1,R^2=H, R^3=OCH_3)



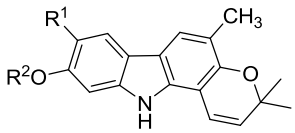
Murrayaquinone A[26] (R^1,R^2=H)
Murrayaquinone B[26]
(R^1=OCH_3, R^2=prenyl)
Murrayaquinone C[26]
(R^1=OCH_3, R^2=geranyl)
Murrayaquinone D[55]
(R^1=OH, R^2=geranyl)
Murrayaquinone E[52] (R^1=OH, R^2=prenyl)



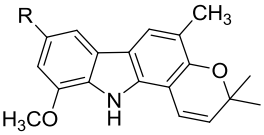
Clausenaquinone A[56]
(R^1=OCH_3, R^2=CH_3, R^3=H)
Koeniginequinone A[57]
(R^1,R^3=CH_3, R^2=H)
Koeniginequinone B[57]
(R^1=H, R^2=OCH_3, R^3=CH_3)



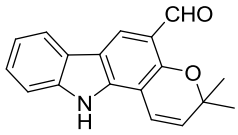
Girinimbine[58] (R=H)
Koenimbine[59] (R=OCH_3)
Koenine[60] (R=OH)



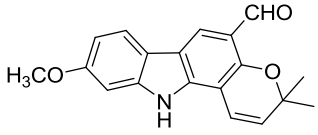
Koenigicine[61] (R^1=OCH_3, R^2=CH_3)
Koenigine[62] (R^1=OCH_3, R^2=H)
Murrayamine-A[63] (R^1,R^2=H)
O-Methylmurrayamine A[64] (R^1=H, R^2=CH_3)



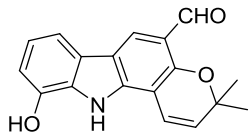
Mupamine[65] (R=H)
Mukonicine[66] (R=OCH_3)



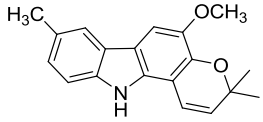
Murrayacine[67]



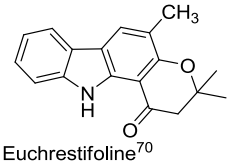
7-Methoxymurrayacine[47]



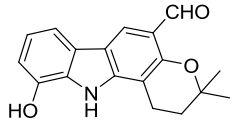
Clauszoline-G[68]



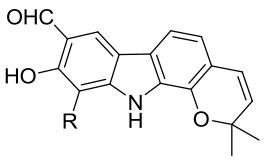
Heptazolidine[69]



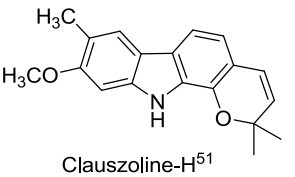
Euchrestifoline[70]



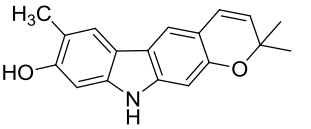
Heptazolicine[71]



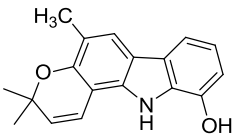
Clauszoline-A[68] (R=prenyl)
Clauszoline-B[68] (R=H)



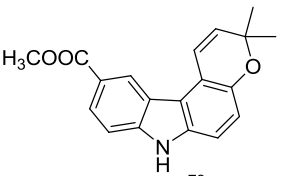
Clauszoline-H[51]



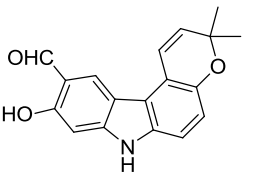
Pyrayafoline B[72]



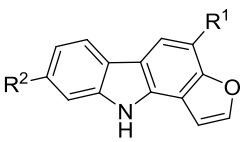
Clauraila B[73]



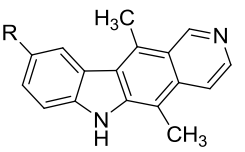
Clauraila C[73]



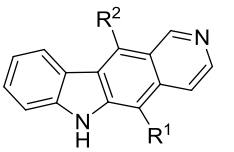
Clauraila D[73]



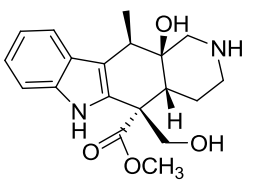
Furostifoline[74] (R1=CH3, R2=H)
Furoclausine-A[75] (R1=CHO, R2=OH)



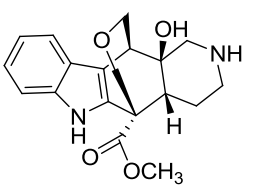
Ellipticine[76](R=H)
9-Methoxyellipticine[76] (R=OCH_3)
9-Hydroxyellipticine[77] (R=OH)



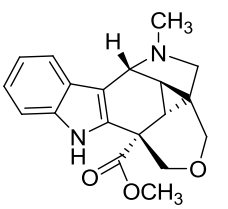
13-Oxoellipticine[77]
(R^1=CHO, R^2=CH_3)
12-Hydroxyellipticine[77]
(R^1=CH_3), R^2=CH_2OH)



Alstilobanines A[78]



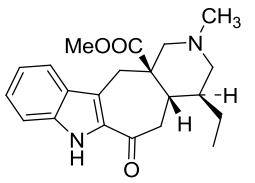
Alstilobanines E[78]



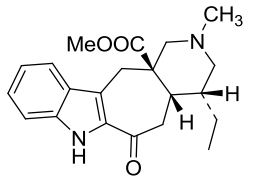
Undulifoline[78]

Carbazole derivatives are also widely used as building blocks for potential organic semiconductors, organic light-emitting diodes, electroluminescent materials, and polymers with other useful electrical properties.[79-83]

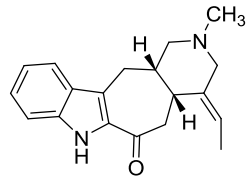
One growing class of biologically relevant indole derivatives are cyclohepta[*b*]indoles (such as one of the six membered ring of the carbazole replaced by a seven membered ring) have been found to posses anti-depressant, anti-cancer, anti-inflammatory activities. Only few cyclohepta[*b*]indole alkaloids were isolated from natural source. These type alkaloids were mostly isolated from the genera *Ervatamia, Pandaca, Caulerpa*. Also the general method for the construction of heterocyclic compounds containing cyclohepta[*b*]indole moiety were very rare in literature. Hence it was a challenging field to explore new and simple synthetic methods for the construction of cyclohepta[*b*]indole bearing heterocycles. Some of the reported alkaloids are given below.



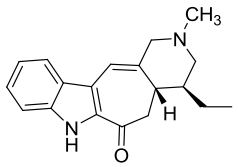
Ervatamine[84]



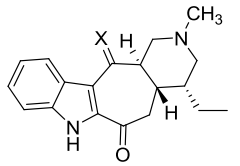
20-Epiervatamine[85]



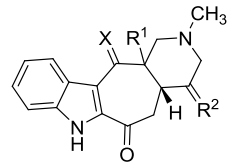
Methuenine[86]



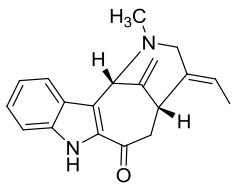
6,16-Didehydro-20-episilicine[87]



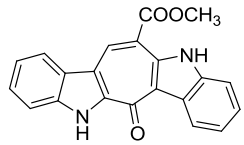
X=O 6-Oxo-16-episilicine[87]
X=H_2 16-Episilicine[87]



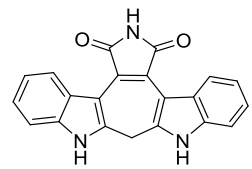
X=O, R^1=α–H, R^2=β-Et
(6-Oxo-16,20-episilicine)[87]
X=H_2, R^1=β–H, R^2=β-Et
(20-Episilicine)[87]



Ervitsine[88]



Caulersine[89]



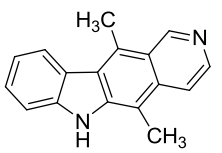
Homoarcyriaflavin[90]

BIOLOGICALLY ACTIVE CARBAZOLES AND CYCLOHEPTA[*B*]INDOLES

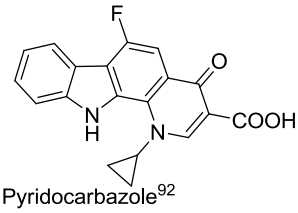
Since then a broad range of structurally interesting carbazole and cyclohepta[*b*]indole alkaloids with useful biological activities has been isolated from diverse natural sources. The pharmacological potential of these natural products initiated the development of novel synthetic methods for efficient routes to carbazoles and cyclohepta[*b*]indoles. In this section, we have summarized some of the important biological and pharmacological activities of these classes of alkaloids.

ANTI-TUMOUR ACTIVE CARBAZOLES AND CYCLOHEPTA[*B*]INDOLES

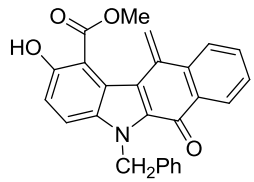
Cancer and related diseases represent one of the major causes of death for humankind. The etiology of cancer is multiple, but great progress has been made in recent times toward the understanding of these diseases with the discovery of oncogenes. Various natural products of plant and animal origin constitute the major sources for compounds affecting such oncogenes. With the passage of time, a wide range of synthetic analogues based on natural products emerged as therapeutically useful anti-tumour agents. Among these natural products, the carbazole constitute one of the important classes of natural products. Also cyclohepta[*b*]indole derivatives exhibit anti-tumour activity. Some of the anti-tumour active compounds are listed below.



Ellipticine[91]



Pyridocarbazole[92]



Benzocarbazole[93]

Anti-biotic carbazoles and cyclohepta [*b*] indoles

Among the various carbazole derivatives, murrayanine (3-formyl-1-methoxycarbazole) was the first carbazole alkaloid isolated from a natural source and it showed antimicrobial properties. Various carbazole and cyclohepta[*b*]indole derivatives showed antibacterial, antifungal and anti-tuberculosis activities and some are given below.

Diverse pharmacologically active carbazoles and cyclohepta[*b*]indoles

N-Alkylamino carbazoles possess significant anti-convulsant and diuretic activity. Rimcazoles is a novel anti-pyretic and neuroleptic agent. It was found to be a specific competitive antagonist of s-sites in the brain. It reverses psychotic conditions induced in humans by phencyclidine and/or s-opiod antagonists, probably by binding to receptors in the brain.[114-116] Ramatroban functions as a novel, dual antagonist of the thromboxane A2 (TXA2) receptor and chemoattractant receptor-homologous molecule expressed on Th2 cells (CRTh2), a newly identified prostaglandin D2 (PGD2) receptor. Certain cyclohepta[*b*]indoles have anti-nociceptive and analgesic. Benzo[6,7]cyclohepta[1,2-*b*]indoles are cytotoxic against murine L1210 leukemia and Lewis lung carcinoma cell lines and have antiproliferative activities. Recently, Zhu and Sanchez-Martinez developed a series of (hetero)aryl analogue of arcyriaflavin A II endowed with noteworthyCDK4/cyclinD1inhibitory activities (IC50<100 nM).

Based on the emerging importance of the carbazole and cyclohepta[*b*]indole derivatives as indicated above, it was felt worthwhile to pay some attention on the synthesis of heteroannulated carbazoles and cyclohepta[*b*]indoles and their biological aspects along with the crystallographic studies of some derivatives.

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Chapter
11

NANOTECHNOLOGICAL ADVANCEMENT IN FISHERIES AND AQUACULTURE

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ABSTRACT

Agriculture is an important component of normal life of human being as it provides food the basic need of everyone. Aquaculture can meet the food needs and livelihood of many fisherman community as it provides cheap source of animal protein. To intensify and meet the demand of several customer's aquaculture and fisheries sectors needs several advanced biotechnological applications. Nanotechnology becoming increasingly popular technology to meet those requirements through several applications. Several nano-materials, nano-particles, nano-devices have been used by several sectors of aquaculture which are the best way as compared to the basic techniques. Pollution has become a significant concern for agriculture and aquaculture due to weather and climate change. Nanotechnology is also helpful for monitoring the several pollution related problems which is helpful for more production in agriculture and aquaculture sector. Seed production is an essential part of aquaculture as increasing fish seed demand which can be achieved by nanotechnology. Fish growth and health management can also be done by several nano particles which have merits over the other traditional methods. Nanotechnology is an advanced form of biotechnology in several sectors to achieve the growing demand and overcome the challenges. Nanotechnology can be used by several researchers in case of agriculture and aquaculture to intensify the production and sustainable ecosystem management. This technology has been used as a novel tool in agricultural sector and its allied sectors.

INTRODUCTION

Aquaculture is an integral part of agriculture as both the sector have solitary aim for production of sustainable food for the human being. With several agricultural developments, the aquaculture developments are also on its way to ensuring the availability of enough and safe food to the human being. Aquaculture sector is an emerging field as part of agricultural sector because fishes are cheap source of protein and our one third of earth surface is covered by ocean. Countries like India (coastline 8129 km^2) surrounded by ocean mainly dependent on fisheries for livelihood. Fishes are now-a-days accepted globally as an ideal non-vegetarian food item as compared to meat, chicken, egg (FAO, 2018).

Nanotechnology is an emerging field of biotechnology in which molecular with electrical properties at nanoscale 1 to 100 nm have been used. Father of nanotechnology, Richard Feynman gave us a useful technology that can be applied to a several sectors.

Nanotechnology and nanoparticles are increasingly recognized for their impending applications in various aspects of human, animals, fishes and animal welfare like development of many pharmaceuticals, food packaging, nano-electronics and techniques like nano bubbles in aquaculture. Nanotechnology helps several sectors like agriculture, aquaculture, industrial, food packaging etc. to be improved as well as revolutionized as compared to before (Lyle *et al*., 2015). Nanotechnology have been proved as upgraded and advanced technology because of two main factors: (1) the merits of nanoparticles which have increased surface area with many antimicrobial properties and many coloring agents and (2) prevention from hazardous polluted materials for environment (Stark *et al*., 2015). Nanotechnology has been used in different sectors of aquaculture such as reproduction, disease diagnosis, absorption of drugs or hormones, vaccines and nutrient deliver, antifouling etc. Many authors such as Singh *et al*., (2017); Haldar and Nath, (2020); Kamalii, et al, (2018); Fakira, (2021); Shah and Mraz (2020); has reviewed about the several applications of nanotechnology in aquaculture, which is vast. Different types and forms of nano-particles have been used in aquaculture to intensify the culture system. Here we reviewed and discussed how nanotechnology can be of immense help for the fisheries, aquaculture and agricultural sectors.

NANOTECHNOLOGY IN WATER MANAGEMENT

Cultured fish species mostly reliant on the water in aquaculture sector. Climate change, several environmental factors and pollution arising problems for aquaculture nowadays. Every parameter (dissolved oxygen level, ammonia level, presence of planktons and different types of microbes) of cultured pond should be in optimum condition and the wastages should be removed periodically. Hu et al, (2013) & Atchudan et al, (2017) used nanoparticles such as Graphene Oxide and Titanium dioxide for the absorption of heavy metals and other organic dyes from the cultured pond. Hu et al, (2006), Park et al, (2013), and Ouyang et al, (2016) used Titanium dioxide for controlling virus, bacteria and algae. Graphene oxide (GO) and graphene Nano-sheets (GNs) have been used by many researchers for removing contaminants and maintain the water quality parameters (Motamedi et al., 2014; Liu et al.,2016; Kuang et al., 2017).

NANOTECHNOLOGY IN FISH BREEDING

Fish breeding is an essential part of aquaculture industry as production of large number of seeds from parent fishes within limited period of time is of beneficial. Several types of synthetic hormones have been used such as: Gonadotropin Relasing Hormone(GnRH), Leutinizing Hormone Releasing Hormone(LHRH) etc. Chitosan-nano conjugated Hormone (LHRH) Nanoparticles showed effective delivery and enhanced reproductive output in female fish of *C. carpio* (Rather *et al.,* 2013). Chitosan-Nano-conjugates had a 13% higher and chitosan gold preparation had a 9% percent higher fertilization rate then bare LHRH.

NANOTECHNOLOGY IN FISH GROWTH

Fish growth is an important parameter as customers want bigger fishes as compared to smaller ones. Fish growth achievement depends mainly healthy and advanced formulated fish diet. Fish feed with some nanoparticles is much more effective than normal fish feed. Tawfik *et al*., (2017) used Nano ZnO for growth enhancement of Nile Tilapia (Oreochromis

niloticus). ZnO Nanoparticles were prepared by chemical co-precipitation method and mixed with fish feed. Fish was fed 2 times daily 3% of body weight for 120 days. Then, growth was estimated in terms of Weight gain (%) and Specific growth rate (SGR) where they observed weight gain and SGR were more when they took 60 mg/kg nZnO. Uzo-God *et al*., (2019) had used dietary macro and nano iron oxide in growth of African catfish (*Clarias geriepinus*) fingerlings and concluded that nFe2O3 and Fe2O3 forms of iron can enhance the general health performance of the fish up to supplemental level of 0.4g/kg feed compared to the conventional basal feed. Oluwasanu *et al*., (2019) had discussed three types of mineral nanoparticles Selenium, Iron and Zinc for the growth of fin fishes and shell fishes.

NANOTECHNOLOGY IN FISH DISEASE MANAGEMENT

Fish disease management is an important factor in aquaculture for preventing mortality and improvement of growth in cultured fishes. Tawfik *et al*., (2017) had evaluated the nonspecific immunity function of Nile Tilapia using *Pseudomonas fluorescence* bacteria with a sub lethal dose 0.2 ml. They used ZnO Nanoparticles with fish feed and evaluated the nonspecific immunity function through quantization of total protein and serum immunoglobulin M (IgM) where they found as compared to the control group the treatment group with 60mg/kg ZnO particle was good. Oluwasanu *et al*., 2019 mentioned dietary zinc, selenium and iron as essential minerals for growth and health animals like fishes. Zinc is helpful for growth, immune booster and higher reproductive behaviors in animals whereas iron is helpful for respiration and immune response of fishes. When these minerals were used at nanoscale they showed more resistant to diseases as compared to control group of fishes.

DNA nano-vaccines are also useful for the disease management. Rajeshkumar *et. al.,* 2009 had used DNA vaccination method to control WSSV of tiger shrimp (*Paenus monodon).* They concluded that by using shrimp feeds with DNA construct containing the VP 28 gene of WSSV encapsulated in chitosan Nanoparticles. The relative survival rates at days 7, 15, 30 was 85%, 65%, 50% respectively whereas 100% mortality has shown by using control shrimp fed (Chitosan/pcDNA 3.1 and Chitosan/PBS complex). Similarly, Vimal *et al.,* (2014) had used CT/TPP NPs with DNA vaccines to control the Nodavirus infection of Asian seabass (*Lates calcarifer*). Ramya *et al*., (2013) used DNA construct containing extra small virus antisense (XSVAS) gene of nodavirus encapsulated with chitosan nanoparticles (NPs) was investigated in giant freshwater prawn (*Macrobrachium rosenbergii*) and concluded that they were having better immunity performance against nodavirus when fed with DNA nano-vaccine containing feed.

NANOTECHNOLOGY IN FEED MANAGEMENT

As Nanomaterials have properties like small size high exposed surface area per unit volume which enhances their chemical reactivity, stability easily taken up by gastrointestinal tract, interaction with organic and inorganic materials, so NMs can be used effectively in feed formulation. Chris *et al*., (2018) mentioned NMs of different types in fish feed which has resulted better fish growth rate, increased immunity power, well fertilization rate with less stress. With the use of NPs as feed supplements the food nutrients can pass to the cells

readily instead of being unused in digestive system. They mentioned about the effective uses of NMs such as Se, Fe, Zn etc. in feed formulation of fishes like *C. carpio*, Shell fishes such as *M. rosenbergii*, *P. monodon* etc. Onuegbu *et al*., (2018) had studied the comparison study between macro and nano ZnO (nZnO) particles in feed formulation of cultured African catfish fingerlings and concluded that nZnO particles have more impact than the macro size. nZnO particles have advantages like feed palatability improvement because of their smaller size, absorption in gastrointestinal tract and bioavailability.

NANOTECHNOLOGY IN DISEASE DETECTION

Disease detection at early stages of aquaculture is more crucial as the harvesting size, appearance and weight of fishes matters a lot. Mainly two types of diseases have been observed in case of fishes: non-pathogenic and pathogenic (Eldahan *et al*., 2021). Pathogenic diseases are much more dangerous as it can spread all over the cultured ponds. Saleh *et al*., (2012) had detected Spring viremia of carp (SVC) of C. carpio prior to amplification of the virus RNA by using gold NPs through colorimetric assay. As AuNPs have non cytotoxicity property they choose colloidal AuNPs for the reaction mixture. If the color remains red then its negative and if color changes from red to blue, its positive. Bacterial and fungal diseases in cultured ponds can also be detected using porous nanostructures and nanosensors (Muruganandam *et al*., 2019). Several other viral diseases of Koi carp, common carp, rainbow trout, atlantic salmon and other shell fishes, also have been detected using nanotechnology (Saleh *et al*., 2012).

NANOTECHNOLOGY IN ANTI-FOULING

Bio-fouling is a phenomenon caused by several marine organisms to the marine engineered vessels which leads to several problems. Anti-fouling paints have been used for the prevention of bio-fouling. Ashraf and Edwin, (2016) used Nano copperoxide incorporated poly ethylene glycol hydrogel as an antifouling coating for cage fishing net. The hydrogel reinforced with 0.004% (wt/vol) copperoxide treated netting material exposed for 90 days to the estuarine environment exhibited excellent fouling resistance with lowest biomass accumulation. Similarly, Vijayan *et al*., (2014) synthesized AgNPs by greener method as coatings for successive bio-fouling control. They choose four different marine biofilm forming bacterial strains, namely, *Salmonella* sp. (JN596113), *E. coli* (JN585664), *S. liquefaciens* (JN596115), and *A. hydrophila* (JN561697) (*in-vitro*). Protective polymer nanocomposites(PNC) coatings with inclusion of small quantities of nanomaterials enable enhanced barrier, and protective behavior towards corrosion resistance and biofouling resistance (Idumah *et al*., 2020).

NANO BUBBLE TECHNOLOGY IN AQUACULTURE

Nowadays super intensive culture for fish species in demand to meet the market supply the stocking density should be more. Large stocking density resulting more ammonia concentration and less oxygen concentration. To overcome this type of problems nano bubble technology can be applicable. Nano bubble technology is meant for more oxygen concentration in cultured water to enhance the fish health and growth without any stress condition. Nano bubble technology can also be helpful for the decomposition of organic matters. Mahasri *et al.,* (2018) had used this technology for nile tilapia (*Oreochromis niloticus*)

and concluded that increase in dissolved oxygen concentration from 6.5 mg/L to 25 mg/L. The dissolved oxygen rate increased upto 0.61 pp/minute for 30 minutes. This technology was also helpful for the cultivation of pacific white shrimp (*Litopenaeus vannamei*) with lower Presumptive Vibrio Count (PVC) value of *Vibrio* species (Mahasri and Harifa, 2019). Nano bubble technology is also helpful for controlling *Vibrio parahaemolyticus* in cultured ponds and increase oxygen level in shrimp farming (Nghia *et al*., 2021).

NANOTECHNOLOGY IN FISH PROCESSING INDUSTRY

Nanotechnology benefits the fish processing industry due to its numerous advantages. Starting from packaging, adding flavors, textures to microbe detection in several seafood products nano-materials take an important part. Chitosan nanoparticles, liposomes or emulsions have been used by several seafood processing industries (Montero *et al*., 2019). Kumar *et al*., (2016) had reviewed several nanoparticles used for the detection of food-contaminating toxins, namely aflatoxin, palytoxin, Botulinium neurotoxin, ochratoxin, zearalenone and HT-2. Fertilizer and pesticides can also be detected in food products with the help of nanoparticles. Vitamins, essential amino acid and hydrogen peroxide can also be detected by this novel technology. Several metal oxide nanoparticles (TiO_2 and ZnO) have been used for the fish gelatin bioactive packaging (Hosseini and Guillén, 2018).

NANOTECHNOLOGY DEVICES USED IN AQUACULTURE

Several Nano-technological devices such as: nanosensors, nanorods, nanotubes, nanobarcodes, nanocheck etc. have been used in aquaculture industry especially for microbe control and detection of several types of pathogens and mislabeling.

Nanosensor

Nanotechnology based biosensors are used for microbe control. Carbon nanotube based biosensors are effectively used for detection of minute amount of microbes. NASA, USA researchers used carbon nanotubes based biosensor for detection of a small amount of micro-organisms from water and food. Lv *et al*., (2016) had done SERS detection of protein biomarkers using gold nanorod based biosensor and concluded the advantage of that a promising alternative for the currently used immunoassays and fluorescence detection, and offer an ultrasensitive, non-destructive, and label-free technique for clinical diagnosis applications. Selvaraj *et al*., (2014) had resulted the beneficial effects of nano colloidal silver for control and detection of several types microbes from cultured water.

Nano-Check

Nano-check is a modern technology produced by Nevada-based Altair nanotechnologies which helps in cleaning of water. It uses 40 nm particles and absorbs phosphates and prevents growth of algae in water (Ashraf et al, 2011). Nanoscale delivery of weedicides a soil-wetting agents can be used for aquatic weed control and mitigation of stress due to climate change and aquatic pollution. Nano-materials like carbon or alumina, with additives like zeolite and iron containing compounds, can be used for the removal of ammonia, nitrites and nitrate contaminants. Ultrafine nanoscale powder made from iron can be used as an effective tool for cleaning up contaminants such as trichloroethane, carbon tetrachloride, and polychlorinated biphenyl to simpler carbon compounds which are less toxic.

Nano-Filtration

Hurtado et al. 2016 had used NF 270 membrane to separate nitrite and nitrate from water of recirculating aquaculture system (RAS). As RAS normally use nitrifying bacteria to control ammonium compounds, there is possibilities of formation of nitrites and nitrates which are toxic to fishes. Lai and Nguyen (2021) concluded that use of three kinds of NF membranes, including NF99, Desal DK and NTR7250 for the purified fish sausage preparation. Deodorizations and refinements of fish oil can also be done using this promising nano-filtration technique (Fang *et al*., 2018).

Nano-Barcoding

Nano-barcoding is mainly used for the detection of microbes and any mislabeling of fish species. Radio frequency ID (Rfid) is chip with a radio circuit incorporating nanoscale component with an identification code embedded in it. These tags can hold more information, scanned from a distance and used as a tracking device as well as a device to monitor the metabolism, swimming pattern and feeding behavior of fish (Ashraf *et al*., 2011). A nano-barcode is a monitoring device in which the processing industry and exporters can monitor the source or track the delivery status of their aqua product until it reaches the market. Nano-barcoding can be used in detection of allergens, viruses, diseases monitoring (Munir et al, 2020). Mainly gold nanoparticles have been used for the detection of pathogenic organisms (Khiyami et al., 2014; Castelani *et al*., 2019).

CONCLUSION

Food is the first need of human being which made our researchers to develop our agricultural and aquaculture production with various ways. Nanotechnology have been used by several researchers in different sectors and resulted in a better and intense way to itself. Nanotechnology proved that it can match the more and more demand of customers with their favorable desires. In aquaculture there are many applications of nanotechnology in water management, feed management, disease management, disease detection, prevention from diseases, reproduction, tracking of the seafood products and detection of mislabeling, which is of immense use. This article can be helpful to know and planning accordingly for the researchers to design their work plan in the field of nanotechnology.

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Chapter
12

BIOSENSORS IN HEALTH CARE

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INTRODUCTION

The current research and development in bioanalytical field is aiming to improve the stability, selectivity and sensitivity of the sensing devices containing immobilized biomolecules. Biologists, physicists, chemists and engineers have worked together to find innovative solutions of a large number of analytical problems by developing biosensors.

A biosensor is a device incorporating a biological sensing element either intimately connected to or integrated within a transducer. Biosensors may be classified according to the biological specificity-conferring mechanism or, alternatively, to the mode of physico-chemical signal transduction. The biological recognition element may be based on a chemical reaction catalysed by, or on an equilibrium reaction with macromolecules that have been isolated, engineered or present in their original biological environment (Thevenot, 1999).

Biosensors have found promising applications in various fields such as biotechnology, cell culture monitoring (Xudong, 2003), agriculture (Christian, 2020) (Antonacci, 2018), clinical diagnosis (Justino, 2016), food analysis (Scognamiglio, 2014), (Arora, 2011) (Mishra, 2012), environmental control (Gupta, 2019), sports medicine, drug delivery and various military situations (Turner et. al., 1987) (Malhotra & Choube, 2003). Among all these, technical development of biosensors for medical care has demanded the greatest attention. In recent years, the technical developments in the field of biosensors provided new outlook with more emphasis on greater sensitivity and stability from single to multi-molecule analysis by using several biomaterials in nanoscale (Goode, Rushworth, & Millner, 2014), (Vigneshvar, 2016).

Increased understanding of the concept of immobilized bioreagents, improved techniques for immobilization and technological advances in the microelectronics and nano technology has significantly contributed to this potential field of research.

The first commercialized biosensor product was a pen style device launched in 1987 by MediSense, developed by Turner's group at Cranfield in collaboration with researchers at the University of Oxford. In 1993, Erickson and Wilding (1993) introduced the i-STAT portable Clinical Analyzer which can measure a range of parameters- glucose, Blood Urea Nitrogen (BUN) sodium, potassium and haematocrit. National Physical Laboratory (NPL),

India has also patented a glucose biosensor based on ampero-metric method. The technology of this first Indian ampero-metric biosensor was transferred to three companies in India and the product is available in Indian markets. The Biomedical Metrology group at NPL carries out a wide range of frontier and applied research activities related to synthesis and characterization of novel electroactive materials such as quantum dots, dendrimers, organic and inorganic nanomaterials, conducting polymers and liquid crystals and thin films and exploitation of their extraordinary properties in the field of biomolecular recognition using various transduction principles such as electrochemical transduction, optical transduction and surface plasmonic resonance etc for biomedical applications, especially in the diagnosis of cardiovascular, food toxins and infectious diseases.

BIOSENSORS

Biosensors are functional analogs, that are based on the direct coupling of an immobilized biologically active compound with a signal transducer and electronic amplifier. The schematic diagram of a biosensor shown in figure-1. Biosensors promise to provide a powerful and inexpensive alternative to conventional analytical strategies assaying chemical species in complex matrices.

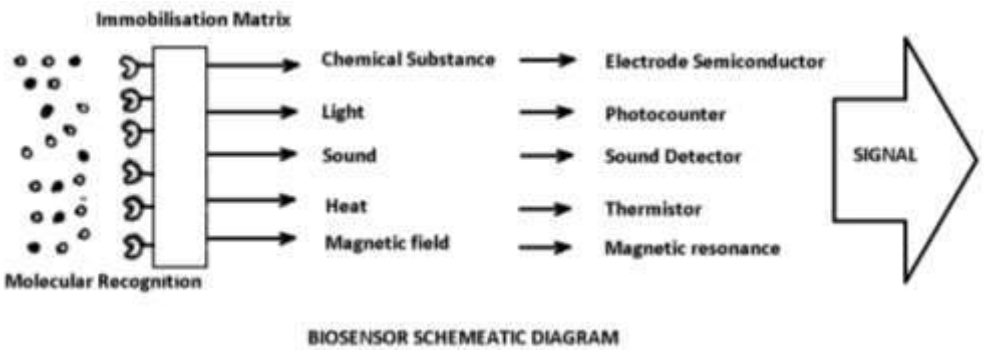

Fig.1: Biosensor Schematic

Bioreceptor or Biocomponents

The bioreceptors are bio recognition components that interact with the specific analyte of interest to produce an effect measurable by the transducer. Specific recognition and high selectivity for the analyte among a matrix of other chemical or biological components is a key requirement of the bioreceptor. The bioreceptors or biochemical transducer may comprise of enzymes, receptors, and antibodies or antigens. The biocomponents commonly used in biosensors are enzymes, tissues, bacteria, yeast, antibodies/antigens, liposomes, organelles, cell membrane components.

Transducer in a Biosensor

The transducer is selected to produce a continuous electronic signal that is directly proportional to the concentration of a chemical or set of chemicals present in a sample. The different type of transducers like optical, calorimetric, electrochemical, piezoelectric or

electromagnetic are used to convert the biological recognition event into a signal that can be analytically processed. The procedure at the biosensor is shown in figure 2.

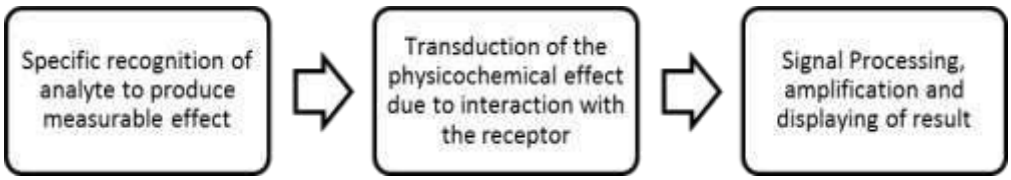

Fig. 2: Activities at Biosensor

A transducer converts the biochemical signal to an electronic signal. The biochemical transducer or biocomponent gives the biosensor selectivity or specificity. The transducer reads the signal, electronically amplifies and displays it. The transducers may be electrochemical, spectroscopic, thermal, piezoelectric, phytochrome sensor and surface acoustic wave technology.

***Optical biosensors*:** are based on the measurement of light emitted or absorbed as a consequence of a biochemical reaction. In such a biosensor, the light waves are guided by means of optical fibres to suitable detectors. e.g. fibre optic sensing based on the absorption, scattering of fluorescence of light by a sample positioned at a distal end with an excitation source and detector located at the proximal end. They can be used for the measurement of pH, 02, or co2 etc. Optical biosensors are also used for colorimetric tests for a number of analytes. Optical biosensors allow the sensitive and selective detection of a wide range of analytes including viruses, toxins, drugs, antibodies, tumour biomarkers, and tumour cells (Damborský, J, & Katrlík, 2016).

***Calorimetric biosensors*:** These biosensors detect an analyte on the basis of the heat absorbed or generated or change in temperature due to the biochemical reaction of the analyte with a suitable enzyme. The integrated circuit temperature sensitive structures have been modified with enzymes. Different substrates, enzymes, vitamins and antigens have been estimated using thermometric biosensors.

***Piezoelectric biosensors*:** These biosensors operate on the principle of generation of electric dipoles when an anisotropic natural crystal is put to mechanical stress. Adsorption of the analyte increases the mass of the crystal and alters its basic frequency of oscillation. They are used for measurement of ammonia, nitrous oxide. carbon monoxide , hydrogen etc.

***Electrochemical Biosensors**:* These are based on the fact that bio-interaction process generates or consumes electrochemical species which produces an electrochemical signal measurable by an electrochemical detector. The electrochemical sensors have several advantages over optical based systems. They can be operated in turbid media, offer comparable instrumental sensitivity and are more amenable to miniaturization. They are based on mediated or unmediated electrochemistry. A number of mediators such as ferrocene and its derivatives, ferricyanide methylene blue etc. are most commonly used. Various conducting polymers · such as polyaniline, polypyrrole etc. have also been used for fabricating biosensor.

The electrochemical biosensors may be further categorised into conductometric, potentiometric and amperometry biosensors based on the electrochemical property measured by the sensors.

The Conductometric Biosensors*:* measure changes in conductance between a pair of electrodes during biochemical reactions.

Potentiometric Biosensors: These biosensors masure potentials at the working electrode with respect to the reference electrode. They function under equilibrium conditions and monitor the accumulation of charge, at zero current, created by selective binding at the electrode surface. For example, ion selective electrodes detect ions such as Na^+, K^+, Ca^{+2}, NH_4^+ biological matrices by sensing changes in electrode potential when the ions bind to an appropriate ion exchange membrane. Guiltbault and Montalvo (1969) were first to devise a potentiometric enzyme electrode for the detection of urea where urease was immobilized at an ammonia selective liquid membrane electrode.

Amperometric Biosensors: These biosensors measure the changes in current on the working electrode due to direct oxidation of the products during biochemical reaction. The amperometric techniques are linearly dependent on analyte concentration and give a normal dynamic range and a response to errors in measurement of current. Oxygen (O_2) and hydrogen peroxide (H_2O_2) being the co-substrate and the product of several enzyme reactions, as well as, artificial redox mediators, such as ferricyanide, NMP+, ferrocene and benzoquinone can be determined amperometrically. Depending on the level of integration, electrochemical biosensors have been subdivided into four generations.

First generation Biosensor: In the first generation, the biocatalyst is either bound to or entrapped between the membranes. which in tum are fixed on the surface of the transducer (Clark and Lyons. 1962; Updike and Hicks, 1967). In these devices analyte concentrate is measured by the electrode based on oxygen consumption or on the basis of production of hydrogen peroxide. These biosensors have been developed for glucose, lactate and ascorbate etc. In such type of enzyme electrodes, oxygen electrode is susceptible to oxygen variation in sample.

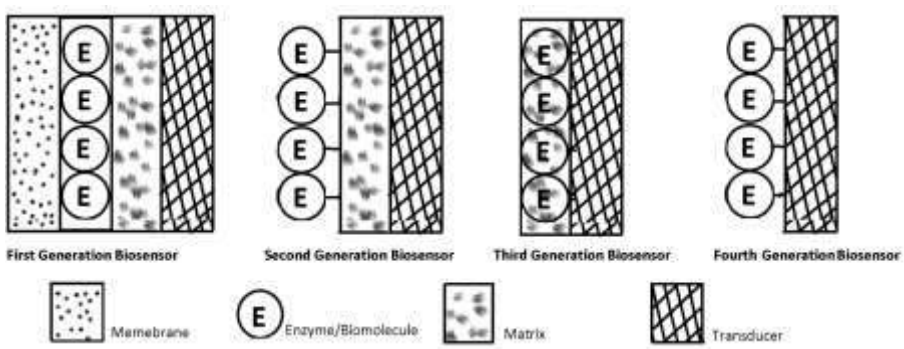

Fig. 3: Scheme of Generation of Biosensor (Source: Chuobey,A.)

Second Generation Biosensor: In the second generation, the biosensor involves covalent fixation or adsorption of the biologically active component to the surface of the transducer and permits elimination of the semi permeable membrane. The electron transfer mediators in these biosensors facilitates the utilisation of lower potentials eliminating the possibility of false results caused by oxidation of impurities in the sample.

Third Generation Biosensor: In the third-generation biosensors conducting polymers such as polyaniline, polypyrrole have been used as immobilisation matrix. These biosensors are stable, cost effective and are easily available. In these biosensors conducting polymers may be used for electron transfer during detection.

Fourth Generation Biosensor: The fourth-generation biosensors directly incorporate the bio components such as enzymes, antigens etc. into matrices. Most commonly used conducting polymers are silicon, and involve microelectrode, microchip or nano technology. These biosensors are suitable for both in vitro and in vivo systems. An in vitro, biosensor measurement takes place in a test tube, a culture dish, a microtiter plate or elsewhere outside a living organism such as the blood glucose monitoring device. In vivo biosensors are implanted in the body, but are not yet fully developed. Wearable biosensors are more commonly used as they are non -intrusive biosensors for real time monitoring of certain health parameters.

ATTACHMENTS OF BIOSENSORS

The biocomponents are attached to the surface of the sensors (polymer, metal, or glass). It is done by coating the surface with the biological elements by using polylysine, epoxy silane, or nitrocellulose in the case of silicon chips. The biocomponents may also be fixed by layered deposition of alternatively charged polymer coatings. Three dimensional lattices such as hydrogel/xerogel are also used to chemically or physically entrap the biocomponents.

APPLICATIONS OF BIOSENSORS

Biosensors have been in demand for rapid and reliable methods for diagnosis of ailments by analysing biological fluids such as blood, serum and urine etc. as well as for self-testing at home for diabetes patients or for other health parameters. Fermentation and bioprocessing industries are using biosensors that can be applied for on-line monitoring in a brewing process. In the food industry the biosensors are used for measurements of constituents of food to predict the shelf-life of food. Most of the methods available in the market are based on enzyme electrodes. Majority of them are one parameter instruments and have been utilized for the measurement of glucose. galactose, uric acid, ethanol, lactate, sucrose and lactose etc. The Glucometer GKM 01 was the first commercial enzyme electrode-based glucose analyser developed in Europe and has been adapted to the quantification of uric acid, lactate and the activity of acetylcholine esterase. The Lipid analysis products are useful for quantitative determination of triglycerides, total cholesterol, low density lipoprotein cholesterol (LDL), high density lipoprotein (HDL) cholesterol, and glucose in capillary whole blood and venous whole blood. Although biosensors have found immense applications in various fields, the use of biosensors in health care monitoring is of utmost importance.

BIOSENSORS FOR HEALTH CARE

Glucose: Detection of glucose has been the most studied analyte in diabetic patients. The level of the glucose can be monitored either in-vivo or in-vitro. The i-STAT 1 analyzer is used in conjunction with i-STAT Cartidges for the Simultaneous quantitative determination of various Analytes(ABG, Electrolytes, Glucose, BUN, Lactate ,Coagulation (PT/INR, ACT),Troponin I, BNP, Chemistries) etc., in whole Blood by Arterial, Venous, Capillary, Cord, MXVN & CPB Sample types. Wide range of glucose testing kits available in the market such as Accu-Chek, OneTouch Verio Flex meter, Dr. Morepen glucose monitor (GlucoOne BG-03) and Apollo Sugar GlucoMe glucometer. There are portable clinical analyser that can measure a range of parameters: sodium, chloride, potassium, glucose, blood urea nitrogen and haematocrit. The sensors are fabricated using thin film microfabrication technology using thin film microfabrication technology on a disposable cartridge or gold-plated test strips.

L-lactate: Lactate measurement is helpful in respiratory insufficiencies, shocks, heart failure, metabolic disorder and monitoring the physical condition. A lactate meter is a portable device that measures the value of the lactate in the whole blood. The determination of lactate value provides clear insights and functionality of the human circulatory system and also the movement of oxygen in the muscles and tissues. Two different technologies have been approached for the development of miniaturized systems. Thin film electrodes have been developed which can be used as either implantable catheter type devices or for in-vivo monitoring in combination with micro dialysis system. For example, Sigma-Aldrich MAK064 Lactate Assay Kit determines lactate concentration by an enzyme assay, which results in a colorimetric product, proportional to the lactate present. Another product is Sensa Core's Lacto spark, which is next-generation, highly advanced ultra-low volume lactate measuring system can measure the lactate value in the blood within 5 seconds. Lacto Spark uses compatible test strips to determine the lactate value, the device requires only 0.5 µl of capillary blood and has a storage capacity of nearly 500 tests.

Urea*:* Urea estimations are of utmost importance in monitoring kidney functions and disorders associated with it. Most of the urea biosensors are based on detection of NH_4^+ or HCO_3^- sensitive electrodes. A blood urea nitrogen (BUN) test is used to determine how well your kidneys are working. It does this by measuring the amount of urea nitrogen in the blood. Urea nitrogen is a waste product that's created in the liver when the body breaks down proteins. Urease hydrolyzes urea to ammonia, the ammonia formed further reacts with a phenolic chromogen and hypochlorite to form a green coloured complex. Intensity of the colour formed is directly proportional to the amount of urea present in the sample. (Gambhir, 2001) had co-immobilized urease and glutamate dehydrogenase on electrochemically prepared polypyrrole/polyvinyl sulphonate for the fabrication of urea biosensor.

Creatinine: It is an analyte used for the determination of renal and muscular dysfunction. Measurement of the creatinine level in human blood and urine reflects the muscular and thyroid functions. The elevated level of creatinine is considered to be as impairment of the kidney. There are numerous methods to measure the concentration of creatinine in blood and urine. An impedimetric device has been used to assay urea and creatinine in serum

using poly(methylvinyl ether)/maleic anhydride modified screen printed electrodes. The other conventional methods such as chromatography, spectroscopy, immune sensor and enzyme-based detections are also used. (Jayasekhar Babu et al., 2022) dissertated use of various nanomaterials chemiluminescence, voltametric, amperometric, conductometric, potentiometric, impedimetric and nano polymer-based creatinine detection methods. Invitrogen™ creatinine urinary detection kit uses The Creatinine Urinary Detection kit is designed to quantitatively measure creatinine present in urine samples. A creatinine standard is provided to generate a standard curve for the assay and all samples should be read off the standard curve. Standards or diluted samples are pipetted into a clear microtiter plate. The color generating reaction is initiated with the Creatinine Detection Reagent, the intensity of the generated color is detected in a microtiter plate reader capable of measuring 490 nm wavelength. The Jaffe reaction used in this kit has been modified to read creatinine levels in urine.

Cholesterol: Abnormal concentrations of cholesterol are related with hypertension, hyperthyroidism, anaemia and coronary artery diseases. Determination of cholesterol based on the inherent specificity of an enzymatic reaction provides the most accurate means for obtaining true blood cholesterol concentration. Off the shelf SD Biosensor Lipido Care is a cholesterol meter and measures a variety of items, including TC, TG, HDL, LDL, LDL/HDL and non-HDL.

DNA biosensors: DNA biosensors have an enormous application in clinical diagnostics for inherited diseases, rapid detection of pathogenic infections, and screening of DNA colonies required in molecular biology. Conventional methods for the analysis of specific gene sequences are based on either direct sequencing or DNA hybridization. Because of its simplicity, most of the traditional techniques in molecular biology are based on hybridization. Several immobilization techniques such as adsorption covalent attachment or immobilization involving avidin-biotin complexation were adopted for a DNA probe to the surface of an electrochemical transducer. The transducer was made from carbon gold, platinum or conducting polymer. In the case of a common sandwich assay the signal generating species is an enzyme such as horseradish peroxidase have been used. Unlike enzyme or antibodies, nucleic acid recognition layers can be readily synthesized and regenerated for multiple uses. DNA biosensors and gene chips have great potential for obtaining sequence-specific information in a faster, simpler and cheaper manner compared to the traditional hybridization(Kavita, V, 2017). Further, increase of interest to DNA based sensors is expected in near future together with a commercial production of these devices and their extensive use.

Remarkable progress has been made in the production of biosensors, transducer technologies and the supplementary technologies, such as microfluidics, wireless data communication, and location/position services that biosensors including wearable biosensors are likely to be healthcare-focused devices (Polat et al., 2022) in times to come.

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Chapter
13

NATURAL PRODUCTS AS POTENT ANTI-CANCER 'COUSIN' OF CHEMOTHERAPEUTIC DRUGS

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ABSTRACT

Accumulating data have provided evidence that most chronic diseases are caused by the dysregulation of multiple genes and signalling pathways. Most of the drugs designed in the pharmaceutical industry are limited to being effective as they are mono-targeted. The treatment of chronic diseases needs to be multigenic and such drugs are not likely to be very effective and exhibit side effects when consumed for long periods. In contrast molecules present in "Mother Nature" are multitargeted and effective over the long term, exhibiting minimal side effects. Thus, it is not too surprising that until very recently, almost 70% of available drugs had their roots in natural resources. Huge efforts have been made over the past few decades to separate unique natural compounds from bacteria, plants, and other living things to evaluate their anticancer characteristics and learn more about how they work. Whether we discuss about chemotherapeutic agents, natural products have also backed up in therapeutics of many other diseases. The history of natural products-based therapies reinforces the exploration and designing of existing concepts, findings, controversies and the hidden challenges loaded with incomparable opportunities against the diseases and their underlying causes.

INTRODUCTION

The diverse chemical nature of products from natural sources makes it a reservoir of bioactive compounds. This nature's gift is beneficial to mankind in many ways. Among the radiating benefits of natural products, its potential for therapeutics needs more intensive exploitation. Natural products through many studies have represented their strong candidature to be used as clinical molecules[1, 2]. The biological complex in natural products can act as a double-edged sword by activating or synergizing our immune response on one side while attenuating the inflammation-mediated immune response on the other side[3]. To meet the rising demand for new drugs which have the potential for the treatment of many diseases, natural products have gained attention constantly among research settings worldwide. The present alternative perspective can minimize the development of resistance, reducing the toxicity and reoccurrence of diseases observed in humans from diverse fields of diseases.

Among the most complex diseases, cancer is a major public health burden worldwide. The annually diagnosed cases and the mortality rate related are rising per year. The

molecular heterogeneity of the tumour microenvironment and the underlying drivers are halting the treatment procedure[4, 5]. For more than a half-century, natural products with remarkable chemical diversity have been widely studied for their anticancer potential [6-10]. Cancer chemotherapy with natural products is an emerging platform of research that can be helpful to prevent, delay or cure cancer. It is still largely unclear how the natural products and their interaction with biological molecules confer the therapeutic dynamics. The rising malignancy raises new challenging objectives for research to discover novel molecules of quality treatment approaches for cancer. Natural products as the modern modalities can reduce side effects and drug resistance associated with the chemotherapeutic approach to cancer treatment.

Cancer and Chemoresistance

Cancer explains a wide array of disease pathologies that arises from cellular growth in an uncontrolled manner. It is one of the trickiest diseases to treat because of its extreme diversity. The interactions between the physical and chemical properties of cancer cells and their surrounding tissues establish interdependent reciprocity which is a challenge for prognostication and treatment [11]. This elevates opportunities in the field of cancer research and its clinical management for exploring avenues and gaining insight toward solving the riddle of potential treatment options. Chemotherapy is an aggressive form of chemical drug therapy meant to destroy cancer cells. It targets directly the growth and proliferation preventing metastasis and invasion into neighbouring cells [12]. It interferes in DNA, RNA, or protein synthesis or the functionality of the target cell leading finally to apoptosis (cell death) [13-15]. Some drugs interrupt the chemical processes involved in cell division. It directly targets the cells that are in the process of splitting. As chemotherapeutic drugs are designed to kill cells that divide quickly, they also target other cells which do similar division. Another notable challenge which surfaced during the last decade is resistance to the already-in-use chemotherapeutic drugs [16, 17]. Cancer cells use a variety of strategies to limit anticancer drug therapeutic effects, resulting in chemotherapy failure. Cancer cells may be mutated & develop pathways that are independent of those blocked by cytotoxic drugs [18]. Drug efflux prevents the optimal reach of drug molecules to their respected target site thus preventing cancer cell death [19]. During the differentiation, deviation occurs in Epithelial-Mesenchymal transition (EMT) which releases survivor signals in cancer cells against drugs limiting the apoptotic pathway [20]. Gene amplification may lead to the overproduction of proteins that are blocked by anticancer drugs or the production of other proteins which mimic the target site avoiding the drug action [18]. Hyphenated DNA damage repair activity is another mechanism which enables cancer cells to revert the damage done by chemotherapeutic drugs and thus help them become resistant to the therapies [18]. The change in molecular signatures during the progression of cancer through several ways brings therapies on a platform with drawbacks in the treatment pipeline. Therefore, effective treatment regimens need to be developed and brought to the clinical setting against the prevalent drug resistance in cancer patients.

Natural products: Alternative rescuers

Natural products encompass any substance produced by a living organism. The use of secondary metabolites from plants, microorganisms, and other natural sources has led to a

more than doubling of life expectancy, making natural products a resounding success in contemporary society [11]. Earlier synthetic compounds were primarily used in clinical settings due to their impressive results. With time issues related to toxicity and resistance started to accumulate making a loophole in the treatment pipeline. Chemists were successful in isolating pure natural products like quinine, morphine, codeine, and other chemicals with therapeutic properties in the late 19th century [12]. Pure compounds enabled accurate dosing to achieve levels within the pharmacological window and reproduce clinical effects. During the 20th and the 21st centuries, natural products or modified natural products managed to enter the drug discovery pipeline used for the treatment of cancer [12]. Since more than 50 years ago, a great deal of research has been done on the anticancer potential of natural compounds, which are now used in clinical settings, and new therapeutic prospects are under development [13]. The combined efforts of research platforms have gained novel compounds, but there are still obstacles to overcome [14-16]. We may be at a turning point where we need to review the approaches to comprehend nature's products and investigate their therapeutic efficacy due to the striking changes in the landscape of cancer therapy. Natural products are readily available, inexpensive, and less toxic sources of chemotherapeutic agents. Furthermore, they have several modes of action to block various targets involved in drug resistance development. Various drug resistance indicators are responsive to natural products. P-glycoprotein and breast cancer resistance protein, for example, can be targeted by a wide range of natural compounds. [17]. A few natural compounds like phenolic acids, flavonoids, stilbenes, coumarins, tannins; alkaloids, nitrogen compounds; organosulfates: isothanates and indoles, allyl sulfates affect DNA damage repair mechanism in cancer cells and re-sensitize it to chemotherapeutic agents [18-21]. The competitive ability of cancer cells brings into consideration the use of natural products for better treatment and to overcome the resistance developed by chemotherapeutic agents. It is now possible to overcome obstacles in boosting the efficiency of drug development, revealing the direct targets of natural products for multifaceted pharmacological effects with the help of new technologies.

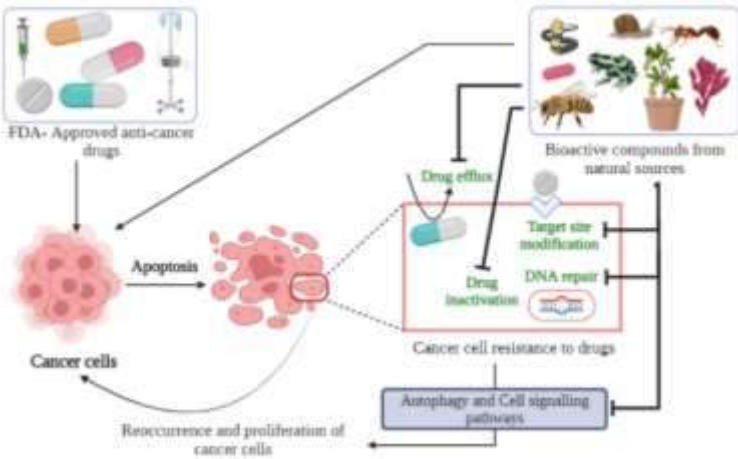

Fig. : Illustration Showing Effect of Natural Products on Chemoresistant Cancer Cells.

Phytochemicals with Anticancer Properties

Plants, either whole or in extract, have been utilised as remedies in Asian countries and Greece since antiquity, and also an astounding number of modern drugs have been developed from them[11]. Accumulating evidence over the past several decades has shown that plants contain natural bioactive products with nutritional values and promising therapeutic properties.

Based on the evidence provided on the complex synergistic interaction of several phytochemicals with anticancer potential, various herbal formulations have been developed to attack malignant cells while inflicting no harm to the body's normal cells. Various phytochemicals having anticancer activity have been classified into five primary phytoconstituents: alkaloids, polyphenols, saponins, tannins, and terpenoids. Using chemicals derived from plants, either alone or in combination, can help combat the side effects of the anticancer drugs that are currently on the market platforms. Intense research into the plant kingdom might offer fresh ideas for the quick creation of brand-new anticancer drugs.

For anticarcinogenic activity whole extract of plants like Withania spp., Berberis spp., Syzygium spp., Aloe spp., Artemisia spp., Coptis spp., Fagonia spp., Curcuma spp., Garcinia spp., Morus spp., Allium spp., Garcinia spp., Drosera spp., Cucurbita spp., and many more are being added each day [12-22]. Also, purified compounds from many plants have been investigated for inhibiting oncogenic pathways. Examples, curcumin, alpha mangostin, plumbagin, Epigallochatechin, resveratrol, Withaferin A, Piperlongumine, lycopene, saponins, isoflavones, cucurbitacins, phytosterols and other polyphenolic compounds have been reported for their anticancerous activity by participating in signalling pathways which are involved in growth, cell differentiation, cells elongation, receptor expression and activation of tumor suppressor genes [12, 13, 19, 22-27]

Anticancer Drugs from Marine Flora

Over 90% of the biomass in the ocean is made up of marine flora, which includes bacteria, actinobacteria, cyanobacteria, fungi, microalgae, seaweed, mangroves, and other halophytes. Due to its distinct biochemical composition marine flora can provide ample opportunities for the discovery of novel medications. They provide considerable potential for the identification of novel anticancer medicines since they are taxonomically varied, highly productive, and physiologically active. Since ancient times, marine floras have been used for therapeutic purposes in India, China, the Near East and Europe. Seaweeds have long been consumed by the inhabitants of China and Japan. Seaweed dietary fibres have a wide range of activities, including antioxidant, antimutagenic, anticoagulant, and anticancer properties [28].

Secondary metabolites produced by marine bacteria have resulted in novel anti-inflammatory medicines (such as pseudopterosins, topsentins, scytonemin, and manoalide), and anticancer agents (such as bryostatins, discodermolide, eleutherobin, and sarcodictyin), and antibiotics (e.g., marinone) [29, 30]. They stimulate and modulate the mucosal immune system by reducing proinflammatory cytokine production via NF-B pathways, increasing the production of anti-inflammatory cytokines like IL-10 and host defence peptides like -

defensin 2, enhancing IgA defences and influencing dendritic cell maturation, and modulating cell proliferation and apoptosis via cell responses to short-chain fatty acids.

Anticancer Drugs from Microorganisms

Microorganisms are a rich source of biologically active small molecules which have been developed into a number of chemotherapeutic drugs. The introduction of these molecules activates the immune system of the body generating a cascade of immune mechanisms which raises the demand for anti-inflammatory cells. This is a method in which microbes indirectly lead to cancer regression. Bacteria are used as vectors for carrying chemotherapeutic biologics thus reducing the toxicity issues and maximizing the effects against cancerous cells. Bacterial toxins from **Clostridium novyi** have been found to disrupt the cancer cells as it grows in anaerobic conditions, which is the optimal condition for the growth of bacteria [31]. **Neospora caninum**, **Bifidobacterium longum**, and BCG vaccine have also shown potential as anticancerous agents [32-34]. In the 19th century, auxotrophic **Salmonella a**nd **Listeria monocytogenes** were used as a carrier for antitumor agents [35]. In a study**, Escherichia coli-induced** infection has been successful in increased expression of major histocompatibility complex I (MHC I) on cancerous cells and high production of CD8+ killer T-cells which leads to disruption of cancer cells [36]. Microbes can also compete with cancer cells for available nutrients and reduce the optimum levels which in result devoid the cancer cells of the supply of metabolic requisites needed for their rapid multiplication. Some bacteria with the help of biofilm formation result in regression of cancer cells by surrounding them and limiting their growth space.

Anticancer Drugs from Animal compounds

The growing field of products from animal sources has been used to define their physiological function such as antioxidative, immunomodulatory, cholesterol-lowering activities and anti-cancer effects [37-39]. The bioactives present in animal sources could specifically hit the target cancer cells without any toxicity. They usually traverse or disrupt the cell membrane of cancerous cells and lead to apoptosis. Although very less studies have documented their development into a potential anti-cancerous drug. It's interesting to note that a variety of animal toxins have potent anticancer properties due to the presence of a cocktail of bioactive compounds which target different physiological processes. These include toxins extracted from the venom of snakes, bees, and scorpions that affect the growth, migration, invasion, apoptosis, and neovascularization of cancer cells [40-42] .

Certain therapeutic molecules from animal toxins include venom from reptiles (Captopril, Exenatide)[43-46] and Molluscs (Ziconotide) [47]. In reptiles extracted and purified antimicrobial peptides such as KT-2, RP-9, anti-tumor peptides T1 and T2, RT-2, Cathelicidin-BF (BF-30) and crotamine also have potential for anti-cancer activity [48-51]. Also, screening of natural products from mammal sources is very limited. Studies have described the inhibition of Angiotensin-converting enzyme (ACE) and the proliferation of cancer cells by bovine peptides such as Caseinophosphopeptides (CPPs) and lactoferrin [52, 53]. Amphibians have also been successful in finding the attention of research groups across the globe. The secretions from amphibian skin and parotid glands have been successful in killing tumor cells thus potentiating their anti-cancerous activity. For example- Aurein,

Dermaseptin, Phylloseptin, XT-7, Alyteserin-2a, and Ascaphian-8, isolated from amphibians have been cytotoxic to tumor cells [54-58].

Toxin from insects contains strong enzymes, proteins and peptides which have been studied to develop new anti-cancerous drugs. Latarcin 2a, Melittin, and Mastoparan have been *in-vitro* tested against different cancer cells but no records have been reported to date for their selective activity against cancer and non-cancer cells [59-63].

CONCLUSION

Natural products are already proven to be potent anti-cancer compounds. Natural product research is a vigorous tool of research to discover novel biologically active compounds with unique mechanisms of action. The regimen of translational research needs to be intensified for the establishment of a formulation which can be used in clinical settings. For safer treatment of cancer, drugs developed from natural products can be a new and effective option for future therapeutics. The complex composition of natural products and even the purified bioactive molecules can stem from the reduction of drug-related toxicity and even reduce the dose by using a combinatorial approach which can reinforce the clinical success in cancer therapeutics. This approach also spurs the search for new and improved anticancer drugs.

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Chapter
14

ECO-FRIENDLY AGRICULTURE: A DEMAND OF FUTURE

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ABSTRACT

In the world up to 811 million people are going hungry and more than 2 billion suffer from the malnutrition. Food security relates to food availability, access and utilization when the person have always has adequate and access to enough safe and nutritious food to maintain and active the healthy life they consider the food secure. A growing population means more mouths for feed using different indicator access adequate food nearly 2.37 billion people or 30% global population lacked access to adequate food in 2020 and it rises 320 million in one year. The world population rich about eight billion but cultivated land reduced so it is challenge for us to produce the more food using plants and it's having major role in food security issue. The Food and Agriculture Organization (FAO) reported that more than ninety percentage food consumed by human cultivated by just thirty plants species.

The climate change is increasing warm it become a challenge to farmer it reduce water and higher pest survival in winter. There is 30,000 species of weeds and 3,000 species of fungi and 10,000 species of plant eating insects occur on earth around to us so the need of protection of crops is necessary. For the protection of crop farmer used specific insecticides which has killed the quickly particular insects. The natural selection of resistant insects, plant and other organisms, the necessities increase use of more powerful control measures. In the eco-friendly agriculture the organic pest control technique encourage predatory beneficial insect and micro organism, careful crop selection and crop rotation. This eco-friendly technique also provides other benefits soil protection, fertilization, pollination, water conservation etc.

An agriculture based on the chemical farming is rapidly depleting the natural resources particularly fresh water, soil, air and fossil fuels. In chemical farming there is also use of large quantities of pesticides, fertilizer for the crop development. In this chemical farming there is also water wastage through high volume irrigation, heavy use of petrochemicals for farm machinery and long distance transport. But in the eco-friendly farming curtails all these. It reduces food contamination and increased food quality. The conventional agricultural practices based on the chemical fertilizer causing greater contamination of food in absence certification and in the wake of unhygienic handling. It also change fertile land into the unfertile due to the over excess use.

Keywords- Food security, Organic pest, Insecticides, chemical farming and eco-friendly agriculture etc.

INTRODUCTION

The idea behind the creation of pesticides was one that hasn't disappeared. The farmer has still wanted to protect their crops from pests without adding. One of the ways pesticides met this need was by using chemicals to target pests, but that left farms around the world with many different, environmentally dangerous problems. The pesticides have been release the chemicals into the environment where they're sprayed. The harmless bugs are killed when they are caught in the spray. Also other animals are hurt when they drink chemical runoff after fields drain into local rivers. The soil is important key farming element it has damaged by the chemical pesticides. The pesticides are sprayed, in the crop then it can alter the soil's pH levels. It make more difficult for crops to grow at next time. The soil structure is weakened; it erodes more easily and gets washed away by heavy rains.

Today in the world there are more than one thousands pesticides used to ensure food is not damaged or destroyed by the pests. The each pesticide has shows the different properties and toxicological effects. In which many are older, cheaper pesticides, like dichlorodiphenyltrichloroethane (DDT) and lindane, has remain for years in soil and water. This chemical pesticide has been banned by countries who signed the 2001 Stockholm Convention an international treaty. It has aims to eliminate the production and use of persistent organic pollutants. The food safety, nutrition and food security are inextricably linked. The food contamination shows that an estimated 600 million almost 1 in 10 people in the world has fall ill after eating contaminated food and 420 000 die every year, resulting in the loss of 33 million healthy life years. In which the children under five years of age carry 40% of the food borne disease burden, with 125 000 deaths every year. The food borne diseases impede socioeconomic development by straining health care systems and harming national economies, tourism and trade. The unsafe food containing harmful bacteria, viruses, parasites or chemical substances causes more than 200 diseases, ranging from diarrhea to cancers. It also creates a vicious cycle of disease and malnutrition, particularly affecting infants, young children, elderly and the sick. The good collaboration between governments, producers and consumers is needed to help ensure food safety and stronger food systems.

In the nature the toxins like mycotoxins, marine biotoxins, cyanogenic glycosides and toxins occurring in poisonous mushrooms. The staple foods like corn or cereals can contain high levels of mycotoxins, such as aflatoxin and ochratoxin, produced by mould on grain. A long term exposure can affect the immune system and normal development, or cause cancer like serious disease. In nature some persistent organic pollutants are compounds that accumulate in the environment and human body. It is known examples are dioxins and polychlorinated biphenyls, which are unwanted by-products of industrial processes and waste incineration. They are found worldwide in the environment and accumulate in animal food chains. The dioxins are highly toxic and can cause reproductive and developmental problems, damage the immune system, interfere with hormones and cause cancer. The heavy metal like lead, cadmium and mercury cause neurological effect and also it damage the kidney. The Contamination by heavy metal in food occurs mainly through pollution of water and soil.

The other chemical hazards in food can include radioactive nucleotides that discharged into the environment from industries and from civil or military nuclear operations, food allergens, residues of drugs and other contaminants incorporated in the food during the process. The eco-friendly farming is a farming method that only uses natural pest control and biological fertilizers to grow crops without using chemicals or pesticides. This method optimizes the energy and nutrient cycles in the agriculture ecosystem. It shows that fertilization increases the organic carbon in the soil; leading to the huge release of carbon dioxide into the atmosphere. The eco-friendly agriculture practices will help farmers to reduce the emission of nitrous oxide and methane from the soil. This method shows positively impacts on water, the surrounding wildlife, land, the atmosphere, and farmers in the long run. Organic farming refers to cultivating crops without the use of harmful chemicals, such as synthetic pesticides. These toxic chemicals make their way into our air, ground and water when they are sprayed, run off with field water and not discarded properly.

OBJECTIVES

- To study the role of agriculture in food production
- To study the effect of population on food arability in world
- To focus on new trends of organic farming and eco-friendly farming
- To aware young generation about food crisis problem

ANALYSIS AND RESULT-

The United Nation's Sustainable development Goal second is for hunger it archive food security and improve nutrition. It also promotes to the sustainable agriculture the plants gives macro nutrients like carbohydrates, lipids and proteins to us in diet. The protein also gets from animal products but many people depend upon plants. The pulses also rich in proteins in India highly vegetarian population occur it depend upon plant products. In India 500 million people depend on non-animal protein source so that the increase in production of pulses is very important. The plant based protein available easily in environment in lowest cost. Sustainable farming is farming in sustainable ways meeting society's present food needs, without compromising the ability for current or future generations to meet their needs. As per the Global Hunger Index, 2018, India was ranked 103rd out of 119 qualifying countries. India needs to adopt a policy that brings together diverse issues such as inequality, food diversity, indigenous rights and environmental justice to ensure sustainable food security. The basic goals of sustainable agriculture are environmental health, economic profitability, and social and economic equity. The eco-friendly agriculture allows us to produce and enjoy healthy foods without compromising the ability of future generations to do the same. The key to eco-friendly agriculture is finding the right balance between the need for food production and the preservation of environmental ecosystems.

The eco-friendly agriculture has helps to replenish the land as well as other natural resources such as water and air. The adoption of eco-friendly practices, farmers will reduce their reliance on non-renewable energy, reduce chemical use and save scarce resources. This

replenishment ensures that these natural resources will be able to sustain life for future generations considering the rising population and demand for food. The eco-friendly agriculture has avoids hazardous pesticides and fertilizers. As a result, the farmers are able to produce fruits, vegetables and other crops that are safer for consumers, workers, and surrounding communities. All the careful and proper management of livestock waste, sustainable farmers can protect humans from exposure to pathogens, toxins, and other hazardous pollutants. In the eco-friendly agriculture any waste a farm produces remains inside the farm's ecosystem. In this way, the waste cannot cause pollution and it help to growing the crops playing role as a fertilizer. A continues use of fertilizer and pesticides to produce adequate food has been a serious threat to soil erosion. Therefore, numerous practices have been developed to keep soil in place, which includes reducing or eliminating tillage, managing irrigation to reduce runoff, and keeping the soil covered with plants or mulch. The use of organic fertilizer and pesticide also keep soil healthy and increase its fertility. The smarter farming and moving food from farm-to-fork in a more efficient manner have helped everyone involved with the agriculture industry. The eco-friendly farms produce a wide variety of plants and animals, resulting in biodiversity. At during crop rotation, plants are seasonally rotated, and this results in soil enrichment, prevention of diseases, and pest outbreaks. The use of solar, hydro-power or wind-farms is ecology friendly. The farmers can use solar panels to store solar energy and use it for electrical fencing and running of pumps and heaters. In the integrated pest management is a combination of pest control techniques for identifying and observing pests in the initial stages. The one also needs to realize that not all pests are harmful, and therefore it makes more sense to let them co-exist with the crop than spend money eliminating them. The eco-friendly agriculture practices examples are as follows.

The Hydroponics and Aquaponics: It has the innovative farming technique, in which the plants grow without soil and get nourished through specialized nutrients that are added in to the water. In hydroponic systems, crops are grown with the roots directly in a mineral solution or with the roots in an inert medium like gravel. The Aquaponics combines the raising of aquatic animals like fish with the growing of hydroponic crops. The water which contains nutrients resulted from the mineralization of fish waste feeds the roots of plants and vegetables which can grow in various mediums. The water is purified by the plants and returns to the hydroponics section of the system. It is best way of eco-friendly farming.

The crop rotation: It is a tried and tested method used since ancient farming practices proven to keep the soil healthy and nutritious. The crop rotation has a logical explanation to it the crops are picked in a pattern so that the crops planted this season replenish the nutrients and salts from the soil that were absorbed by the previous crop cycle. For example, row crops are planted after grains to balance the used nutrients. It is also best way of eco-friendly farming, it avoid the use of chemical fertilizers.

The organic farming: It is incredibly popular because it doesn't use too many different farming approaches than conventional farming. It is also a downside as this means it still employs damaging farming techniques like tilling. Tilling is common practice for traditional and organic farms alike. It's when soil is prepared for agriculture by digging, stirring and overturning it, like when using a hoe or rake. But it damages the soil by destroying its

natural structure, which makes soil erosion and surface runoff occur faster. Too much tillage even causes the soil to lose nutrients and organic matter. In sum, while organic farming may limit the earth's exposure to harmful chemicals, it still subjects the land to other harmful practices and helps to practice eco-friendly farming. Today the organic farming currently covers about 2.8 million hectors area or two per cent of India's net sown area of 140 hectors area. The natural farming is the fastest growing sustainable agricultural practice in India and has been adopted by around 800,000 farmers. The Integrated Pest Management (IPM) has achieved a coverage area of five hectors area after decades of sustained promotion.

The agro-forestry: It is a farming method which involves growing shrubs and trees among other plants and vegetables. It combines forestry and agricultural practices to guarantee a sustainable and highly productive approach to land use. The system mimics forest ecosystems found in nature and it's designed to comprise multiple layers of food forests. It includes perennial plants such as fruit trees, perennial herbs, mushrooms, and other vegetables on the ground level and underground root vegetables. Compared to traditional farming systems, agro-forestry can double crop yields and significantly decreases the need for chemical fertilizers or pesticides.

The sustainable farming involves the use of alternative energy sources such as hydropower, solar power or wind farms which are eco-friendly. Solar panels can be used to run pumping and heating systems. Also, hydroelectric power sourced from river water can be used for various farming machinery. Farmers can compare energy consumption rates by using an online energy compare site to identify the best suitable power sources.

Poly-culture Farming: The farming has involves growing multiple crop species in one area. These species often complement each other, and greater diversity of products can be produced at one plot while fully utilizing available resources. The high biodiversity makes the system more resilient to weather fluctuations, promotes a balanced diet and applies natural mechanisms for preservation of soil fertility.

Permaculture: It is a food production system with intention, design, and smart farming to reduce waste of resources and create increased production efficiency. The focus is on the use of perennial crops such as fruit trees, nut trees, and shrubs that all function together in a designed system that mimics how plants in a natural ecosystem would function.

In agriculture, sustainable farming is becoming the need of the hour the world over. Efforts for sustainable farming are on the right track in India, but at a slower pace. So there is a need of policy intervention to give boost to sustainable farming practices. Eco-farming combines modern science and innovation with respect for nature and biodiversity. It ensures healthy farming and healthy food. It protects the soil, the water and the climate. It does not contaminate the environment with chemical inputs or use genetically engineered crops. And it places people and farmers consumers and producers, rather than the corporations who control our food now at its very heart. It is a vision of sustainability and food sovereignty in which food is grown with health and safety first and where control over food and farming rests with local communities, rather than transnational corporations.

The healthy soil is important to a good crop for that purpose use old techniques like tilling the land, plowing etc. still work wonders. The Manure, fertilizers, cover crops etc. also help improve soil quality. The crop rotations prevent the occurrence of diseases in crops, as per studies conducted. In nature there is some natural pest eliminators like bats, birds, insects etc. work as natural pest eliminators. Farmers build a shelter to keep these eliminators close. Ladybugs, beetles, green lacewing larvae, and fly parasites all feed on pests, including aphids, mites and pest flies.

The principles of eco-farming are as follows-

- **Biodiversity:** For the promoting diversity in crops, instead of monocultures like corn and soy, is essential to protecting nature.
- **Smarter food production and yields:** The eco-agriculture can create higher yields to help feed the world.
- **Food sovereignty:** The producers and consumers, not corporations, it should control the food chain and determine how food is produced.
- **Food Resilience:** The diverse and resilient agriculture, not monoculture crops, is the best way to protect communities from shocks from climate and food prices.
- **Rewarding rural livelihoods:** The eco-agriculture is instrumental in rural development, food security and fighting poverty.
- **Sustainable soil:** The soil fertility can improve using eco-farming methods and refraining from chemical fertilizers and inputs.
- **Ecological pest protection:** The farmers can control pest damage and weeds effectively through natural means instead of chemical pesticides.

The eco-farming agriculture is a holistic production management system which promotes and enhances agro-ecosystem health, including biodiversity, biological cycles, and soil biological activity. It emphasizes, the use of management practices in preference to the use of off farm inputs, taking into account that regional conditions require locally adapted systems. The organic farming methods combine scientific knowledge and modern technology with traditional farming practices based on thousands of years of agriculture. The organic farming relies heavily on the natural break down of organic matter, using techniques like green manure and composting, to maintain nutrients taken from the soil by the previous crops. The organic farming uses a variety of methods to improve soil fertility, including crop rotation, cover cropping, and application of mulching. These benefits are both complementary and cumulative in overall effect on farm health. However, there are various major advantages of organic farming:-

It increases productivity at lower cost there is misconception among the people that organic farming leads to loss in productivity. It is also proven that after a short period of drop in yields, organic farming is more productive than chemical farming. The environmental friendly Conventional agriculture based on chemical farming is rapidly depleting natural resources particularly fresh water, soil, air and fossil fuels. In chemical

farming there is also use of large quantities of pesticides, fertilizer etc. and there is also water wastage through high volume irrigation, heavy use of petrochemicals for farm machinery and long distance transport etc. but organic farming curtails all these. It reduces food contamination and increased food quality Conventional agricultural practices based on chemical fertilizer causing greater contamination of food in absence certification and in the wake of unhygienic handling.In the control of pesticides there is some eco-friendly methods are used in agriculture like as follows.

Microbial pesticides- It has either indigenous or genetically engineered microbes, it consists bacteria fungi, virus and protozoa it protect plants from the attack of pests. The Bastus thuringensis is a soil bacterium that produces natural toxin known as Bt-toxin which binds to the gut of larval pests (coleopteran, lepidoptera) black flies, mosquitoes, thereby killing them. Spores of this bacterial strain are sprayed over crops, which secrete delta endotoxin that is highly lethal to the pests. It is very specific to pest of cabbage, potatoes and other crops. Biocides have also been developed from Bacillus sphaericus that are effective against beetles. A pseudomonas bacterium is also endowed with pesticidal properties. Recently insecticides prepared from Bacillus thuringiensis (type H14) and B. sphaericus are available in powdered form and are commercially available which are effective against 90 species of insects, Protozoans that are used for this purpose in agriculture belong to groups Mattesia and Lambronella. The genes of Bacillus thuringiensis transferred to Pseudomonas sp. or other indigenous soil bacteria make them a genetically modified biopesticide. It is highly effective against various pests. The genetically engineered insect resistant plants produced from genes transferred from Baculovirus, are quite effective against specific fungus and nematodes. Viral pesticides are entomopathogenic virus (Baculoviridae) extensively used as they are ecofriendly. Reoviridae is also an effective biopesticide that selectively kills pests, but has no adverse effects on pollinating insects, mammals other useful animals.

Biopesticide- Bio-pesticides or biocides are chemical substances, natural materials or, microorganism, or their derivatives and minerals that selectivity kill target pests(3), bio-pesticides are species-specific toxins that target only few species, but otherwise remain harmless to animals like birds, mammals including human and non-target useful insects. The bio-herbicides on the other hand kills only selective and harmful weeds. Being biological product, these substances are highly degradable, less toxic and hence, do not contribute to environmental hazards. The bio-pesticides are widely used in organic farming, as they leave no residues and decompose easily in nature. They are required in small amounts and are easy to apply in crop fields forming an integral part of the integrated pest management programme. The bio-pesticides are species specific toxins and target only few specific pests, but otherwise remain harmless to other animals like birds, mammals including humans and non-target useful insects. The bio-herbicides only kill selective weeds. Neem, mahua, tobacco are common plants with pesticidal properties. Asparagus is effective against nematodes, vegetable oil against brucid, rice and maize weevil, and Bougainvillea has antiviral activity. Being natural biological products, these substances are easily degradable and less toxic hence do not contribute to environmental hazards. Overall

they prevent biodiversity loss, help in sustainable soil management, and protect biological crops, animal and public health.

Effect of pesticides- The pesticides are wide range of chemicals that prevent, destroy or control population of pests. These are classified according to the nature of their target or by their chemical structure and physical state. These occur as inorganic, synthetic, or as bio-pesticides. The various groups of insecticides include organochlorines (DDT), organophosphates, and carbamates (thiocarbamate and dithiocarbamates). Synthetic, persistent pesticides are extremely harmful, and tend to accumulate in the biota inflicting health damage. The damage of the central nervous system has leading to paralysis. The Organophosphates parathion, malathion, Organophosphate and carbamates inhibit the acetylcholinesterase, affecting the function dazinon, folidol are not accumulated by the organisms, but these inhibit cholinesterase activity. The erbicides are lethal to weeds and applied in water bodies to control algal population and other aquatic plants. Phenoxy compounds selectively kill broadleaved weeds. Phenoxy and benzoic acid destroy conductive tissues of plants. The triazines interfere with photosynthesis, destroying floral diversity. The toxicity of these harmful chemicals not only restricts unwanted aquatic weeds, but is extended to fish and other aquatic organisms as well. These are acutely dangerous to organisms including man. Insecticides may harm the useful animals in two ways. Insectivorous birds or other animals are directly poisoned from the affected insects they consume or eradification of insect population reduce the availability of food for these animals, which eventually perish. Thousands of animals including Britain's grey partridge have been affected. The application of herbicides eventually leads to disruption of the entire aquatic food chain.

So the in the future for saving of soil fertility and good, healthy crops production the need of eco-friendly agriculture has very demand, It has help to protect the nature and also protect the health of human. The excess use of chemical fertilizer and pesticides had destroyed the link of food chains also decrease the soil fertility and production of crops. In the human due to chemicals many serious diseases also occur. To the avoid like this different problem of nature the eco-friendly farming is necessary.

CONCLUSION

In the world about two million tons of pesticides are utilized annually, where the China is the major contributing country, followed by the USA and Argentina, which is increasing rapidly. In the year 2020, the global pesticide usage has been estimated to increase up to 3.5 million tones. The Food and Agriculture Organizations reports shows the 4.1 million tones of substances applied globally in 2015, that is, 35% greater than in 2001. The projected 9.77 billion people in 2050 and the expected land conversion into arable production, the global pesticide applications are likely to increase. The pesticides are substances or mixtures of substances that are mainly used in agriculture or in public health protection programs in order to protect plants from pests, weeds or diseases, and humans from vector-borne diseases, such as malaria, dengue fever, and schistosomiasis. The insecticides, fungicides, herbicides, rodenticides, and plant growth regulators are typical examples residues of pesticides can be found in a great variety of everyday foods and beverages, including for

instance cooked meals, water, wine, fruit juices, refreshments, and animal feeds. The washing and peeling cannot completely remove the residues. The industrialization of agriculture has brought a series of problems including economic, social, and environmental impacts that local populations cannot manage.

The overproduction of food, export-oriented monocultures, the demand for cheap labor, and the other characteristics of industrialization have clearly failed to solve the problems of hunger and malnutrition. On the contrary, inequitable food distribution, overexploitation of land and water sources, the overuse of agrochemicals, and the degradation of the natural environment are some of the results of the dominant agricultural .It estimates in the1991 suggest that about 240 million hector lands is chemically degraded. The land due to nutrient depletion about 136 million hector has affected, the Stalinization damaged about 77 million hector lands, and the acidification degraded about six million hector lands. In another way about 11million hector lands is affected by soil pollution. The agricultural mismanagement 58 % and deforestation 28 % are the main causes of chemical degradation of soil. However, excessive use of chemical fertilizers has led to several issues such as serious soil degradation, nitrogen leaching, soil compaction, reduction in soil organic matter, and loss of soil carbon. In addition, the efficacy of chemical fertilizers on crop yield has been decreasing over time. All this problem are decreases by the adoption of eco-friendly method in the agriculture it is demand of the future world for the good and healthy environment.

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Chapter
15

MITIGATION OF MILD STEEL CORROSION IN ACID MEDIUM BY GREEN INHIBITOR

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INTRODUCTION

"Corrosion can be defined as the deprivation of a material due to a reaction with its environment". Degradation infers weakening of physical properties of the material. This can be a weakening of the material owing to a damage of cross-sectional area, it can be the devastating of a metal because of hydrogen embrittlement [1]. Materials can be polymers, metallic elements, ceramic ware or mechanical mixtures of two or more materials with various assets. Mostly metals undergoing corrosion are electrochemical in nature [2]. Fumes of acids such as hydrochloric acid and sulphuric acid and dust of caustic soda also accelerate corrosion [3].

Some of the familiar methods to control corrosion are selection of material, protective coatings, inhibitors, design, etc.. Inhibitors are the substances when added in minor quantities inhibit the rate of corrosion. In repetition, inhibition of corrosion studies have become concerned towards safety contemplation and towards human health [4, 5]. In modern era, the researchers have been fixated on the applying environmentally friendly compounds like extracts of plants, deceased nontoxic medicines, etc. which comprises many organic compounds [6, 7]. The mechanism of the corrosion inhibition process lies behind the principle of adsorption [8].

It has been observed that leaves, barks, stem of easily and naturally available trees were found to possess corrosion inhibition property. Hence the present work was carried out to examine the IE of ***Barleria cristata*** as a green corrosion inhibitor in controlling corrosion of mild steel (MS) in acid medium.

EXPERIMENTAL METHODS

In South India, it is known to be as December Flower as it blooms in December and is normally strung into garlands of flower.

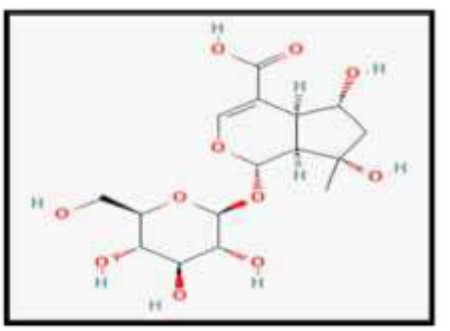
Phytochemical Constituents of *Barleria cristata* [9]

S. No.	Phytochemical constituents	Methanol Extract	Ethanol Extract	Aqueous Extract
1	Alkaloid	+	+++	-
2	Carbohydrates	+	++	-
3	Flavanoids	+	+++	+
4	Saponin	+	++	+
5	Tannins	+	+	+
6	Steroids	+	+	+
7	Phenolic Compounds	+	++	+
8	Amino Acids	-	-	-
9	Proteins	-	-	-

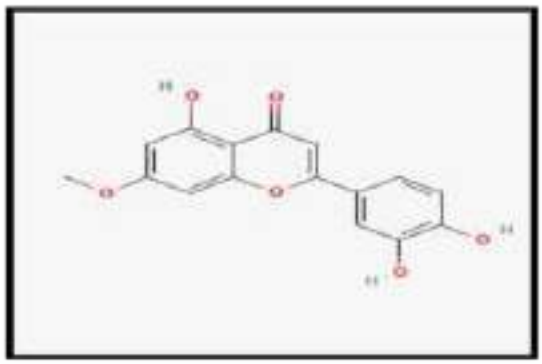
+++ = High; ++ =Moderate; + =Present; -=Absent

Active components present in B*arleria cristata*

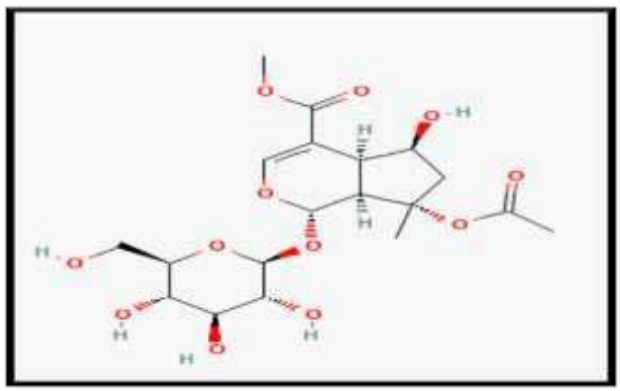
Shanshiside



7-Methoxy Luteolin



Barlerin



Medicinal Uses

Several extracts examined from B. cristata leaves, bark, seed, etc have shown pharmacological activity in both in-vivo and vitro studies. Several preclinical studies have been focused on the anti-bacterial, anti-inflammatory, antidiabetic and antioxidant activity [10-14].

Mild steel composition

MS specimens (0.0260%-S, 0.060%-P, 0.41% -Mn, 0.100%-C and remaining percentage is iron) of dimensions 1x4x0.1 cm were polished and was degreased with acetone and carried out for mass loss method.

Acid

H_2SO_4 used of G.R. Grade (MERCK CHEMICALS)

Weight Loss Method

Loss in weight was performed in H_2SO_4 medium.

IE (%) = $\frac{Wi-Wo}{Wo} \times 100$

W_o = Loss of weight in blank

W_i = Loss of weight in the presence of different concentrations of inhibitor

Potentiodynamic Polarization Studies

Polarization experiment were done from 800mV to 250mV at a constant identical to mass loss measurements and carried out using MS specimens in 1.0 N H_2SO_4, with and without the addition of the inhibitor. Current in mA and potential in mV were plotted. From the graph the Tafel slope (in mV/decade) and the corrosion potential (in mV/decade) were calculated.

Impedance measurements

AC impedance studies was carried out using the same polarization instrument. Both real and imaginary part were examined at various frequencies in ohms.

RESULT AND DISCUSSION

Mass loss studies

Table 1 gives the IE of various concentrations of Barleria cristata in 1.0 N H2SO4 medium. The inhibition process is dependent on nature and means of adsorption on the MS surface [15].

Table 1: Mass Loss Studies Parameters

Inhibitor Concentration (%)	Corrosion Rate, (g cm^{-2} hr^{-1})	IE (%)
H_2SO_4	-	-
0.2	0.00500	83.25
0.4	0.00017	89.42
0.6	0.00011	92.95
0.8	0.00008	94.71
1.0	0.00005	96.03

ADSORPTION ISOTHERMS

The adsorption isotherms are helpful in predicting the nature of metal-inhibitor interaction.

Langmuir adsorption isotherm

The Langmuir adsorption isotherm values are presented in table

Graph is plotted between 3+ log C/θ and 3+1og C is found to be linear straight line as shown in figure l [16].

Table 2: Langmuir Adsorption Isotherm Parameters

Inhibitor Concentration (%)	3+log (C/θ)	3+log C
H_2SO_4	-	-
0.2	3.6964	2.3010
0.4	3.9269	2.6021
0.6	4.1201	2.7782
0.8	4.2529	2.9031
1.0	4.3836	3.0000

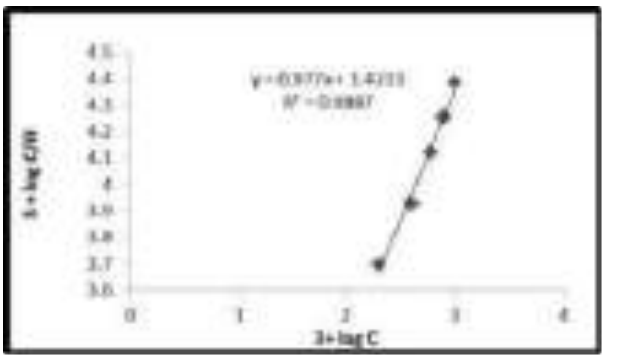


Fig. 1: Langmuir Adsorption Isotherm

TEMKIN ISOTHERM

The linear plot of θ against log C is obtained as displayed in figure 2 indicates that Temkin isotherm was negative and found to be obeyed and "a" value indicate repulsion existing in the adsorption layer and the tabulated results are displayed in table 3 [17-19].

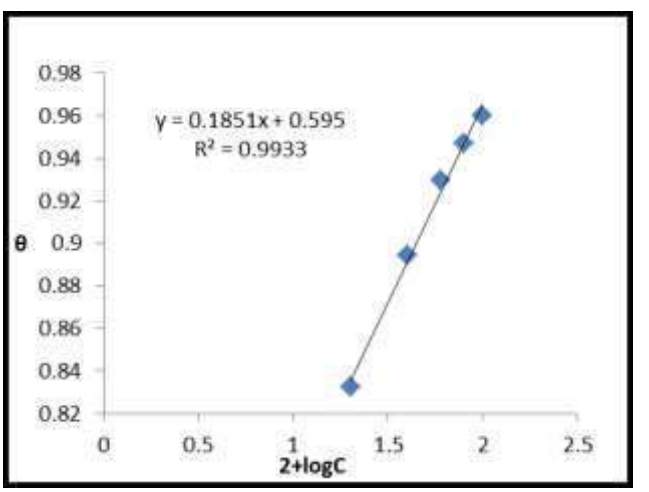


Fig. 2: Temkin Adsorption Isotherm

Table 3: Temkin Adsorption Isotherm

Inhibitor Concentration (%)	θ	2+ log C
0.2	0.8325	1.3010
0.4	0.8942	1.6021
0.6	0.9295	1.7782
0.8	0.9471	1.9031
1.0	0.9603	2.0000

Florry-Huggins adsorption isotherm

The adsorption parameter is shown in table 4 and the graph plotted between 3+ log (θ /C) and 3+ log (1- θ) and is found to be linear as revealed in figure 3.

Table-4: Florry-Huggins Adsorption Isotherm

θ	Inhibitor Concentration (%)	3+log (θ/C)	3+log (1- θ)
0.8325	0.2	3.6193	2.2240
0.8942	0.4	3.3493	2.0245
0.9295	0.6	3.1901	1.8482
0.9471	0.8	3.0733	1.7235
0.9603	1.0	2.9824	1.5988

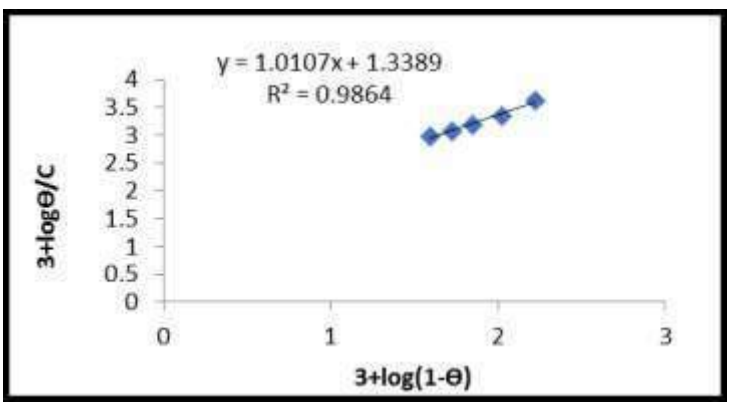


Fig.3: Florry-Huggins Adsorption Isotherm

El-awady Isotherm

A graph is obtained by plotting 2 + log (θ /(l- θ) vs 2+ log C and linear straight line is obtained as shown in figure 4 and the values are tabulated in table 5 [20].

Table 5: El-awady Adsorption Isotherm Parameters

Inhibitor Concentration (%)	2+log C	θ	1- θ	(θ/1-θ)	2+log(θ/1-θ)
0.2	1.3010	0.8325	0.1675	4.9701	2.6964
0.4	1.6021	0.8942	0.1058	8.4518	2.9269
0.6	1.7781	0.9295	0.0705	13.1844	3.1201
0.8	1.9031	0.9471	0.0529	17.9036	3.2529
1.0	2.0000	0.9603	0.0397	24.1889	3.3836

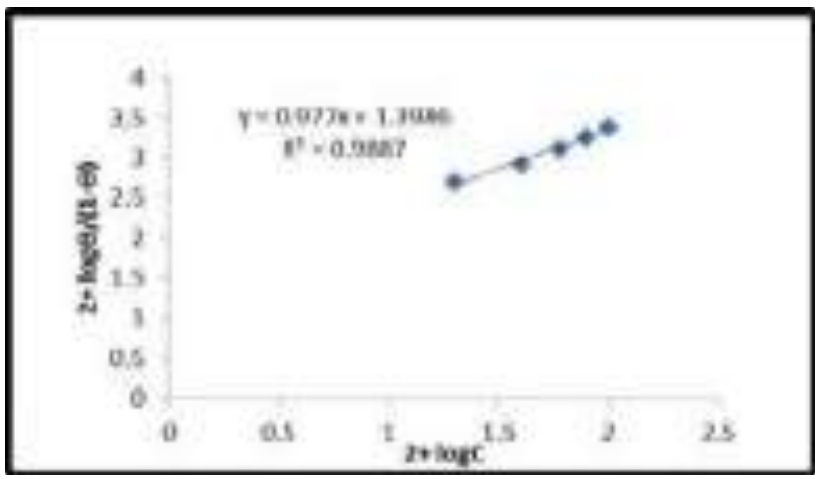


Fig.4: El-awady Adsorption Isotherm

Free Energy Change

The changes in ΔGoads of inhibitor on MS surface is correlated to the adsorption constant as

(ΔGoads) = -2.303RTlog (Kads x 55.5)

From the results shown in table-6, most of the results of ΔGoads were observed to be negative and less than the threshold value of -20kJ/mole which indicates the adsorption is spontaneous and physical adsorption type [21].

Table 6: Free Energy Change Parameters

Medium	Inhibitor Concentration (%)	K_{ads}	ΔG (kJ/mole)
Barleria	0.2	24.8507	18.2480
	0.4	21.1294	-17.8061

cristata leaves extract	0.6	21.9739	-17.9048
	0.8	22.3794	-17.9509
	1.0	24.1889	-18.1468

Table 7: Adsorption Isotherm Parameters

Medium	Isotherm	Slope	R^2	a	1/y
Barleria cristata leaves extract	Langmuir Isotherm	0.9770	0.9887	-	1.023
	Temkin Isotherm	0.1851	0.9933	-0.4313	5.405
	Florry-Huggins Isotherm	1.0107	0.9864	-	0.990
	El-awady Isotherm	0.977	0.9889	-	1.023

Potentiodynamic Polarization Studies

The values of polarization parameters are tabulated in table 8 and figures 5-7. It can be noted that the phyto-components diffuse from the bulk of the solution and becomes absorbed on MS surface [22, 23].

Medium	Inhibitor,(%)	$I_{corr.}$, mV	$-E_{corr.}$, mV	B_a.,mV/dec	B_c.,mV/dec	IE(%)
H_2SO_4	-	282.153	490.185	46.357	155.861	-
Barleria cristata	0.2	110.250	484.896	45.690	129.698	60.9254
	1.0	30.293	491.079	47.771	138.379	89.2636

Table 8: Polarization Parameters

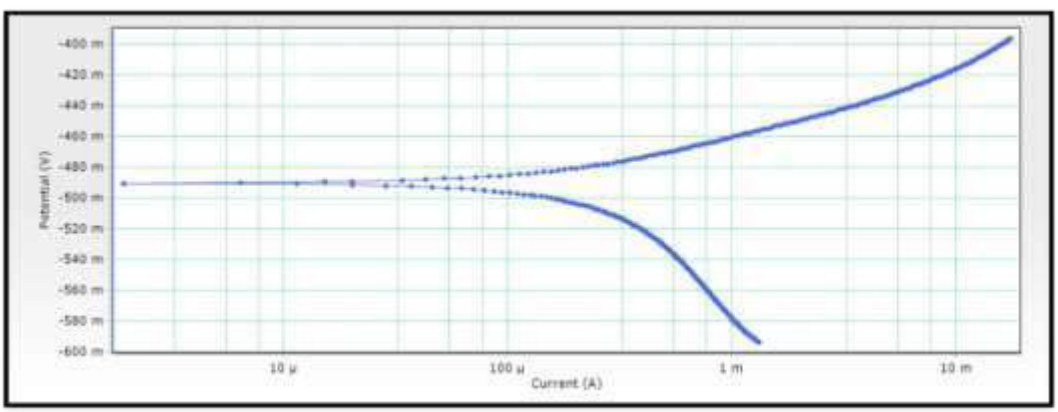


Fig.5: Polarization Graph for the Specimen in Blank H_2SO_4

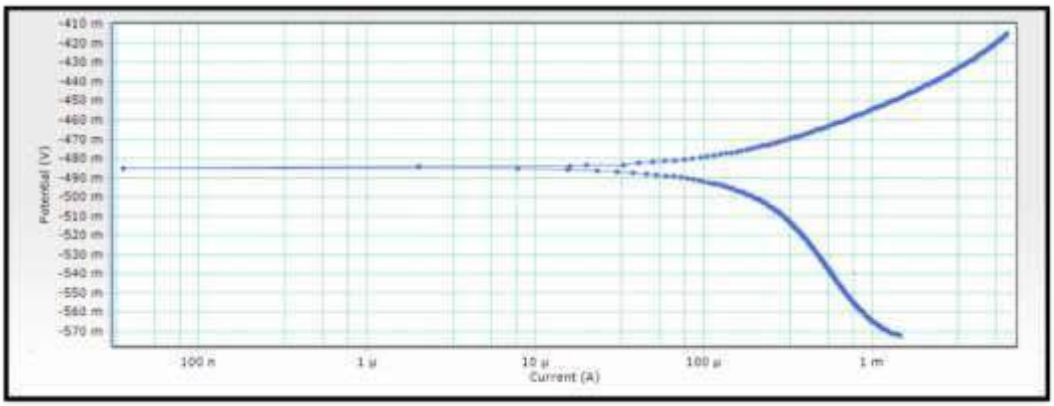


Fig.6: Polarization Graph for the Specimen at Lower Concentration of BC Leaves Extract

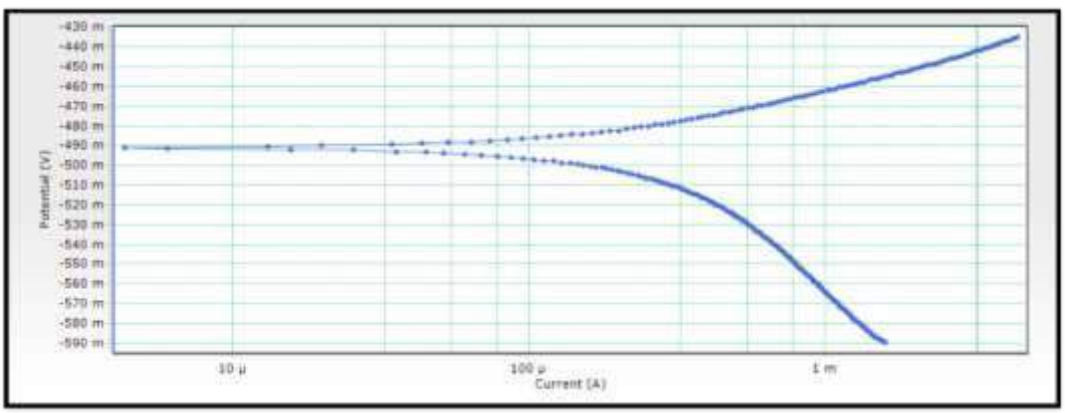


Fig.7: Polarization Graph for the Specimen at Higher Concentration of BC Leaves Extract.

AC Impedance Study

Table 9 and figures 8-10 shows the AC impedance value for different concentrations of the inhibitor. There is increase in the values of Rt and decrease in the values of Cdl with the concentration of the inhibitor which confirms the protective film formation on MS surface [24, 25].

Table 9: Corrosion Impedance Parameters

Inhibitor(%)	R_t, Ohm cm^2	C_{dl},F/ cm^2	IE(%)
H_2SO_4	17.00	220.52	-
0.2	37.58	732.68	83.66
1.0	50.65	506.50	96.70

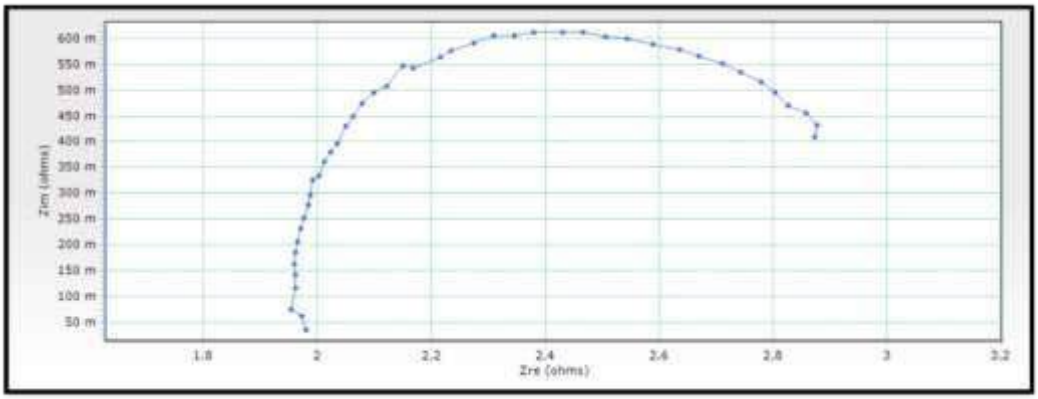


Fig.8: Impedance Diagram for the Specimen in Blank H_2SO_4.

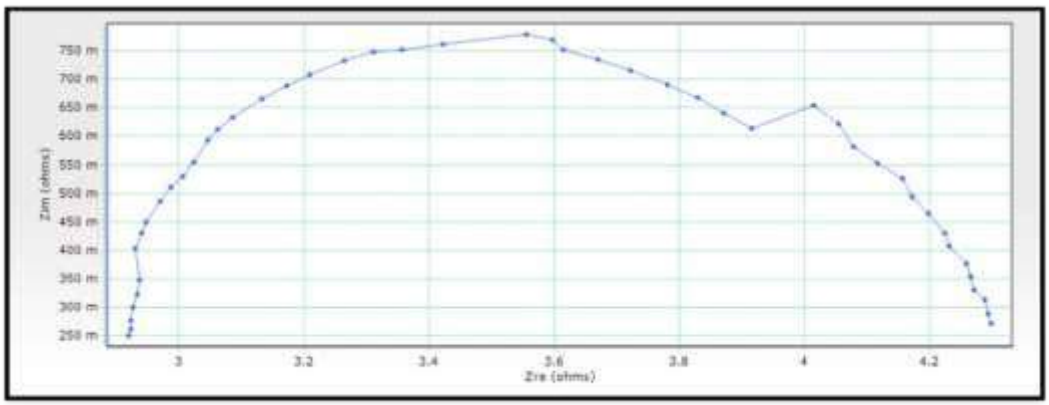


Fig.9: Impedance Diagram for Specimen Studied at Lower Concentration of BC Leaves Extract.

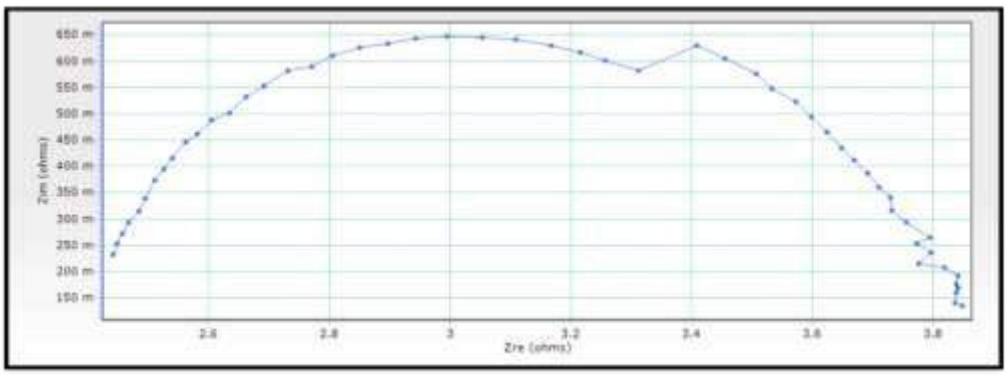


Fig.10: Impedance Diagram for Specimen Studied at Higher Concentration of BC Leaves Extract.

Mechanism of Corrosion Inhibition

1. The variation in the values of CR in mass loss technique and the increase in the values of R_t and decrease in the C_{dl} values obtained from the impedance study and the tafel slope obtained determining the corrosion current, corrosion potential, variation in the values of anodic and cathodic potential confirms the inhibitor is of mixed type.
2. There exists a complex between Fe^{2+} and the inhibitor molecules which prohibit the corrosion process without possibility of adsorbing of the aggressive ions such as Cl^-.

CONCLUSION

The IE values determined by the mass loss method, polarization and impedance measurements show close agreement. The corrosion decreases with increasing addition of *Barleria cristata* leaves extract probably due to the progressive adsorption of the inhibitor on the MS surface. The inhibition of corrosion may be due to the mode of adsorption of any of the phyto-chemical constituents present in the leaves extract onto the MS surface. Langmuir, Temkin, Florry-Huggins, El-Awady adsorption isotherm and the kinetic thermodynamic model show the best fit results for the studied inhibitor. The changes in the values of ΔG is accompanied by physical adsorption type. The protective film formation is confirmed by AC impedance studies.

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DECLARATION

All views and opinion expressed in the book are the sole responsibility of the author concerned. Neither the Editors or nor the Publisher can in anyway be held responsible for them.

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Chapter
16

TRENDING INNOVATIONS IN PHARMACEUTICAL INDUSTRY AND HEALTHCARE

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ABSTRACT

The pharmaceutical industry has been conventionally sluggish to embrace new technologies, but the newest pharmaceutical health drifts are indications of a considerable archetype budge in the industry. The most recent technologies, like additive manufacturing, Augmented Reality/Virtual Reality, and artificial intelligence (AI), facilitate pharmaceutical companies speed up the research and development processes, produce custom-made products, and perform testing in inventive ways. Eventually, all these technologies build healthcare further effectual and proficient, renovate the understanding for patients and suppliers. Pharmaceutical healthcare technology is growing globally. In addition to India and the United States of America, countries that are considering speedy development in pharmaceutical healthcare technology include the United Kingdom, Germany, Switzerland, Israel and Belgium. This article highlights the latest pharmaceutical healthcare technology drifts and how they are influential on the industry and the prospect of healthcare as we recognize it.

CURRENT TOP PHARMA HEALTHCARE TECHNOLOGY TRENDS:

Healthcare technology venture is at a record high, having a growth of 48% to hit Dollar 52 Billion in 2021. Following are the areas which are powering the major changes. Here are the topmost pharmaceutical health tech drifts that will tremble up the industry is shown in the following figure:

Artificial Intelligence (Ai)

AI is enticing progressively more fundamental in pharmaceutical and healthcare zone. As per information by Grand View Research, the worldwide Artificial Intelligence healthcare sector market size will attain a stunning Dollar 35 billion by 2030, rising at an aggregate CAGR (Compound Annual Growth Rate) of 42% in this instance.

The utilization of artificial intelligence is enhancing the drug discovery and development progression. Many Startups are investigating the use of these tools to deal with the different confrontations in the pharmaceutical industry, such as automation and optimization of the industrialized practices, in addition to scheming effectual marketing and post-launching tactics. Patient recognition is a critical stage in the drug discovery and development course, particularly for accomplishment of clinical trials.

Artificial Intelligence is by now influencing the pharmaceutical industry with its enormous prognostic and data analytics capability. This application of Artificial Intelligence technology facilitates pharmaceutical and healthcare professional to explore prototypes in data sets to realize the inferences, advantages, and success rates of new drugs prior to inducting them into the market.

Pangaea Data, a United Kingdom startup and In-vivo AI, a Canada based startup, employs Artificial Intelligence together with ML (Machine Learning) for RWE studies (real-world evidence) and clinical trial processes. Using ML-equipped software, Pangaea Data startup can scan electronic health records and In-vivo AI aiding to check new drugs and choose the most excellent potential contenders for the medicines. These startups also generating a documentation of Artificial Intelligence model for a range of disease sections.

Big Data Management and Analytics

One of the prevalent faltering obstructions in the launching of new drugs is the expenditure of research and development. Development of a new chemical molecule as a drug candidate compound or medicine of biological origin can cost approximately about 3 billion dollars. By controlling big data, pharmaceutical researchers can abbreviate investigation sequences, progressing to the rapid discovery and delivery of new drugs. Big data can in addition assists to resolve side effects of a drug in advance, which trim down the time desirable for different stages of clinical trials. The expenses of research and development blow up the price of medications, so limiting the Research and Development phases can aid controlling the overheads of medication for patients. (1)

The pharmaceutical manufacturing industry needs high-performance arrangements to scrutinize the bulky degree of data created throughout the drug discovery and development progression. Pharmaceutical manufacturing companies use third party clients to share the data with associates, turning the data management a vital area of spotlight. Furthermore, these techniques of analytics are employed on approximately all types of medical data obtained from records of the patients, hospital data and medical imaging, to exemplify a few. Pryml, a startup unit from Belgium, generates an artificial report of the classified data accessible with pharmaceutical units. This facilitates the confidential allocation of this data with third-party hubs for business appliance or research partnership.

Single-Use Processes and Flexible Production

More and more pharmaceutical units are implementing SUT (single-use technology) in their industrial practices. This swing is enduring as there are more production companies becoming attentive towards the awesome features of this tool.

Single-use technology equipped production units can improvise the progress of high-tier practices at a superior scale. With condensed maintenance procedures, pharmaceutical manufacturing companies by now already employing Single-use technology information for rapid turnaround and improvement in time-period and simplified processes.

Machinery operating on Single-use technology is simple to establish, taking about only one or two hours in comparison to stainless steel setups that will require a couple of weeks. Additionally, system continuance is comparatively uncomplicated, with no requirement for sterilization annual cleaning, validations, and bare minimum monitoring. SUT processes lessen the menace of cross-contamination of products, and maintaining a sterilized production environment will become very simple.

While Single-use technology is a comparatively newer technological advancement, its advantages are extensive, making it very hard for pharmaceutical manufacturers to overlook. The prospect of Single-use technology is dazzling, and more pharmaceutical units will connect to the mainstream in next decade and afar. (2)

The pharmaceutical manufacturing industry is searching new ways of production processes because of the vibrant market dynamics, such as tiny batches for precision medicine. Single-use bioreactors are becoming popular as they condense downtime and boost productivity. These bioreactors accomplish it by removing complicated processes such as cleaning and validation stages amid split production steps. New kind of bioreactor schemes and nonstop production processes meet the mounting spotlight on biopharmaceutical products. Additionally to the eliminating downtime, incessant production has squat power requirements, accomplishes high manufacturing, and lessens the quantity of waste. Single-use technology bioreactors are progressively more accepted choice for simplifying manufacturing procedures.

A Scotland startup Cellexus and Belgian startup unit Secoya Technologies presenting new technologies that formulates single-use airlift bioreactor arrangements. The single-use arrangement can be employed for a range of fermentation and cell cultures and these startups have attained growth of bacteria, microalgae, yeast, and intensification of bacteriophages and utilization in chemical synthesis, evaporation, micro-encapsulation, and crystallization processes.

Precision Medicine

Precision medicine tenders a new loom to diagnosis of diseases, its treatment, and disease prevention. This particular technology employs the genes of the patient and his/her lifestyle to assist physicians to make accurate, data-supported diagnostic assessment.

With a Compound Annual Growth Rate of 11%, market value of the precision medicine will surpass 100 billion dollars by 2025. This expansion relates a great deal to the

accomplishment of freshly embattled treatments. The booming accomplishment of precision medicine will involve a new clinical, regulatory, technical and economic composition. That way, medical practitioners can provide the accurate therapy to the correct patient at the exact time. If the development projections are no matter which to go by; this will be one of the mainly unsettling pharmaceutical healthcare-technological tendencies of the time.

ExactCure, a France unit startup is offering a software elucidation to simulate the use of population pharmaco-kinetics, in addition to scientific literature data, for real-time calculation of effectiveness and drug interaction, on each personality. ExactCure is working on drug-specific contact models for drugs under examination for the management of COVID-19.

A Switzerland startup unit Tepthera is coming with platform technologies for the detection of T cell antigens. The MEDi platform assists in the fast detection of tumor-specific antigens from leukocyte antigens of human patient. After the collection of antigens, the software solution recognizes tumor-specific epitomes and then continuously monitors antigen-specific T cells. (3)

Additive Manufacturing and Bioprinting

The necessity for precision medicine is also forcing pharmaceutical manufacturing companies to rethink about the manufacturing procedures. A lot of research is happening for creating superior 3D printing machines that can print tissues and cells. 3D printing of human cells and tissues has immense appliance in drug development, regenerative medicine, and organ engineering. This permits the expansion of age or physiologically reliant pharmaceutical formulations, as well as precision pills. Bio-printers also facilitate to push in novelty in bio-inks, microfluidics, and tissue engineering.

FabRx is a UK startup which produces M-3DIMAKER, a 3D printer for preparing custom-made pills. M-3DIMAKER uses tools for direct powder extrusion. It produces pills with properties such as sustained release or delayed dose, and multidrug component pills. The printer also facilitates small batch-wise production for clinical trials and precise custom-made dosage formulations for individual use.

The US-based startup unit Frontier Bio is offering FLUX-1, a 3D bio-printer for printing human tissues. An Indian company, Avay biosciences private ltd. Manufactures Avay Mito Bio 3D printers, Chennai produces organs, cells and tissues for transplanting, drug discovery and drug development, disease model generation and tissue engineered foods.

These organs printed using 3D-printing technology is replacing living human matters at some stage in clinical trials. Bio-ink, a fluid suspension of living cells and the main constituent of 3D printed tissues and organs helping to generate human tissue in laboratories. This machinery forms micro-organs and tissues those respond in the similar manner the human body acts to new drugs and medicines. Bio-ink using genes obtained from a patient are enabling to reconstruct bigger, more composite organs. It is now even allowing pharmaceutical manufacturing companies to produce personalized drugs appropriate for a particular patient.

Other advantages of bio-printing to the pharmaceutical manufacturing industries include:

- Testing of drug toxicity of a particular dosage form and its dosage
- Modeling of diseases and testing of a range of treatment measures
- Measuring metabolic actions of different drugs in living tissue

The major application of 3D-printed organs is helping to minimize expenses connected with clinical trials whilst plunging the time-frame essential to endorse new drug substances. (4).

Blockchain

Blockchain technology is incredibly important for the pharmaceutical manufacturing industry in each juncture of the manufacturing and supply of drugs. The stakeholders in the pharmaceutical industry are, normally, very reticent concerning their datasets owing to the sensitive type of the data. Blockchain technology is in addition being exposed to deal with the utilizion of bogus medicines and inferior drugs that are entering into the pharmaceutical distribution chain and taking life of thousands of patients each year. The computerization and digitalization of operations compose blockchain a capable measure to track and secure the pharmaceutical operation ecosystem.

Infosys, leading software company in India is providing pharmaceutical supply chain distribution application software solutions to worldwide industries. PharmaTrace, a Germany startup and Veratrak, a British startup are tendering a blockchain-based bionetwork to safeguard the datasets and install smart contract in the pharmaceutical manufacturing industry. (5)

Real-World Data and Extended Reality

Real-world data (RWD) is one among the rising pharmaceutical healthcare technological drift that is playing a very important function in health-care resolutions. For case in point, the U.S. Food and Drug Administration (FDA) employ Real-world data together with real-world evidence (RWE) to find out safety of the product and discover adverse effects ahead of taking regulatory conclusions. Health care professional utilize these two technological advancements to backup reporting conclusions and formulate guiding principles on therapeutic aspects in clinical pharmacy practice. Additionally, medical, healthcare and pharmaceutical manufacturing producers employ RWD with RWE to maintain clinical trial plans such as rational and simple clinical trials. The industries are in addition adopting RWD with RWE to shore up observational documentation and novel curative course of therapy routines.

Computers, biosensors, wearable devices, and Mobile devices amass and store up health-associated datasets. This database then aids health-care professionals to devise and accomplish enhanced clinical trial data. As the datasets are so inherently coupled to technological aspects in all industrial sectors, we can anticipate RWD and RWE to continue as a nucleus part of pharmaceutical and healthcare technology development trend for the predictable prospect. Real-world data (RWD) and real-world evidence (RWE) are

renovating modernization in the pharmaceutical manufacturing industry. RWD comprise of patient health condition, treatment datasets, and health information collected regularly. The accessibility of real-world data facilitated by the wearable technology, Internet of Things (IoT) and sensors, and is streamlining the way the pharmaceutical industry is working.

Mixed reality (MR), virtual reality (VR), and augmented reality (AR) is making possible the visualizations effects like by no means previously. Pharmaceutical startup units are discovering the potentials of extended reality technology in pharmaceutical research and production field. Extended reality paraphernalia allow database-rich and important real-time location dependant communication amongst research panels. Startup units are building human escalation in pharmaceutical arena is now actuality all the way through extended reality wearable tools.

Nanome, a United State based startup unit, offering a Virtual Reality cooperation venture for atomic, molecular, and protein visualization.. It accede researchers to devise proteins, iterates the 3D configurations, and also to work in a virtual terminal with worldwide group members.

The Germany startup unit Goodly Innovations is developing OptiworX, an Augmented Reality set for pharmaceutical and biopharmaceutical production units. Furthermore, this set support all store and floor processes like production, filling, primary packaging, and secondary packaging etc. (6, 7)

INTEGRATED WEARABLE TECHNOLOGY

Integration of Wearable technology lets pharmaceutical industry units to execute more than merely manufacturing, marketing, and selling the drugs. This expertise offers patients much better options to handle their health conditions and take decisive choices. Today by now a wide range of remote patient health care monitoring devices are available those allow physicians to account observations for urine, glucose and blood pressure data outputs and maintain dosage on persistent conditions like asthma, hypertension and diabetes etc.

Japanese drug manufacturing company, Daiichi-Sankyo, in partnership with other Health-Care Centers produced a device called as the mobile wrap-around that keep an eye on data of patients detected with atrial fibrillation disorder and provide comments to medical practitioners. Roche is one more company coupled my-Sugr app with the Accu-Check glucometer, making possible the diabetic people to experience a special, more receptive system to deal with the ailment. With the help of this paired device, patients can register in and follow easy steps, which permit them to keep a check on their sugar levels (8)

DIGITAL THERAPEUTICS AND CURATIVE THERAPIES

Digital therapeutics send evidence-based therapeutic interference by means of software to check, handle, or take care of physical, behavioral, and mental conditions. These non-pharmacological, technology based solutions are moreover unconnected or employed along with medications, therapies, or devices. Digital therapeutics permit every individual person have better control over their health effects.

A US-based startup, Cognivive, proffer evidence-based digital therapeutics for the management of neuro-cognitive and neuro-motor disturbances. Its neuro-rehabilitation therapy uses a medical device to aid patients to recuperate from a paralysis stroke. A Germany startup unit Dopavision is producing a smartphone-based digital therapeutic for the management of myopia particularly children. This solution accomplishes the dopamine activation, a neurotransmitter that has a vital function in eye growth control. Dopavision is at present enterprising pre-clinical trials of the digital therapeutics.

Curative therapies like cell and gene therapies are becoming popular where usually genetic material is inserted into the cells to recompense the atypical genes or to compose a favorable protein. Genetically engineered viruses are the most familiar vectors employed for gene therapy.

Mogrify is a UK startup which is developing a proprietary straight cellular translation platform for transmogrifying grown human cells. Mogrify is developing cell therapies for auto-immune, cancer immunotherapy, musculoskeletal and, additionally respiratory and ocular diseases. The United State unit Lacerta Therapeutics is a clinical-stage gene therapy startup offering treatments for the lysosomal storage diseases and central nervous system defects. (9)

IN-SILICO TESTING

Product development of cosmetic preparations is expensive and lingering, in particular on every occasion industries try to find out latest ingredient components. Nowadays, more industries are opting for in-silico screening tests to deal with such production troubles.

In-silico screening tool come together with datasets and simulation software's that amass molecule details and interactions with skin proteins. In pharmacological studies, in-silico screening confirms how a possible cancer-causative candidate interacts with proteins implicated in the cancer development process.

There is a variety of possible applications for in silico screening, as it helps zones that depend on biological research such as drug and food toxicology research, and cosmetic development to attain the following:

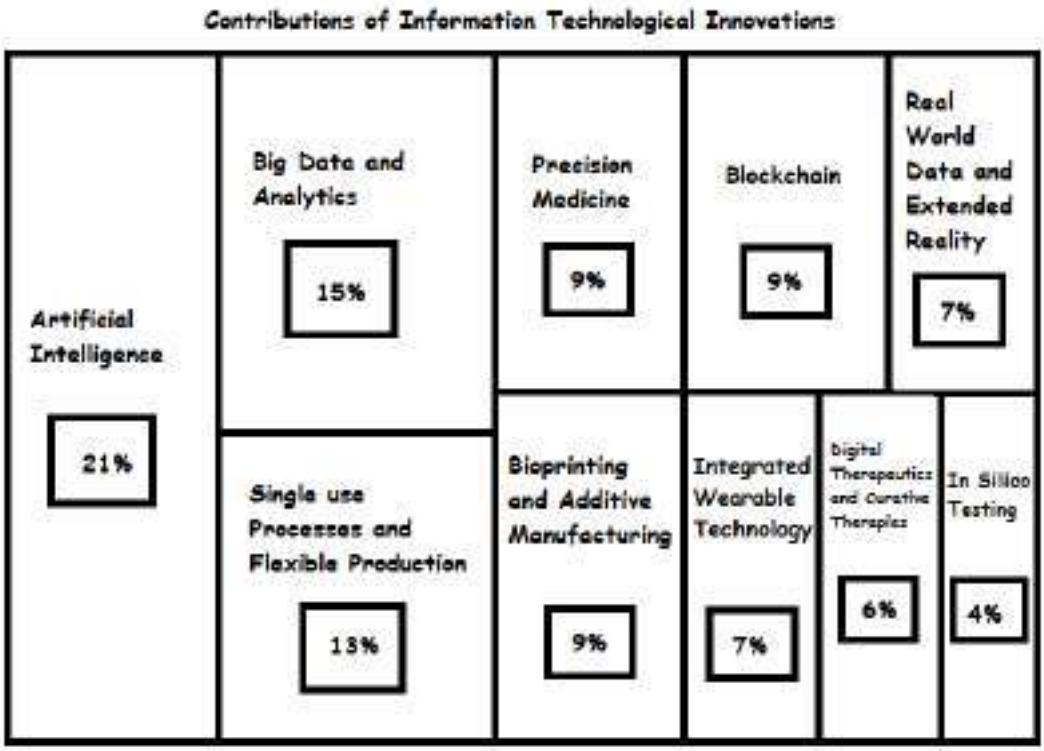
- Improvise products
- Recognize possible active candidates for a particular target
- Demonstrate the biological activities and health applications of molecules

One real-world model for in-silico technology is the GPDB dataset, which stores details of plant extracts and natural product molecules.

CONCLUSION

Sustaining regulatory compliance is an immense challenge for pharmaceutical companies relies on Information Technology systems to impel escalation and competence. As the technologies change, consequently do the regulations. Accordingly, any company faces a continuous combat to keep on rationalized with the most up-to-date industrialized processes and IT integration is the need of the hour.

Information Technology will forever acts an important function in the pharmaceutical manufacturing, and about 50% of industries aver this digital expertise scarcity is the prevalent hesitant obstruction for digital revolution in the pharmaceutical sector. (10)



By adopting of the latest technological innovations, pharmaceutical manufacturers might locate themselves in the market looking for a newer, more contemporary elucidation with the help of evolving technology. In an industrial environment power-driven by modernization, pharmaceutical companies cannot afford to fail to keep up with technology. However, manufacturers don't have the resources to ordeal each and every trend in healthcare that emerges. Pharmaceutical hubs can trounce this barrier by circumspectly estimating which healthcare technology remedies offer the most excellent return on investment (ROI).

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