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Contemporary Trends in Chemical, Pharmaceutical and Life Sciences Volume IV

Editors:
Dr. Bassa Satyannarayana
Mr. Mukul M. Barwant

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Volume IV

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PREFACE

The field of chemical, pharmaceutical, and life sciences has experienced unprecedented growth and transformation over recent decades. This volume, *Contemporary Trends in Chemical, Pharmaceutical and Life Sciences* seeks to capture and present the current advancements, research, and trends that are shaping these dynamic fields today.

The compilation of research and review articles in this volume highlights the interdisciplinary nature of modern science, where boundaries between chemistry, pharmacology, and biology are increasingly blurred. This synergy is driving innovation, leading to new therapeutic strategies, cutting-edge technologies, and a deeper understanding of the fundamental processes of life.

This book aims to provide readers, whether they are seasoned researchers, educators, or students, with a comprehensive overview of the latest developments. It also serves as a platform for scientists and scholars to share their findings and contribute to the collective knowledge in these fields.

We are at a pivotal moment in history where the convergence of disciplines is opening new avenues for exploration and discovery. The contributions in this volume reflect the dedication, creativity, and intellectual rigor of the scientific community, and we hope that it will inspire further research and innovation.

I would like to extend my gratitude to all the authors who have contributed to this volume, as well as the reviewers whose insights have ensured the quality and relevance of the content. It is our sincere hope that this book will serve as a valuable resource for all those engaged in the chemical, pharmaceutical, and life sciences.

Editors:
Dr. Bassa Satyannarayana and Mr. Mukul Machhindra Barawnt

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Chapter 1

ANTIMICROBIAL RESISTANCE TO CIPROFLOXACIN: MECHANISMS, CONSEQUENCES AND INTERVENTIONS FOR SUSTAINABLE USE

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ABSTRACT

Antibiotics have revamped the treatment of diseases, saving countless lives and improving public health. However, misuse and overuse of these drugs have led to the development of antimicrobial resistance. When microbes adapt to antibiotics and develop resistance, antimicrobial resistance occurs. Human activity is speeding up the process, otherwise AMR is a slow process and happens over a period of time. Understanding the mechanism of AMR of antibiotics is important to combat this rising threat and sustaining drug efficacy.

KEYWORDS: Antimicrobial Resistance**,** Ciprofloxacin, Antibiotics, AMR.

INTRODUCTION

Antibiotics have revamped the treatment of diseases, saving countless lives and improving public health. However, misuse and overuse of these drugs have led to the development of antimicrobial resistance. When microbes adapt to antibiotics and develop resistance, antimicrobial resistance occurs. Human activity is speeding up the process; otherwise AMR is a slow process and happens over a period of time. Understanding the mechanism of AMR of antibiotics is important to combat this rising threat and sustaining drug efficacy.

Fluoroquinolines are class of antibiotics that can treat gram positive and gram negative bacteria by inhibiting DNA synthesis in bacteria. Ciprofloxacin – second generation fluoroquinoline drug is a broad spectrum antibiotic treats pneumonia, urinary tract infections, bone, joint infections, typhoid, and gastrointestinal infections and sexually transmitted diseases[1-4].However, the emergence of antibiotic resistance to ciprofloxacin, has become a serious problem in the medical community.[5, 6].

Understanding the complex mechanisms of AMR of Ciprofloxacin, seeking strategies to reduce the use is important to address this challenge. Resistance mechanisms to fluoroquinolones such as ciprofloxacin are often associated with alterations in antibiotic sites, overexpression of efflux pumps, plasmid-mediated resistance, enzyme inactivation and biofilm formation. Altogether, these mechanisms reduce the activity of ciprofloxacin against bacteria, allowing them to survive and multiply even when exposed to antibiotics.

MECHANISM OF ACTION

Ciprofloxacin exerts its antibacterial activity by targeting bacterial DNA molecules and Topoisomerase IV, Which is involved in DNA replication and transcription processes necessary for bacterial growth and survival. This process inhibits cell division and causes cell death

Antibiotic resistance to ciprofloxacin includes genetic mutations that alter drug targeting, increased antibiotic reflux, horizontal transfer of resistance genes, enzymatic degradation of ciprofloxacin, bacteria embedded within biofilms, all of which together reduces ciprofloxacin resistance.

The mechanisms of antimicrobial resistance to fluoroquinolone drugs, specifically centering on Ciprofloxacin, emphasize the multifaceted strategies bacteria engage to elude the effects of this important antibiotic. Antimicrobial resistance to fluoroquinolone drugs, such as Ciprofloxacin, arises from a complex interplay of bacterial defense mechanisms and genetic mutations. Enhanced Understanding these mechanisms is crucial in resisting the increasing threat of resistance and preserving the effectiveness of these antibiotics.

ANTIMICROBIAL RESISTANCE MECHANISM

TARGET SITE MUTATION

The primary mechanism of resistance involves mutations in the target sites of fluoroquinolones. Ciprofloxacin employs its antimicrobial activity by inhibiting bacterial DNA gyrase and topoisomerase IV, essential enzymes involved in DNA replication and repair. Mutations in the genes encoding these enzymes can alter the binding sites of Ciprofloxacin, reducing its efficacy and allowing bacteria to survive exposure. Antimicrobial resistance due to target site mutations is a critical mechanism that significantly impacts the efficacy of antibiotics. This mechanism involves genetic alterations in the target sites of antibiotics, leading to reduced binding affinity and effectiveness of the drug against bacteria[7, 8].

Recent research by Redgrave et al.[1] explored the evolutionary dynamics of target site mutations in antimicrobial resistance. The study highlighted the adaptive nature of bacteria in acquiring mutations that confer resistance to antibiotics, emphasizing the importance of exploring these mechanisms to combat the spread of resistance. Understanding the genetic and molecular basis of these mutations is crucial for developing effective strategies to combat resistance and preserve the efficacy of antibiotics in clinical practice. Mutations in DNA gyrase and topoisomerase IV that confer resistance to fluoroquinolones, elucidating the molecular mechanisms underlying this form of resistance

EFFLUX PUMP OVEREXPRESSION

Efflux pumps are active exporters that push out undesirable substances from cells. In bacteria, an efflux pump over expression is an important path for eliminating antibiotics. When bacteria activate efflux pumps, they can reduce the intracellular concentration of ciprofloxacin, which reduces the antibiotic's ability to eradicate bacteria and favors bacterial survival[9].

PLASMID-MEDIATED RESISTANCE

Plasmids are small, circular DNA molecules that may be transferred between bacteria by conjugation. Conjugation may occur by direct cell-to-cell contact between bacteria. Plasmids can carry antibiotic-resistance genes that allow the bacteria to be resistant to a number of antibiotics at the same time. This phenomenon is called multidrug-resistance. The transfer of resistance-encoding genes among bacteria may promote the dissemination of resistance to antibiotics. Plasmid-mediated resistance is a mechanism of acquiring resistance genes through a plasmid to help bacteria spread resistance to antibiotics[10].

ENZYMATIC INACTIVATION

Enzymatic inactivation is one of the intelligent defense mechanism that bacteria have developed to counter the effect of antibiotics, thus enabling them to survive and thrive in the presence of antibiotics. Bacteria develop enzymes that can modify or break down antibiotics and neutralizes the antibiotic's effectiveness. These enzymes chemically alter the drug, making it unable to bind to its target in the bacterial cell. The drug thereby cannot bind to its target within the bacterial cell. This modification inhibits Ciprofloxacin from carrying out its stipulated function of killing the bacteria, giving them a survival benefit. In essence, it's like bacteria have their chemical laboratory where they deactivate the drug and go on living[11].

BIOFILM FORMATION

Biofilm formation can also contribute towards developing resistance against Ciprofloxacin, as this is a very common bacterial defense mechanism. The embedded bacteria within the biofilm have less susceptibility to the antibiotics because the physical barrier created by the biofilm matrix limits the entry of Ciprofloxacin and other antimicrobial agents into the bacterial cells. When the bacteria come together to form biofilms, they pack themselves in together and produce a sticky matrix that traps them in a protective layer. Biofilm shield protects bacteria not only from antibiotics but also makes it a little difficult for the immune system to clear out[12].

IMPACT OF RESISTANCE

The emergence of antimicrobial resistance to ciprofloxacin compromises the effectiveness of ciprofloxacin in the treatment of bacterial infections. This is likely to result in treatment failure, prolonged durations of illness, and complications for patients. Furthermore, the transmission of resistant bacteria strains in healthcare settings and communities poses a significant public health threat.

Antimicrobial resistance goes far beyond an individual patient; it extends to whole communities and healthcare systems. Resistant bacteria spread quickly, sometimes to epidemic proportions, which makes control very challenging. This can result in the need for stronger and more expensive antibiotics, longer hospital stays, and an increased risk of serious complications[13-15]

To deal with antimicrobial resistance, collaborative effort is needed among health care professionals, researchers, policymakers, and the general public to handle the challenge

TO ADDRESS THE CHALLENGE OF ANTIMICROBIAL RESISTANCE TO CIPROFLOXACIN, IT IS ESSENTIAL TO IMPLEMENT COMPREHENSIVE STRATEGIES

Antibiotic stewardship plays a vital role in addressing antimicrobial resistance in fluoroquinolone drugs. Antibiotic stewardship involves various strategies, such as promoting appropriate antibiotic prescribing practices, ensuring the right dosage and duration of treatment, and discouraging unnecessary antibiotic use. Healthcare facilities can establish guidelines and protocols for antibiotic use, conduct regular reviews of antibiotic prescriptions, and provide education to healthcare professionals on the importance of judicious antibiotic use. These efforts can help prevent the misuse and overuse of antibiotics, which are significant contributors to the development of antimicrobial resistance[13].

Surveillance programs are important in monitoring antimicrobial resistance in fluoroquinolone drugs such as Ciprofloxacin. A systematic collection, analysis, and reporting of data on antibiotic

resistance patterns in bacteria are fundamental parts of surveillance programs geared toward identifying trends and emerging resistance mechanisms.

Surveillance programs inform strategies to overcome antimicrobial resistance to public health policy makers. Based on the patterns of prevalence for Ciprofloxacin resistance in the community; policymakers may be able to develop evidence-based interventions to ensure that this important antibiotic remains effective[14].

Infection control is probably one of the most fundamental measures put in place to combat and reduce the inappropriate use of antibiotics like ciprofloxacin. Hand hygiene, clean environment, and strict infection prevention protocols will prevent the passage of bacteria from one patient to another as well as reduce risks of infection that may require antibiotic treatment. By emphasizing infection control measures, healthcare providers can contribute to the overall efforts to combat antimicrobial resistance and ensure the continued effectiveness of antibiotics like Ciprofloxacin[15-17].

CONCLUSION

Antimicrobial resistance requires a multifaceted approach that includes antibiotic stewardship, infection control measures, surveillance programs, and research into new antibiotics. By addressing the factors contributing to resistance, promoting responsible antibiotic use, and implementing effective infection prevention strategies, we can work towards preserving the efficacy of ciprofloxacin and other vital antibiotics.

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Chapter 2

NUTRITIVE STATUS OF MEDICINAL PLANTS

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ABSTRACT

Plants that possess therapeutic properties or pharmacological effects on the human body are generally noted as medicinal plants. Medicinal plants offer a range of vitamins, minerals, and bioactive compounds that benefit for human health. These plants also synthesize and accumulate secondary metabolites like alkaloids, sterols, terpenes, flavonoids, saponins, glycosides, cyanogenics, tannins, resins, lactones, quinines and volatile oils etc., are compounds which play important roles in defense mechanisms, pollination and plant communication. Nutrients are essential compounds required for human health to function properly, growth, development and immune health. Food is the major source for serving nutritional needs, but with growing modernization some traditional ways are being given up. Medicinal plants provide a dual advantage: nutritional enrichment and medicinal therapy, offering a sustainable way to improve health outcomes and well-being. These plants not only enhance individual health but also contribute to environmental sustainability and economic development through agriculture, pharmaceuticals, and wellness industries.

KEYWORDS: Medicinal Plants, Nutrients, Metabolites, Health, Benefits.

INTRODUCTION

Medicinal plants are invaluable due to their broad spectrum of health benefits for boosting immunity and reducing inflammation to support mental well-being and cardiovascular health. These plants serve as natural remedies in traditional remedies in traditional healing system and are also sources of modern pharmaceutical compounds. Plants provide a variety of essential nutrients such as carbohydrates, proteins, healthy fats, vitamins and minerals. Deficiencies in these nutrients can lead to various health issues, while adequate intake offers numerous health benefits. A balanced diet rich in fruits, vegetables, lean proteins, whole grains and healthy fats can help ensure the body receives these vital nutrients. A diverse diet rich in plant-based foods can meet most nutrient needs and offers numerous health benefits due to the abundance of fiver, vitamins, minerals and antioxidants. This approach supports overall wellness, reduces disease risk and is associated with heart, brain and digestive health.

FUNCTIONS OF NUTRIENTS IN PLANT SOURCES

Nutrients have one or more basic functions; they provide energy, contribute to body structure and regulate chemical processes in the body. These basic functions allow us to detect and respond to

environmental surroundings, move, excrete wastes, breathe, grow and reproduce. Some important nutrients and their benefits are tabulated below.

Fig 1: Important Nutrients

Table 1: Important Nutrients and their benefits

Sl.No.	Nutrients	Benefits	Examples
1	Carbohydrates	Provide energy for the body especially to the brain and muscles and support digestive health through fiber content.	Whole grains, root vegetables, legumes and fruits
2	Proteins	Support muscle growth, immune function and cell repair.	Legumes, nuts, seeds and soy products.
3	Healthy Fats	Support heart health, brain function and hormone production.	Avocados, olives, nuts and plant oils.
4	Fiber	Aids in digestion, helps to control sugar levels, lower cholesterol and supports weight management.	Whole grains, fruits, vegetables, legumes and seeds.
5	Vitamins: Vitamin A	Supports vision, immune function and skin health.	Carrots, sweet potatoes and dark leafy greens.
	Vitamin B	Helps in energy production, brain function and red blood cell formation	Whole grains, legumes, nuts and leafy greens.
	Vitamin C	Acts as an antioxidant, boosts immunity and aids collagen production	Citrus fruits, bell peppers, broccoli and strawberries

	Vitamin D	Helps to maintain calcium and phosphorous levels, improves the immune system and keeps brain and cell health	Fortified cereals and fortified milk
	Vitamin E	Supports skin health and acts as an antioxidant	Nuts, seeds and green leafy vegetables
	Vitamin K	Helps for blood clotting, wound healing and bone health	Broccoli, spinach, kale and blue berries
6	Minerals; Calcium	Important for bone health and muscle function	Leafy greens, fortified plant-based milks
	Iron	Supports oxygen transport and energy production	Lentils, beans, spinach and quinoa.
	Magnesium	Involved in muscle and nerve function and energy production	Nuts, seeds, whole grains and leafy greens
	Potassium	Regulates fluid balance, blood pressure and muscle contractions.	Bananas, potatoes, tomatoes and beans
	Zinc	Helps for wound healing and cell division	Legumes, nuts and seeds whole grains and fortified cereals.
	Magnesium	Helps the body release stored energy, reduce fatigue and maintain healthy bones and teeth	Bananas, avocado, spinach, legumes and nuts.
7	Antioxidants	Protect cells from oxidative stress, reduces the risk of chronic diseases such as heart disease, cancer and neurodegenerative disorders	Blue berries, strawberries, nuts, seeds, and green tea and dark leafy vegetables.
8	Phytochemicals	Act as antioxidants, support immune function and help to prevent chronic diseases.	Fruits, vegetables, nuts, seeds and whole grains.

HISTORY OF MEDICINAL PLANTS

The use of medicinal plants dates back thousands of years around the world. The earliest known records of medicinal plant use come from Mesopotamian clay tablets, dating to around 2600 BCE. These tablets mention plants like myrrh and opium for treating various ailments. Ancient Egyptians were known for their herbal knowledge, documented in texts like the Ebers Papyrus which lists hundreds of remedies, including garlic, aloe Vera and frankincense. They used these plants for healing wounds, digestive issues and spiritual purposes.

Around 1500 BCE, Ayurvedic medicine in India documented the therapeutic use of plants in texts like Rig-Veda and Atharvaveda. Ayurvedic practices used turmeric, ginger and Ashwagandha for treating inflammation, digestive health and stress. Chinese medicine dating back over 2,000 BCE years incorporates plants like ginseng and licorice. The Shen Nong Ben Cao Jing is one of the oldest Chinese texts, categorizing herbs and plants by heir medicinal properties. Greek physician Hippocrates known as the "Father of Medicine" promoted plant-based treatments. Later, Roman physician Dioscorides wrote De MateriaMedica, an extensive pharmacopoeia of herbs, which served as a primary resource for medicinal plant knowledge in Europe for over a thousand years.

During the middle Ages, monasteries in Europe preserved ancient herbal knowledge, translating works by Greek and Roman scholars. Monks cultivated medicinal plants in their gardens and treated ailments using herbs like chamomile and sage. The Renaissance brought renewed interest in botany and explorers discovered new medicinal plants in Asia and America. In the 16th century, herbs like cinchona bark, which contains quinine, were used to treat malaria. Herbalists like Nicholas Culpeper published books on medicinal plants making herbal knowledge more accessible.

In recent decades, there has been renewed interest in herbal medicine and alternative therapies, often supported by scientific research. Herbal medicine is now integrated into complementary and alternative medicine practices, and medicinal plants are being studied for their roles in treating chronic diseases, inflammation and infection.

Fig 2: Some Important Medicinal Plants

BENEFITS OF MEDICINAL PLANTS

Medicinal plants also known as healing herbs have many benefits, including;

Health: Medicinal plants can help prevent and manage heart diseases, cancer and diabetes. They can also help reduce blood clots and have anti-inflammatory and anti-tumour properties.

Economic: These plants are a major source of income and employment for millions of people. The global market value for medicinal plants is estimated to be around 400 dollar billion.

Traditional Medicine: Medicinal plants have been used in traditional medicine practices since prehistoric times. For example, willow bark has been used for thousands of years to relieve pain and reduce fever.

Anxiety and Stress: Some medicinal plants like lavender can help reduce anxiety.

Nausea: Ginger is known for easing nausea and used for digestion.

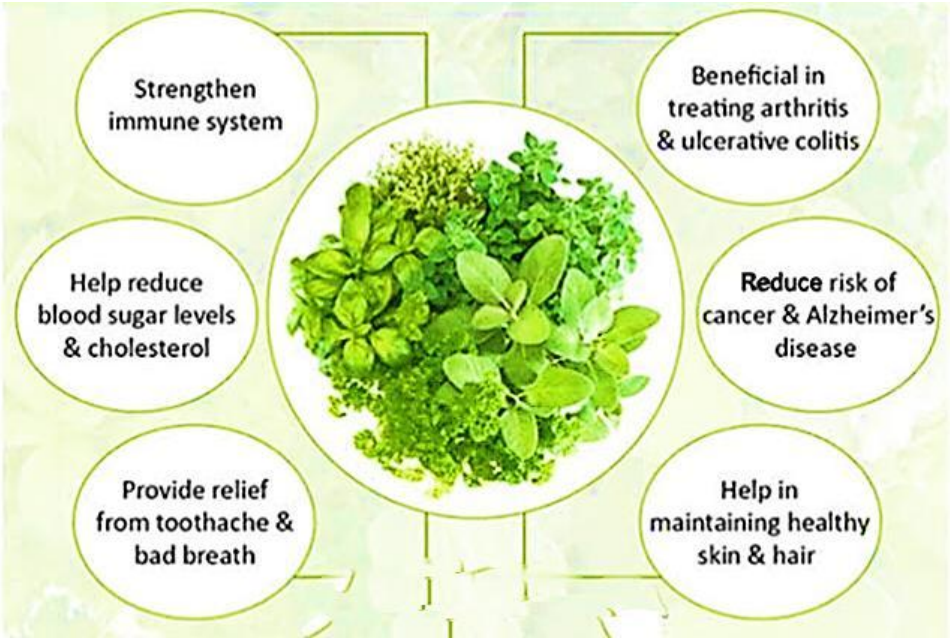

Fig 3: Important Benefits of Medicinal Plants

NUTRITIVE VALUES OF MEDICINAL PLANTS

Medicinal plants are species of the plant kingdom, whose parts such as flowers, leaves, roots, stems, fruits and seeds are directly used or used in some preparation as a medicine. Around 50,000 medicinal plants are used worldwide with a significant number having well-documented therapeutic properties. According to the Botanical Survey, India is home to more than 8,000 species of medicinal plants. Terminaliachebula is popularly is known as "chebulicmyrobalan" or "king of medicine". It is a native plant of Southeast Asia and is mentioned in Indian and Chinese traditional systems of medicine. It belongs to the family Combretaceae and is found to grow mostly in tropical and subtropical belts.

The nutritive status of medicinal plants is crucial as it highlights their role in both traditional medicine and dietary nutrition. Many of these plants are not only valuable for their therapeutic properties but also for their rich nutrient content, which supports overall health.

SOME MEDICINAL PLANTS AND THEIR NUTRITIONAL VALUE

1. Oats (*Avena sativa*): Oats especially in the form of milky oats and oat straw are highly nutritious.

Fig 4: Oats (*Avena sativa*)

Nutrients in Oats:

Minerals: Magnesium, Calcium, Iron

Vitamins: Vitamin A. C and B-complex (except B12)

Benefits of Oats: Oats have been linked to improve cognitive function and mental health. Consuming oat-based teas or extracts helps stress and anxiety freeness and making them ideal for mental well-being.

2. Cilantro (*Coriandrum sativum*): Cilantro leaves and seeds are rich in essential minerals and vitamins.

Fig 5: Cilantro (*Coriandrum sativum*)

Nutrients in Cilantro:

Minerals: Copper, magnesium and potassium

Vitamins: Vitamins A, C and K

Benefits of Cilantro: This plant aids in digestion, supports liver function and helps for regulation of cholesterol and blood sugar levels when consumed regularly.

3. Mint Family (Lamiaceae):

Peppermint (*Mentha piperita*): This plant is known for its dual warming and cooling effects

Fig 6: Peppermint (*Mentha piperita*)

Nutrients in Peppermint: Rich in antioxidants and potassium

Benefits of Peppermint: Leaves of this plant is used to improve concentration and digestion, often consumed in tea form to alleviate post-meal discomfort.

ii) Oregano (*Origanum vulgare*): Oregano oil is used for topical applications.

Fig 7: Oregano (*Origanum vulgare*)

Nutrients of Oregano: This herb is rich in antioxidants and quercetin

Benefits of Oregano: This plant has anti-inflammatory and antibacterial properties.

iii) Spearmint (*Menthas picata*): This herb is also known as garden mint, common mint, lamb mint and mackerel mint.

Fig 8: Spearmint (*Menthas picata*)

Nutrients of Spearmint: Magnesium, potassium and volatile oils

Benefits of Spearmint: This plant is used for digestion and improves gastrointestinal health.

4. Tulsi (*Ocimum sanctum*): It is commonly known as holy basil and it is widely cultivated throughout the Southeast Asian tropics.

Fig 9: Tulsi (*Ocimum sanctum*)

Nutrients in Tulsi:

Vitamins: Vitamin A and C

Minerals: Calcium, zinc, iron

Antioxidants: Eugenol

Benefits of Tulsi: This plant is used to boost immunity, reduces the stress and has anti-inflammatory properties.

5. Neem (*Azadirachta indica*): In traditional Ayurvedic medicine, people have used the bark, wood, sap, leaves, flowers, fruits, seeds and oils from the neem tree.

Fig 10: Neem (*Azadirachta indica*)

Nutrients in Neem:

Minerals: Calcium and magnesium

Phytochemicals: Flavonoids, tannins, carotenoids and fiber

Benefits of Neem: This tree is commonly known for antimicrobial, anti-inflammatory and skin health

6. Amla (*Phyllanthus emblica*): All parts of this plant are used for medicinal purposes, especially the fruit which has been in Ayurveda as a potent Rasayana and in traditional medicine for the treatment of diarrhea, jaundice and inflammation.

Fig 11: Amla (*Phyllanthus emblica*)

Nutrients in Amla:

Vitamins: High in vitamin C

Minerals: Iron

Phytochemicals: Polyphenols

Benefits of Amla: This tree is mainly used to support immunity, aids digestion and has antioxidant properties.

7. Turmeric (*Curcuma longa*): Like other colorful plant-based foods, turmeric is rich in phytonutrients that may protect the body by neutralizing free radicals and shielding the cells from damage.

Fig 12: Turmeric (*Curcuma longa*)

Nutrients in Turmeric:

Vitamins: Vitamins C and E

Minerals: Manganese

Phytochemicals: Curcumin

Benefits of Turmeric: This plant is used to support joint health, boosts immunity and has inti-inflammatory properties

8. Ginger (*Zingiber officinale*): Ginger has been used for thousands of years for the treatment of numerous ailments such as colds, arthritis migraines and hypertension.

Fig 13: Ginger (*Zingiber officinale*)

Nutrients in Ginger:

Vitamins: Vitamin B6

Minerals: Manganese and magnesium

Phytochemicals: Gingerol

Benefits of Ginger: It is used for digestion and reduces nausea and has anti-inflammatory properties.

9 Aloe Vera (*Aloe barbadensis* miller): Aloe vera is a cactus-like plant that grows in hot, dry climates. It is cultivated in subtropical regions around the world.

Fig 14: Aloe Vera

Nutrients in Aloe Vera:

Vitamins: Vitamin A C and E

Minerals: Calcium, magnesium and potassium

Phytochemicals: Folic acid

Benefits of Aloe Vera: It is used to hydrate the skin, helps for digestion and has healing properties for wounds.

10. Garlic (*Allium sativum*): Garlic is utilized as a spic and flavoring ingredient which is found to have fundamental nutritional components. This plant also has a high medicinal value and is used to cure a variety of human diseases.

Fig 15: Garlic

Nutrients in Garlic:

Minerals: Manganese, selenium and sulfur compounds.

Phytochemicals: Allicin

Benefits of Garlic: It is used to lower the blood pressure, improve heart health and has antibacterial properties.

CONCLUSION

Medicinal plants are invaluable in both traditional and modern medicine, providing natural and holistic options for many health issues. These plants are often more affordable than pharmaceuticals, especially in rural areas where these plants grow abundantly and can be harvested sustainably. This can make healthcare more accessible in low-income regions. In many cultures, medicinal plants have historical significance and are integral to traditional healing practices. This cultural connection can enhance acceptance and adherence to natural remedies. However, careful consideration is essential due to potential variability, dosage challenges and interaction risks.

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Chapter

3

THE EFFECT OF NANOPARTICLES ON QUORUM SENSING OF BACTERIA

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ABSTRACT

Bacterial cell communicates with each other by the quorum sensing process. The bacterial cell secretes biochemical compound known as auto inducers that is responsible for quorum sense of bacteria. The secreted molecules regulate the gene expression for virulence, biofilm formation and pigment production. Quorum quenching is the inhibition of quorum sensing process to control the pathogenicity and biofilm formation of bacteria. The quorum quenching is achieved by various enzymes and chemicals. The inhibitors are found natural or produced by microorganisms. Recently, Nanoparticles has great attention due to its size dependent properties. Among various synthesis method of nanoparticles biosynthesis process has attracted because of its non-toxic and ecofriendly processes. The metal and metallic nanoparticles such as silver, zinc oxide, titanium oxide nanoparticles showed efficient antimicrobial agents. The metal and metallic nanoparticles inhibit the quorum sensing of bacteria by inhibiting the components (auto inducer) of quorum sensing. The quorum sensing inhibition ability of the nanoparticles reduces the virulence and biofilm formation of nanoparticles; as a consequence the nanoparticles are alternative to conventional antimicrobial agents.

KEYWORDS: Quorum Sensing, Bacteria, Quorum Quenching, Inhibitors.

INTRODUCTION

The scientists Kenneth Nealson, Terry platt and Woodland Hastings first reported the Quorum sensing (QS) in 1970 (Nealson et al.1970). Bacterial species utilize quorum sensing to synchronize gene expression depends on the density of its local population (Jugder, 2022). Bacteria can communicate with each other by the dispersed biochemical molecules which are secreted by bacteria. The secreted molecule is beneficial for intra and inter bacterial species message and organizing bacterial cell activities such as motility, production of toxin, formation of bio-film, bioluminescence, sporulation, production of pigment, antibiotic production (Yada *et al.*, 2014; Pangastuti *et al.*, 2019). The secreted biochemical molecules are known as autoinducers (AI). Owing to the bacterial species density increases, the secreted autoinducers accumulate in their surrounding environment and bacterial species check the changes in cell number then modify the gene expression (Rutherford and Bassler, 2023).

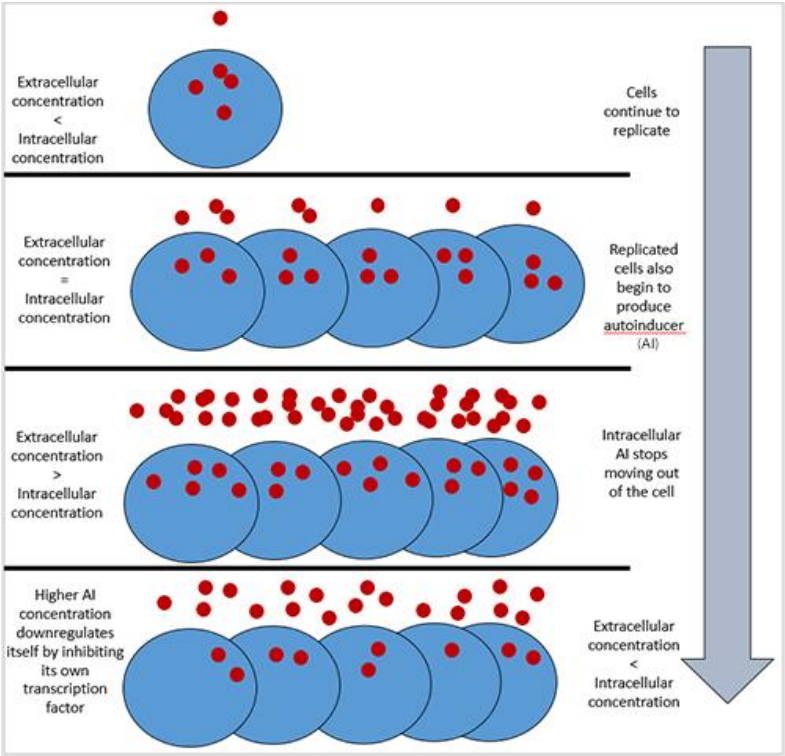

Fig 1: How quorum sensing works. Source: Jon Windsor (2020)

The mechanism of quorum sensing is based on the three basic principles, the primary principal is the signaling molecule (AI) is produced by bacterial species disperse away therefore the concentration is below the threshold necessary for detection due to the low density of bacterial species, whereas the high density of bacterial species leads to local high concentration of autoinducers which permitting detection and response. The second principle is the receptors found in the cytoplasm or membrane recognizes the autoinducers. Finally the principle behind the quorum sensing is the production of autoinducers as a result of recognizing the autoinducers in addition to activating gene expression to coordinate the behaviors of bacterial community (Kaplan and Greenberg 1985; Novick *et al.,* 1995; Seed *et al.,* 1995).

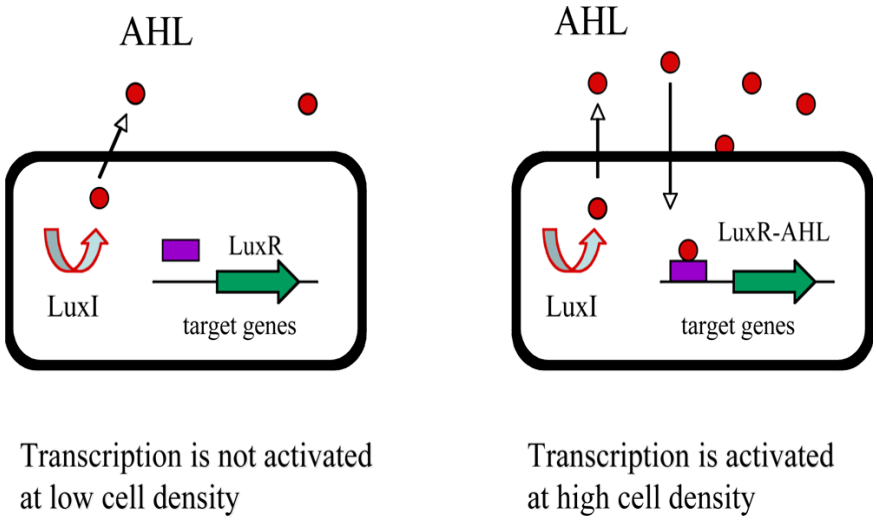

Fig 2: Low and High density of AIs effects of quorum sensing on transcription (Source: Li and Tian 2012)

The Quorum sensing is exhibited by the both gram positive and gram negative bacteria. Gram positive bacteria, both the bacteria utilize various types of quorum sensing system. Gram positive bacteria secreted oligopeptides via its cell wall and use the processed oligopeptides as autoinducers, whereas gram negative bacteria use acylatedhomoserine lactones as autoinducers (Miller and Bassler 2001). In gram positive bacteria the quorum sensing is occurred by peptides as auto inducing peptide (AIP), AIP combine with related membrane-bound histidine kinase receptor as a result of binding the receptor's kinase is activated and passes phosphate to a related cytoplasmic response regulator, the phosphorylated response regulator activates the transcription of the genes expression changes. Alternatively the AIPs control the gene expression changes by passing the AIPs back to the cytoplasm; there it can interact with transcription factors to control transcription factors activity leads to gene expression changes. Gram negative bacteria secrete small chemical molecules including acyl homoserine lactones (AHL). The auto inducing molecules produced by gram negative bacteria disperse across the inner and outer membrane while the high concentration of AIs are found adequately, AIs attach with cytoplasmic receptor which are transcription factors as a consequence of reaction the AI-attached receptors regulate gene expressions in the quorum sensing regulon (Wei *et al.*, 2011; Rutherford ST and Bassler BL, 2012).

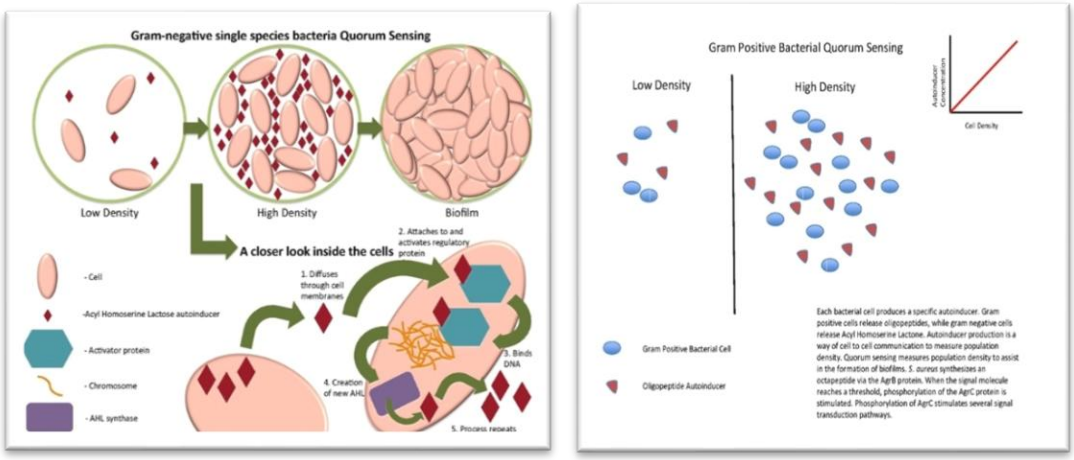

Fig 3: Mechanism of quorum sensing in Gram positive and Gram negative bacteria

The effect of quorum sensing in bioluminescence is first recorded in *Aliivibriofischeri*, the bioluminescent bacteria. The bioluminescence is regulated by auto inducer known as N-acyl – homoserinelactones, when the auto inducer is sufficiently found; the transcription of luciferase is induced as a consequence the bacteria produces bioluminescence. The bacteria *Pseudomonas aeruginosa* utilizes quorum sensing to organize the formation of biofilm, crawling motility, production of exopolysaccharide, virulence and cell aggregation. *Acinetobacter sp* produces N-acyl – homoserine lactones and also degrade the AHL molecules. The cell division of the *Escherichia coli* is partially regulated by the AI-2 mediated quorum sensing (Ahmer, 2004; Sauer *et al.*, 2002; Chan *et al.*, 2011; Igbinosa *et al.*, 2012).

QUORUM QUENCHING

The Quorum quenching is known as the inhibition of Quorum sensing, the quorum quenching is accomplished by deactivating the signaling molecules by employing enzyme. The autoinducer N-

acyl – homoserine lactones (AHL) is degraded by three types of enzyme including lactonases, amidases and oxidoreductases. The enzyme lactonase cleave the lactone ring, amidase hydrolyze the amide bond of the AHLs and divided it into fatty acids and homoserine lactone and the oxidation of acyl chain or reduction of 3-oxo-AHLs to 3-hydroxy-AHL is achieved by oxidoreductase. The enzymes that are degrading AHL present naturally and are formed by bacteria, archea and eukaryotic organisms. (Sikdar and Elias2020).

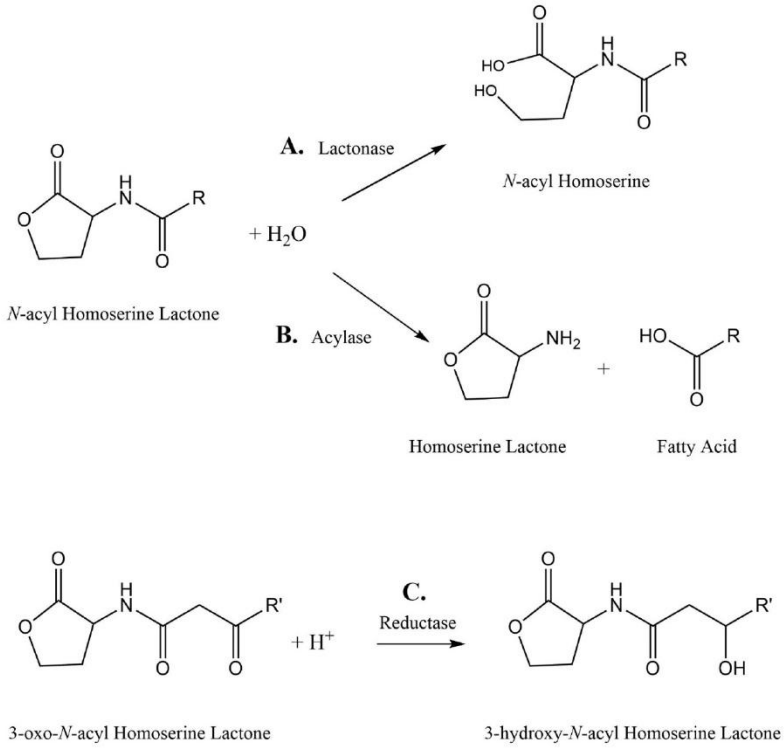

Fig 4: Enzymatic degradation of AHL. Source (Sikdar and Elias, 2020)

NANOPARTICLES IN QUORUM QUENCHING

Nanotechnology have gained much attention in recent times for developing of nanoparticles as quorum sensing inhibitors, this lead to the advancement of alternative antibacterial therapies (Singh *et al.*, 2015). The small size, high surface area to volume ratio, high percentage of molecules on the surface makes the nanoparticles is promising tool for inhibiting quorum sensing and biofilm formation (Mishra *et al.*, 2022). Nanoparticles can effectively intrude quorum sensing molecules, and nanoparticles have several advantages including reducing toxicity, conquering resistance and economical (Kanak *et al.*, 2023). Various methods are employed for the synthesis of metal nanoparticles, the methods including physical, chemical, enzymatic and biological methods. Among different method biological processes for the fabrication of metal nanoparticles have many advantages (Chitra and Manohar, 2022).

The metal and metallic nanoparticles are chiefly attracted due to its quorum quenching abilities. Among various metal nanoparticles, silver nanoparticles studied extensively for its anti-quorum sensing activity. The previous studies showed that silver nanoparticles reduced the synthesis of AHL in two soil *pseudomonas* species and silver nanoparticles inhibiting biofilm formation and virulence factors including LasA protease, LasBelastase, pyocianin, pyoverdin, pyochelin,

rhamolipid and alginate of *Pseudomonas aeruginosa* by reducing the levels of AHL and its transcriptional regulators LasIR and RhIiR in *Pseudomonas aeruginosa.* The virulence factor such as prodigiosin and protease of uropathogen*Serratia marcescens* and *Escherichia coli* is reduced by inhibiting quorum sensing of virulence factor. The TiO2 nanoparticles were incorporated with silver chloride and its showed anti-quorum sensing activity against *Chromobacteriumviolaceum*, the studies showed that the concentration of ATNPs was 20 times lower than the bactericidal concentration (Holban *et al.* 2016; Mohanty *et al.,* 2016; Singh *et al.,* 2015; Naik and Kowshik, 2014; Lee JH, 2014).

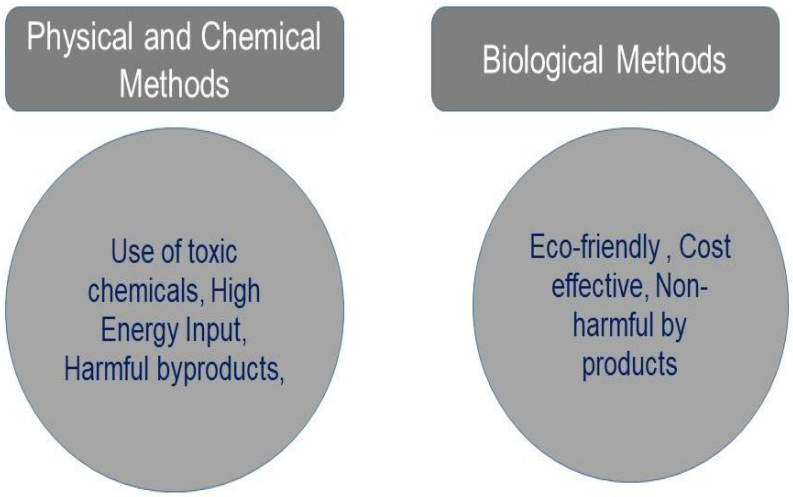

Fig 5: Different Approach of Nanoparticles Fabrication. Source: (Chitra *et al.,* 2023)

Zinc oxide nanoparticles inhibit the biofilm formation and pyocyanin, *Pseudomonas* quinolone signal, pyochelin production of *Pesudomonas aeruginosa*. Previous study reported that the zinc oxide nanoparticles decreased the pathogenicity of bacteria by inhibiting the quorum sensing and biofilm formation (Khan *et al.,* 2020). The authors of the previous study reported that the bacterial mediated synthesized silver nanoparticles showed quorum sensing inhibition to control the occurrence of multidrug resistance in *Chromobacteriumviolaceium* (Anju and Sarada, 2016).

CONCLUSION

This review focused on the role of nanotechnology in the inhibition of quorum sensing of bacteria which control the formation of biofilm, pigment, bioluminescence, pathogenicity by autoinducers. The metal and metallic nanoparticles have effect on autoinducers activity thus it reduces the pathogenicity and biofilm formation of bacteria. The nanoparticle shows the promising tool compared to other materials due to nanoparticles size and high surface area. The nanoparticles could be alternative to conventional antimicrobial agents owing to their ability to inhibit the quorum sensing.

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Chapter 4

PESTICIDE EFFECTS ON CROP

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ABSTRACT

Pesticides have played a crucial role in enhancing agricultural productivity in India, especially since the Green Revolution. This chapter examines the dual nature of pesticide use, highlighting its benefits in ensuring food security and farmers' income while addressing the significant challenges posed by health risks, environmental degradation, and economic burdens. The World Health Organization estimates that pesticide exposure contributes to numerous health issues, including acute poisoning and chronic diseases. Furthermore, the environmental consequences include the decline of beneficial organisms, soil and water contamination, and the emergence of pesticide-resistant pests. The need for sustainable alternatives is paramount, with strategies such as Integrated Pest Management (IPM), organic farming, precision agriculture, and biological control emerging as viable solutions. Government initiatives and regulatory frameworks must evolve to support these practices and promote public awareness among farmers. Case studies, including the endosulfan tragedy in Kerala and the rise of Bt cotton, illustrate the complex dynamics of pesticide use in India. This chapter emphasizes the urgent need for collaborative efforts among policymakers, researchers, and farmers to transition towards more sustainable agricultural practices that balance productivity with environmental and human health.

KEYWORDS: Pesticides, Agricultural productivity, Food security, Health risks, Environmental impact, Integrated Pest Management (IPM), Organic farming, Bio-pesticides, Pesticide resistance, Sustainable agriculture, Crop yields, Human health, Ecosystem disruption, Regulatory frameworks, Case studies, Precision agriculture, Biodiversity, Soil and water contamination, Community engagement, Sustainable alternatives.

INTRODUCTION

Pesticides have significantly contributed to enhancing agricultural productivity in India, aiding in the country's journey toward self-sufficiency in food production. The Green Revolution of the 1960s marked a pivotal moment in Indian agriculture, where the introduction of high-yielding varieties of crops and the extensive use of chemical fertilizers and pesticides transformed the agricultural landscape. However, the indiscriminate use of these chemicals has resulted in adverse effects on human health and the environment, raising questions about their long-term sustainability and safety.

This chapter explores the implications of pesticide use in India, including health risks, environmental consequences, and potential sustainable alternatives. It aims to provide a balanced view of the benefits and drawbacks associated with pesticides and emphasize the urgent need for more sustainable agricultural practices.

PESTICIDE USE AND ITS CONSEQUENCES

Pesticides play a crucial role in protecting crops from pests and diseases, thereby ensuring food security and agricultural profitability. They serve as a frontline defense against a myriad of threats, from insects to fungal infections. In India, the adoption of pesticides has led to increased crop yields and has been instrumental in boosting farmers' incomes. However, the benefits of pesticides are often overshadowed by the dangers they pose to human health and the environment.

The health implications of pesticide use are profound and far-reaching. The World Health Organization (WHO) estimates that pesticide exposure contributes to approximately 200,000 deaths globally each year, with India being one of the most affected countries (Aktar *et al.,* 2009). Farmers, agricultural workers, and even consumers can experience acute poisoning from direct contact or consumption of contaminated food. Chronic exposure can lead to severe health issues, including respiratory problems, hormonal imbalances, neurological disorders, and even cancers. Studies have found significant correlations between pesticide exposure and increasing rates of illnesses in agricultural communities, highlighting the need for urgent action to protect human health.

Moreover, the negative effects of pesticides extend beyond human health. They disrupt ecosystems, harm beneficial organisms such as pollinators, and contaminate soil and water sources. Pollinators, including bees and butterflies, play a critical role in food production by aiding in the pollination of many crops. The decline in pollinator populations, exacerbated by pesticide use, threatens food security and biodiversity. Furthermore, the contamination of soil and water bodies can have long-lasting effects on ecosystem health, affecting not only agricultural productivity but also the overall balance of local environments.

The over-reliance on chemical pesticides has also led to the emergence of pesticide-resistant pests, creating a vicious cycle that necessitates the application of even more toxic chemicals (Goulson, 2013). As pests evolve and develop resistance, farmers often resort to using higher doses or switching to more hazardous alternatives, further endangering human health and environmental stability. This cycle not only increases the financial burden on farmers but also exacerbates the ecological crisis.

THE NEED FOR ALTERNATIVES

Given the myriad challenges associated with pesticide use, there is an urgent need for alternatives that prioritize environmental sustainability and human health. Collaborative efforts among policymakers, researchers, and farmers are essential to promote awareness and develop safer alternatives to chemical pesticides. Transitioning away from harmful pesticides requires innovative solutions that integrate ecological principles and leverage the benefits of modern technology.

Several promising strategies are already gaining traction in India. The introduction of bio-pesticides, derived from natural materials, presents an effective alternative to synthetic chemicals. Bio-pesticides target specific pests without harming beneficial organisms, making them a safer choice for both humans and the environment. Additionally, organic farming practices, which eschew synthetic

inputs in favour of natural methods, have gained popularity among environmentally conscious consumers. Genetically modified crops, such as Bt cotton, illustrate the potential to control pests while minimizing environmental damage and health risks. These crops are engineered to produce a protein toxic to specific pests, significantly reducing the need for chemical insecticides.

However, these alternatives face challenges, including high costs, limited accessibility for small farmers, and a lack of awareness. Many smallholder farmers, who constitute a significant portion of India's agricultural workforce, struggle to afford the initial investment required for transitioning to organic or bio-pesticide practices. Additionally, a lack of training and education on alternative pest management methods can hinder adoption. Addressing these challenges requires targeted government interventions, farmer education programs, and community-based initiatives that promote sustainable agriculture.

GOVERNMENT AND POLICY INITIATIVES

India's regulatory framework for pesticide use is governed by the Insecticides Act of 1968, which regulates the import, manufacture, sale, and use of pesticides. The Central Insecticides Board and Registration Committee (CIBRC) oversees the approval of new pesticides and monitors their safety standards. While this regulatory framework is in place, enforcement challenges, particularly in rural areas, lead to widespread misuse. Many farmers resort to unregistered or counterfeit pesticides, which are often less effective and more harmful (Gupta, 2016). These practices undermine the integrity of agricultural systems and pose serious risks to health and the environment.

To address these challenges, the Indian government has promoted Integrated Pest Management (IPM) through various programs. IPM is a holistic approach that combines biological control, cultural practices, and resistant crop varieties to manage pests effectively while minimizing reliance on chemical pesticides. However, the adoption of IPM remains limited due to a lack of infrastructure, training, and awareness among smallholder farmers. The government must enhance efforts to provide resources, training, and support to farmers to encourage the widespread adoption of IPM practices.

Organic farming has been advocated as a more sustainable alternative to conventional agriculture. In 2016, Sikkim became India's first fully organic state, setting an example for the rest of the country. This achievement demonstrates that large-scale organic farming is possible and can yield economic benefits while safeguarding environmental health. Organic farming avoids synthetic chemicals, relying instead on natural methods like crop rotation, composting, and biological pest control. While this approach reduces environmental and health risks associated with pesticides, it is often more labour-intensive and yields lower compared to conventional farming methods (Pretty, 2005). Policymakers must recognize the potential of organic farming and invest in supporting farmers transitioning to these practices through subsidies, training programs, and research initiatives.

CASE STUDIES OF PESTICIDE IMPACT

1. The Endosulfan Tragedy in Kerala: One of the most notorious cases of pesticide misuse in India occurred in the Kasaragod district of Kerala, where endosulfan was aerially sprayed on cashew plantations for decades. This led to severe health problems, including birth defects, cancer, and neurological disorders among the local population. Public protests and scientific studies ultimately resulted in a nationwide ban on endosulfan in 2011, highlighting the dangers of persistent organic

pollutants and spurring calls for stricter pesticide regulations (Gupta, 2016). The endosulfan tragedy serves as a stark reminder of the consequences of unchecked pesticide use and the importance of regulatory oversight in safeguarding public health.

2. Pesticide Poisoning in Punjab: Punjab, one of India's most agriculturally productive states, faces severe environmental and health issues due to the overuse of pesticides. Studies have shown high levels of pesticide residues in soil, water, and food, contributing to rising cancer rates in the region. The daily train service from Punjab to Rajasthan, nicknamed the "cancer train," is filled with cancer patients seeking treatment. This situation has raised awareness of the risks of pesticide overuse and prompted a push toward more sustainable farming practices (Singh, 2019). The plight of Punjab's farmers underscores the need for a comprehensive strategy to mitigate the harmful effects of pesticides while ensuring food security.

3. Bt Cotton and Reduced Pesticide Use: A success story in Indian agriculture is the introduction of Bt cotton, a genetically modified crop that produces a toxin harmful to bollworms. Since its introduction in 2002, Bt cotton has significantly reduced the need for chemical insecticides, resulting in higher yields and lower pesticide costs for farmers. However, concerns remain about the long-term environmental impact of genetically modified crops and the potential for pests to develop resistance to Bt toxins (Yu, 2008). The case of Bt cotton highlights the complexity of technological solutions in agriculture, where benefits must be carefully weighed against potential ecological consequences.

FUTURE DIRECTIONS FOR SUSTAINABLE PEST MANAGEMENT

India's agricultural success hinges on balancing productivity and sustainability. While pesticides will likely remain part of the agricultural landscape, their role must be carefully managed to mitigate risks to human health and the environment. Several approaches hold promise for reducing pesticide dependence while maintaining crop productivity.

1. Precision Agriculture: The use of precision agriculture technologies, such as drones, satellite imagery, and sensors, allows for monitoring crop health and applying pesticides more efficiently. By targeting pesticide applications only to areas needing treatment, farmers can reduce pesticide use and environmental impact while saving costs. Precision agriculture holds the potential to revolutionize farming practices, ensuring that resources are utilized judiciously. Although still in its early stages in India, government support and investment could position precision agriculture as a key tool for sustainable pest management (Gagic *et al.,* 2019). This technology can enable farmers to make informed decisions based on real-time data, enhancing productivity while minimizing environmental harm.

2. Biological Control: Utilizing biological control agents, such as predators, parasites, and pathogens, presents a promising alternative to chemical pesticides. Introducing natural predators like ladybugs and spiders can help control aphid populations without chemical insecticides. Similarly, microbial pesticides, which use bacteria, fungi, or viruses to target specific pests, offer environmentally friendly pest control options. Expanding the use of biological control agents in India could help reduce reliance on synthetic pesticides (Kogan, 1998). Research and investment in developing effective biological control strategies can enhance the resilience of farming systems while preserving biodiversity.

3. Agroecological Approaches: Agroecology emphasizes integrating ecological principles into agricultural practices, offering a holistic approach to pest management. Promoting biodiversity, soil health, and ecosystem resilience reduces the need for chemical inputs and enhances farming systems' sustainability. Key practices include crop diversification, intercropping, and using cover crops. Encouraging farmers to adopt these practices could create more sustainable and resilient agricultural systems in India (Pretty, 2005). Agroecology not only supports pest management but also contributes to soil fertility, water conservation, and overall ecosystem health.

4. Public Awareness and Education: Educating farmers about the risks of pesticide overuse and promoting safer alternatives is vital for reducing pesticide-related problems in India. Government programs, NGOs, and research institutions can play a crucial role in providing training and resources to farmers, particularly smallholders who may lack access to modern pest management tools. Raising public awareness of health and environmental risks associated with pesticides can also drive demand for safer, pesticide-free food, encouraging a shift toward sustainable agricultural practices. Community engagement and farmer cooperatives can foster knowledge sharing and collaboration, enhancing the effectiveness of educational initiatives.

5. Strengthening Regulatory Frameworks: Improving enforcement of existing pesticide regulations and updating safety standards based on the latest scientific knowledge is essential for protecting public health and the environment. The Indian government should continue phasing out the most hazardous pesticides while promoting safer alternatives. Strengthening monitoring and enforcement mechanisms, particularly in rural areas, will be critical for ensuring compliance with pesticide regulations and providing farmers access to safer pest control options. Collaborative efforts between government agencies, research institutions, and farmers can create a robust regulatory framework that prioritizes safety and sustainability.

CONCLUSION

Pesticides have played a crucial role in boosting agricultural productivity in India, helping the country achieve self-sufficiency in food production. However, their widespread and often indiscriminate use has led to significant environmental, health, and economic challenges. From contaminating water sources to declining pollinator populations, the impact of pesticides on ecosystems and human health cannot be overlooked. The consequences of pesticide misuse necessitate a reevaluation of agricultural practices and policies.

The future of pest management in India lies in adopting more sustainable practices that balance the need for high crop yields with the imperative to protect human health and the environment. Integrated Pest Management, organic farming, precision agriculture, and biological control offer promising alternatives to chemical pesticides. However, these solutions must be made accessible to all farmers, particularly smallholders, who constitute the backbone of India's agricultural sector.

Policymakers, researchers, and farmers must work together to develop and implement strategies that reduce pesticide dependence while ensuring food security. By promoting awareness, improving access to safer alternatives, and strengthening regulatory frameworks, India can move toward a more sustainable agricultural future, one that protects both its people and its environment. The time for action is now, as the health of current and future generations and the integrity of ecosystems depend on the decisions made today.

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Chapter

5

BIOLOGICAL ACTIVITIES OF MEDICINAL PLANTS - PHARMACOLOGICAL ACTIVITIES OF ENICOSTEMMAAXILLARE

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ABSTRACT

Indian culture is the birthplace of Ayurvedic medicine. People have adopted it as their way of life from ancient times. The literature examines the different medicinal plants that are employed as treatments for various illnesses. One of the plants is called Enicostemmaaxillare. In a few local languages, it is also known as Vellaruku, Nahi, Mamajjaka, etc. It is primarily found in the coastal regions of India, Gujrat, Tamilnadu, and the Godawari basin. Diseases such as fever, anorexia, poor digestion, liver disorders, diabetes, snake bites, worms, wound healing; blood purification, etc. are reported to be effectively treated by it. Folklore people usually drink it in the form of swarasa. This essay aims to investigate the names, properties, and medicinal uses of Enicostemmaaxillare, as well as references to it in contemporary and Ayurvedic literature.

KEYWORDS: Enicostemmaaxillare, Vellaruku, Mamajjaka, Nahi, Pharmacological Activities.

INTRODUCTION

The perennial glabrous medicinal herb Enicostemmaaxillare (Lam.) A. Raynal belongs to the Gentianaceae family. With a broad distribution in Africa, America, and Asia, the plant is highly adapted to a variety of environmental, climatic, and soil conditions. (Abirami *et al.,* 2012; Ahamad *et al.,* 2020).

The original range of the species encompasses the following countries: Angola, Assam, Botswana, Cocos (Keeling) Islands, Ethiopia, Gulf States, India, Jawa, Kenya, South Africa, Lesser Sunda Islands, Malawi, Mozambique, Namibia, Oman, Pakistan, Saudi Arabia, Somalia, Sri Lanka, Sudan, Swaziland, Tanzania, Vietnam, West Himalaya, Yemen, Zambia, and Zimbabwe. In addition, E. axillare has been brought to and naturalized in a number of additional areas. There have been reports of it from countries in the Americas including Venezuela, Brazil, and Colombia. Furthermore, observations of E. axillare have been made in Australia and the Pacific islands. This species' widespread tolerance to a variety of environments is reflected in its global distribution. (Deepake *et al.,* 2012; Rana *et al.,* 2012; Shashina and Nampy, 2014).

Although E. axillare is often known as "Indian whitehead" in English, it is also referred to regionally as "Mameyjavo," "NanuKariyatun" in India, and "Makgonatsohle" in South Africa. It has a well-established reputation for being used in traditional medicine to manage, treat, and cure a variety of

illnesses, especially in rural areas where access to healthcare is severely limited. (Saravanan *et al.,* 2012). Because it is thought to be able to treat all illnesses, its local name in South Africa, "makgonatsohle," translates to "omnipotent." The plant is used to cure skin conditions, tumors, sporadic fevers, venereal infections, helminthiasis, and as a blood cleanser in the traditional medical system of India. (Saravanan *et al.,* 2012).

A secoiridoid glycoside called swertiamarin is regarded as the primary chemo taxonomical marker for the species. The presence of different phytochemicals has been linked to the significant pharmacological properties that the extracts of E. axillare showed, including antioxidant, anti-inflammatory, antimutagenic, antidiabetic, hepatoprotective, and anti-arthritic activities, as demonstrated by several pharmacological studies. (Gite *et al.,* 2010; Leelaprakash *et al.,* 2011; Nampaliwar *et al.,* 2012).

Existing studies have not showcased the medicinal value of *E. axillare*, and to the best of our knowledge, phytochemistry, pharmacology potentials, and toxicity study. Hence, the present review aimed to extensively review and summarize previously published articles on the botany, traditional medicinal uses, pharmacological potentials, clinical applications, and toxicology of *E. axillare*, to provide an in-depth reference for researchers to discover its therapeutic potentials for further investigation and full utilization.

E. AXILLARE IN AYURVEDIC LITERATURE

The Vedic literature has no references to E. axillare. There is no mention of this plant in either Brihattrayi or Laghuttrayi. Several Nighantu (Ayurvedic Materia Medica) references this herb. The Herb was first recorded in Lakshmanadi Varga's Shodhal Nighantu (12th century AD). Shaligram Nighnatu, written later in the 1800s, made reference to this phenomenon. Nighnatu Adarsha and Priya Nighnatu from the 20th century also make reference to it.

USES IN FOLKLORE MEDICINE

Folklore information and Ethnomedicinal studies about plants and herbs elucidate their importance in the management of human diseases and ailments all over the world (Odebunmi *et al.,* 2022). Plants have been utilized by humans for health purposes since ancient times, particularly in developing countries. A significant portion of the global population relies on plants as a crucial source of food and primary healthcare (Guler *et al.,* 2021; Gune € s *et al.,* 2018)

TAXONOMY

Kingdom	Plantae
Subdivision	Angiospermae
Class	Dicotyledonae
Subclass	Gamapetalae
Serius	Bicarpellatae
Order	Gentianales
Family	Gentianacae
Genus	Enicostemma
Species	axillare

NOMENCLATURE

The word Enicostemma is probably formed from the three words, "en" means inside, "icos" means 20 and "stemma" means wreath or circle due to the many flowers arranged in circles in the leaf axils along the stem.

GEOGRAPHICAL DISTRIBUTION

This tropical genus is widely distributed in South America, Africa, and Asia. E. littorale grows in many diverse habitats from savannas, grasslands, forests to beaches, from wet to very dry and also survives in a very saline environment.

MORPHOLOGY OF E. AXILLARE

It is an erect, perennial herb attaining height of 15-20 inch, simple or branched at the base (Figure: 1). Stem cylindric, glabrous with a decurrent ridge below each leaf, internodes short 0.8 to 1.5 cm long. Leaves are opposite decussate, lanceolate, 3 to 6 by 0.5 to 0.7 cm, sessile, often narrow, green in colour, apex obtuse, 3 nerved, venation pinnate, upper surface rough, lower glabrous. Flowers are small white with green lines, drying yellowish, sessile or subsessile; white with green lines, drying yellowish, sessile or subsessile; whorled and in clusters, 5- merous (rarely 3-, 4-, or 6- merous); calyx narrow, 3 to 4 mm long, campanulate; divided down halfway to 2/3, thin, persistent in fruit, with colleters. Corolla small, white, 6 to 8 mm long, tubular to funnel shaped at the base contains numerous seeds. Ovary is without nectary disk; stigmas capitate, slightly bilobed. Fruit a capsule, obovoid, seeds rounded, not winged. Root is slender, tapering, rough, secondary root filiform, 5 to 15 cm length, 0.3 to 2.5 cm in diameter, light yellow externally, creamish white internally. Stamens inserted below the sinuses, just above the middle of the tube; filaments 1.5–2.3 mm long, with a double hood at the insertion point (MurukesuMudaliyar KS 1988, Kannusamipillai S.1998, Kirtikar KR 2003).

Figure 1: Enicostemmaaxillare

Flowering and Fruiting season: From July to November.

Collection: October-November.

PHARMACOLOGICAL PROPERTIES OF E. AXILLARE

The antibacterial activity of the methanolic extract of E. axillare leaves was demonstrated in a dose-dependent manner against E. coli, Proteus mirabilis, Bacillus subtilis, Klebsiella penumoniae, and Enterococcus (Nila and Karthikeyan, 2017). Moreover, Aspergillus niger and Candida albicans were well combated by the ethanol extract of E. axillare subsp. littorale (Leelaprakash *et al.,* 2012).

The study examined the anticancer effect of a methanolic extract of the total plant material of E. axillare subsp. littorale against Dalton's ascetic lymphoma in albino mice. The mice with tumors had a noticeably longer mean survival time when the extract was added. Additionally, administration of the extract increased peritoneal cell counts, while intraperitoneal injection of Dalton's ascitic lymphoma (DAL) cells reduced the formation of tumor cells in rats. Furthermore, the modified hematological indices, protein, and packed cell volume (PCV) in the experimental mice were suppressed by the methanol extract (Kavimani & Manisenthlkumar, 2000).

The diabetic rats' blood glucose and thiobarbituric acid reactive substances (TBARS) were markedly decreased after receiving the aqueous extract (2 g/kg), but their glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) activities were elevated. Moreover, the plant extract was more potent than the standard medication, insulin. Sonawane *et al.,* discovered that cold and hot aqueous extracts of E. axillare subsp. littorale decreased blood glucose, serum triacylglycerol, and cholesterol levels in type 1 diabetic rats. Furthermore, research showed that swertiamarin, the main ingredient in the E. axillare subsp. littorale hot water extract, had antidiabetic activity and improved lipid parameters in rats suffering from type 1 diabetes (Sonawane *et al.,* 2010).

In hypocholesterolemic rats with hepatoma, the aerial portion of E. axillare subsp. littorale isolated in ethanol decreased serum cholesterol. Furthermore, by free cholesterol esterification in high-density lipoprotein, the extract increased the activity of cholesterol acyltransferase (Gopal *et al.,* 2011).

E. axillare subsp. littorale demonstrated antacid and antipyretic properties in a different investigation. The study found that an aqueous extract of the plant's aerial portions (100–400 mg/kg bw) significantly lowered the body temperature that lipopolysaccharide-induced hyperthermia in mice over the course of five hours. The extract showed antacid potency in the in vitro experiment that was comparable to a reference antacid medication employed in the study, indicating that the extract has antacid-like and antipyretic qualities (Garad *et al.,* 2012).

The antiulcer properties of the aerial portions of E. axillare subsp. littorale were examined in rats that were ulcerogenic due to pyloric ligation, aspirin, and ethanol. Acidity, gastric secretion volume, free acidity, and gastric pH all decreased in a dose-dependent manner in this study when the aqueous extract was administered prior to the production of ulcers. Furthermore, the aqueous extract of E. axillare subsp. littorale inhibited serum albumin's denaturation in a dose-dependent manner. On the other hand, the methanol extract demonstrated anti-inflammatory and anti-ulcer properties. According to Roy *et al.,* (2010), the latter was connected to its antioxidant activity.

Preclinical research on E. axillare has revealed immunomodulatory potential. In a study, the weight of the spleen and thymus, as well as the lymphocyte and total leukocyte counts, were significantly increased by the methanolic extract of the entire E. axillare plant at 200 and 100 mg/kg bw. Additionally, a dose-dependent increase in the antibody titer value was observed. The methanolic extract of E. axillare substantially and dose-dependently reduced the generation of proinflammatory cytokines and nitric oxide. At 25 and 10 μg/mL, the plant extract induced a phagocytic response in the in vitro portion of the investigation. The authors reported that the E. axillare extract inhibited the

generation of pro-inflammatory cytokines and affected humorally and cell-mediated immune activities. (Saravanan *et al.,* 2012).

CONCLUSION

Enicostemaaxillare (Nahi) is the subject of this review, which also includes basic science, pharmacological information, clinical data, and Ayurvedic literature. The entire plant known as panchang is said to be helpful in treating a number of ailments, such as diabetes, obesity, pyrexia, cough, stomach aches, and snake bites, according to Ayurvedic literature. The critique of ethnobotany implies that individuals employ traditional medicine to address a range of ailments. Using published research articles from journals, a comprehensive evaluation of the literature is carried out, showing that the researchers looked into the phytochemical analysis, medicinal properties, and potential for treating a variety of disorders of the plant. This work is the outcome of a thorough analysis of the literature, which showed that more study of Enicostemmaaxillare in relation to disorders in vivo and in vitro is required.

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Chapter 6

THE ROLE AND DECLINE OF AMPHIBIANS IN ECOSYSTEMS

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INTRODUCTION

Amphibians play a pivotal role in maintaining the balance of ecosystems. They contribute significantly to biodiversity, pest control, nutrient cycling, and ecosystem health. However, over the past few decades, amphibians have faced unprecedented declines worldwide. Factors such as habitat loss, pollution, climate change, and emerging diseases like chytridiomycosis have pushed many species toward extinction. Understanding the importance of amphibians, the causes of their decline, and the strategies for their conservation is essential for maintaining healthy ecosystems and ensuring biodiversity's longevity (Wake & Vredenburg, 2008).

This chapter explores the vital role amphibians play in ecosystems, the factors driving their decline, and the broader ecological consequences of losing amphibian populations. The final section outlines key conservation strategies and global initiatives aimed at mitigating these losses.

AMPHIBIANS: KEY CONTRIBUTORS TO ECOSYSTEM FUNCTION

BIODIVERSITY AND POPULATION CONTROL

Amphibians are vital for maintaining biodiversity in both aquatic and terrestrial ecosystems. They help control insect populations, thereby reducing the prevalence of pests that damage crops and spread diseases. For example, frogs and toads consume large quantities of mosquitoes, contributing to the reduction of diseases such as malaria and dengue (Blaustein & Kiesecker, 2002).

Additionally, amphibians occupy multiple trophic levels, acting as both predator and prey. Their presence ensures the smooth functioning of food webs. Tadpoles, which consume algae, prevent overgrowth in aquatic systems, and adult amphibians serve as prey for numerous predators, including birds, mammals, and fish.

AMPHIBIANS AS BIOINDICATORS

Amphibians' permeable skin makes them sensitive to environmental changes, particularly pollution, temperature shifts, and habitat alterations. As such, they serve as bioindicators—species whose health reflects the overall health of the environment (Hocking & Babbitt, 2014). A decline in amphibian populations often signals larger ecological problems, including water pollution, climate stress, or habitat degradation.

NUTRIENT CYCLING AND ECOSYSTEM HEALTH

Amphibians contribute to nutrient cycling in both terrestrial and aquatic ecosystems. By feeding on organic material and algae, tadpoles help break down detritus, promoting decomposition. The

movement of amphibians between water and land also facilitates the transfer of nutrients across ecosystems, enriching soils and supporting plant growth (Whiles *et al.*, 2006).

DRIVERS OF AMPHIBIAN DECLINE

HABITAT DESTRUCTION

Habitat loss is one of the primary drivers of amphibian decline. Wetland drainage, deforestation, and urbanization have significantly reduced the areas where amphibians can live and breed. Fragmentation of habitats isolates populations, making it difficult for amphibians to migrate, find mates, or access resources. This leads to reduced genetic diversity and, ultimately, population declines (Stuart *et al.*, 2004).

POLLUTION AND ITS EFFECTS

Pollution has devastating effects on amphibian populations due to their sensitive skin, which allows for easy absorption of harmful chemicals. Industrial pollutants, pesticides, and heavy metals disrupt amphibian reproductive systems and immune responses, leading to deformities, sterility, and increased susceptibility to diseases (Sparling *et al.*, 2010).

Table 1: Pollutants Affecting Amphibians and Their Effects

Pollutant Type	Source	Effect on Amphibians	Citation
Pesticides (e.g., atrazine)	Agricultural runoff	Hormonal disruption, sterility, deformities	Hayes *et al.*, 2010
Heavy Metals (e.g., mercury)	Industrial emissions	Neurological damage, reduced survival rates	Blaustein *et al.*, 2012
Endocrine Disruptors	Plastics and personal care products	Altered reproductive systems, skewed sex ratios	Sowers *et al.*, 2009

CLIMATE CHANGE AND AMPHIBIANS

Climate change represents one of the most critical and escalating threats to amphibian populations globally, primarily due to the species' sensitivity to environmental conditions such as temperature and moisture. Amphibians have evolved to thrive within specific ecological niches, relying on stable temperatures and water availability for critical life processes such as breeding, foraging, and thermoregulation. This dependence makes them particularly vulnerable to the fluctuations caused by climate change. As global temperatures rise, many amphibian species are facing increased stress. For example, temperature shifts can directly affect amphibians' physiological processes, such as metabolism, growth rates, and reproductive success. Amphibians are ectothermic animals, meaning they regulate their body temperature through external sources. When their external environment becomes too hot or too cold, they struggle to maintain homeostasis, leading to weakened immune systems, impaired reproduction, and increased mortality rates. Furthermore, climate change is significantly impacting weather patterns, leading to unpredictable precipitation events, extended droughts, and altered seasonal cycles. These changes can drastically affect amphibian breeding habitats. Many amphibians rely on temporary water bodies, such as ponds and vernal pools, for reproduction. With changes in precipitation patterns, these breeding sites may dry out prematurely, causing massive losses of eggs and larvae. Additionally, erratic weather patterns can cause mismatches in the timing of breeding and food availability, particularly for amphibians that depend

on synchronized seasonal cues for reproduction. If breeding occurs at the wrong time, newly hatched larvae may face food shortages, leading to higher mortality rates and population declines (Corn, 2005). Even in areas where water remains available, the timing and intensity of rainfalls can be unpredictable, disrupting the delicate balance that amphibians depend on. In some regions, amphibians are being forced to shift their range to higher altitudes or latitudes in search of suitable climates, but this often comes at the cost of increased competition for resources, habitat fragmentation, and exposure to new predators and diseases. As climate change accelerates, amphibians may struggle to adapt fast enough, leading to widespread declines and extinctions.

DISEASE AND THE SPREAD OF CHYTRID FUNGUS

Another significant threat to global amphibian populations is the emergence of infectious diseases, particularly chytridiomycosis. This disease is caused by the fungal pathogen Batrachochytrium dendrobatidis (Bd), commonly known as chytrid fungus, which has been responsible for dramatic amphibian population declines and extinctions across various continents. Chytridiomycosis has been identified as one of the deadliest wildlife diseases ever recorded, affecting hundreds of amphibian species globally. Chytrid fungus spreads rapidly in water, making aquatic and semi-aquatic amphibian species particularly vulnerable. It affects both larval and adult amphibians by infecting the keratinized tissues in their skin. Amphibians rely heavily on their skin for respiration, hydration, and maintaining electrolyte balance, so even minor disruptions in skin function can have lethal consequences. As the chytrid infection progresses, it causes thickening and hyperkeratosis of the skin, impairing these vital functions and eventually leading to death through dehydration, asphyxiation, or cardiac arrest (Berger *et al.,* 1998). The spread of chytrid fungus has been exacerbated by human activities, including the global trade of amphibians for the pet industry and research purposes. Additionally, climate change may indirectly influence the spread of chytrid fungus by altering the environmental conditions that favor its growth. Chytrid thrives in cooler, moist environments, and as amphibians are forced to migrate to higher altitudes due to climate change, they may inadvertently move into areas where the fungus is more prevalent, increasing their risk of infection.

This deadly disease has had devastating impacts on biodiversity, with entire populations being wiped out in just a few years. Some species have gone extinct in the wild, and others have experienced catastrophic population declines. While certain species have shown some resistance or recovery, the vast majority of affected amphibians continue to struggle against the spread of this disease. Conservationists have focused efforts on developing disease management strategies, but the spread of chytridiomycosis remains a global challenge.

CONSEQUENCES OF AMPHIBIAN DECLINE

The decline of amphibian populations has far-reaching consequences, affecting not only the species themselves but also the ecosystems in which they play essential roles. Amphibians serve as keystone species in many ecosystems, contributing to the balance of food webs, regulating insect populations, and maintaining biodiversity. The loss of amphibians can have cascading effects, leading to ecological imbalances, biodiversity loss, and economic costs.

IMPACT ON FOOD WEBS

Amphibians occupy a crucial niche in many food webs, serving as both predators and prey. They help control insect populations by feeding on a wide variety of invertebrates, including many pest species that can damage crops or spread diseases to humans. In the absence of amphibians, insect populations can surge, leading to increased pest pressures on agriculture and higher incidences of vector-borne diseases such as malaria and dengue fever. Moreover, amphibians are an essential food source for a range of predators, including birds, mammals, reptiles, and other amphibians. The loss of amphibians from ecosystems can cause these predator populations to decline, leading to further disruptions in the food web. In some cases, the decline of amphibians can lead to trophic cascades, where the entire structure of the ecosystem becomes destabilized due to the loss of a keystone species (Whiles *et al.*, 2013).

LOSS OF BIODIVERSITY AND ECOSYSTEM RESILIENCE

Amphibians are among the most diverse groups of vertebrates, with over 7,000 known species. Their decline represents a significant loss of biodiversity, weakening the overall resilience of ecosystems. Biodiversity is critical for the stability and functioning of ecosystems, as it helps them withstand environmental stresses and recover from disturbances. When amphibians are lost, ecosystems become more vulnerable to other threats, such as invasive species, habitat degradation, and climate change. The decline of amphibians also reduces the genetic diversity within populations, making species less adaptable to changing environmental conditions. This loss of genetic diversity further exacerbates the risk of extinction, as populations become more susceptible to diseases, extreme weather events, and other environmental changes (Blaustein *et al.*, 2011).

ECONOMIC AND ECOLOGICAL COSTS

The decline of amphibians carries significant economic costs, particularly in agricultural regions where amphibians provide natural pest control services. Without amphibians to regulate insect populations, farmers may need to rely more heavily on chemical pesticides, which can be costly and have negative environmental impacts. The increased use of pesticides can also lead to the development of pesticide-resistant pest species, further compounding the problem. Additionally, the decline of amphibians can impact ecotourism industries, particularly in regions rich in amphibian biodiversity, such as tropical rainforests. Ecotourism is an important source of income for many communities, and the loss of amphibians can reduce the appeal of these natural areas to tourists. As amphibian species disappear, the economic benefits of ecotourism may diminish, leading to reduced income for local communities and less funding for conservation efforts (Gascon *et al.*, 2007).

CONSERVATION STRATEGIES FOR AMPHIBIAN PROTECTION

Given the critical role that amphibians play in ecosystems and the numerous threats they face, it is essential to implement comprehensive conservation strategies to protect these species. Conservation efforts must address the various factors contributing to amphibian declines, including habitat loss, climate change, pollution, disease, and overexploitation.

HABITAT CONSERVATION AND RESTORATION

One of the most effective strategies for protecting amphibians is the conservation and restoration of their natural habitats. Amphibians rely on specific environmental conditions for breeding, foraging, and survival, so the preservation of wetlands, forests, and other critical habitats is essential.

Conservation efforts should focus on protecting existing habitats from destruction and degradation, particularly in areas where amphibians are most vulnerable. Restoration efforts are also critical in areas where habitats have been lost or degraded. Reforestation, wetland restoration, and the creation of habitat corridors can help amphibian populations recover by providing them with suitable breeding and foraging sites. Habitat corridors, in particular, are important for allowing amphibians to migrate between fragmented habitats, enabling them to maintain genetic diversity and adapt to changing environmental conditions (Semlitsch, 2000). Legal protections for critical habitats, such as the establishment of nature reserves and protected areas, are also crucial for the long-term survival of amphibians. These protections can prevent further habitat loss and ensure that amphibians have access to the resources they need to thrive.

POLLUTION CONTROL MEASURES

Amphibians are highly sensitive to pollution, particularly in aquatic environments where they spend much of their life cycle. Pollution from agricultural runoff, industrial waste, and urban development can contaminate amphibian habitats, leading to developmental abnormalities, reduced reproductive success, and increased mortality. To protect amphibians from the harmful effects of pollution, it is essential to implement pollution control measures, particularly in areas near amphibian habitats. Buffer zones around wetlands can help reduce the amount of pollutants entering these sensitive ecosystems, while the reduction of pesticide use and the regulation of industrial emissions can mitigate the impact of pollution on amphibian populations (Mann *et al.*, 2009). In addition to reducing pollution, efforts should be made to monitor and assess the health of amphibian populations in polluted areas. By tracking changes in amphibian populations and their habitats, conservationists can identify areas where pollution control measures are most needed and adjust their strategies accordingly.

CAPTIVE BREEDING PROGRAMS AND DISEASE MANAGEMENT

Captive breeding programs have been a key tool in preventing the extinction of critically endangered amphibian species. These programs involve breeding amphibians in controlled environments, such as zoos or research facilities, with the goal of reintroducing them into the wild once their populations have recovered. Captive breeding programs are particularly important for species that have been severely impacted by habitat loss or disease, such as chytridiomycosis. By breeding amphibians in captivity, conservationists can protect them from the immediate threats they face in the wild, while also working to develop treatments and management strategies for diseases like chytrid fungus (Griffiths & Pavajeau, 2008). Disease management is a critical component of amphibian conservation, particularly in the case of chytridiomycosis. Efforts are being made to develop treatments for chytrid fungus, including antifungal medications and probiotics that can help amphibians resist infection. Additionally, conservationists are working to identify amphibian species that are naturally resistant to chytrid fungus, with the hope of breeding these individuals to create more resilient populations.

POLICY AND GLOBAL INITIATIVES

Amphibian conservation requires international cooperation and coordination, as many of the threats facing amphibians are global in nature. Policies such as the Convention on Biological Diversity (CBD) and global initiatives like Amphibian Ark aim to protect amphibian species through research,

public awareness campaigns, and coordinated conservation actions. Amphibian Ark, for example, is a global initiative that focuses on the conservation of amphibians through captive breeding, habitat restoration, and disease management. By collaborating with governments, NGOs, and research institutions, Amphibian Ark works to prevent the extinction of amphibian species and ensure their long-term survival (Gascon *et al.,* 2007). In addition to global initiatives, national and local policies play an important role in amphibian conservation. Governments can enact laws to protect amphibian habitats, regulate the use of pesticides and pollutants, and fund research and conservation efforts. Public awareness campaigns can also help educate communities about the importance of amphibians and the actions they can take to protect these species.

CONCLUSION

The decline of amphibians is a critical environmental issue with far-reaching consequences for ecosystems, biodiversity, and human well-being. As bioindicators, amphibians signal broader environmental problems, and their loss disrupts food webs and weakens ecosystem resilience. Addressing the drivers of amphibian decline—habitat destruction, pollution, climate change, and disease—requires global collaboration and sustained conservation efforts. Protecting amphibians is essential for preserving the health of ecosystems and ensuring the continued provision of vital ecosystem services.

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Chapter

7

EXPLORING THE LARVICIDAL POTENTIAL OF *DIDEMNUM PSAMMATODE* AGAINST *ANOPHELES STEPHENSI*: A NOVEL BIOCONTROL APPROACH

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INTRODUCTION

Vector-borne diseases, particularly those spread by mosquitoes, pose a significant global health challenge. The use of synthetic chemical insecticides has been the primary approach to control mosquito populations. However, their widespread use has led to several environmental and health concerns, including the development of resistance in mosquito populations, toxicity to non-target organisms and pollution. Consequently, there is an urgent need for alternative, eco-friendly larvicides that are effective, safe, and sustainable. In this context, marine-derived compounds offer a promising solution. Previous studies have highlighted the potential of various marine organisms as sources of natural larvicides. *Didemnum psammatode*, a colonial ascidian found in tropical and temperate seas, is one such organism that exhibits a wide range of biological activities, including antimicrobial, antifouling, and cytotoxic properties. However, its larvicidal activity against mosquito larvae remains underexplored.

This study aims to investigate the larvicidal activity of *Didemnum psammatode* extracts against mosquito larvae. By evaluating its efficacy, the research seeks to contribute to the development of novel, marine-based larvicides that could offer a sustainable alternative to synthetic chemicals. Additionally, the study will explore the chemical composition of the extracts to identify the active compounds responsible for larvicidal activity. Understanding the potential of *Didemnum psammatode* as a larvicide could pave the way for innovative strategies in mosquito control, aligning with global efforts to combat vector-borne diseases through environmentally friendly approaches.

While numerous marine organisms have been investigated for their bioactive properties, the larvicidal potential of *Didemnum psammatode* remains largely unexplored. Existing research on ascidians like *Polyclinum indicum* and *Phallusia nigra* has revealed significant larvicidal activity, suggesting that ascidians, including *Didemnum candidum*, may hold promise as natural larvicides (Sundararajan, *et al.,* 2017, Rahuman, *et al.,* 2018, Paripooranaselvi and Meenakshi, 2012).

This study aims to bridge the knowledge gap by assessing the larvicidal efficacy of *Didemnum psammatode* extracts, which have not yet been evaluated for mosquito larvicidal activity.

MATERIALS AND METHODS

COLLECTION OF ANIMAL MATERIAL

Samples of colonial ascidian *Didemnum psammatode* Sluiter, 1895 were collected during the low tide from the intertidal rocky area of Hare Island. The samples were washed with seawater to remove sand, mud and overgrowing organisms at the site collection and then transported to the laboratory. Identification up to the species level was carried out based on the key to the identification of Indian ascidians by Meenakshi, 1997.

SYSTEMATIC POSITION

Didemnum psammatode belongs to Phylum: Chordata: Subphylum: Urochordata; Class: Ascidiaceae; Order: Enterogona; Suborder: Aplousobranchia; Family: Didemnidae; Genus: *Didemnum*; Species: *psammatode*

ANIMAL MATERIAL

Ascidians commonly called 'sea squirts' are an interesting group of marine, sedentary organisms found to occur in abundance in the Tuticorin coast. It is sessile and filters feeding. It lives on plankton that it filters from seawater with a mucous net.

Plate – 1 shows the colony of *Didemnum psammatode*. It is thin and soft. In the test spicules are few, but abundant ovoid faecal pellets are present. Live and preserved colonies are grey in colour.

PREPARATION OF POWDER

The specimens were dried under shade. The dried animals were homogenized to get a coarse powder. The dried powders of the tunicate -*Didemnum psammatode* were used.

PREPARATION OF EXTRACT

Didemnum psammatode was dried, ground into a fine powder, and placed in a Soxhlet extractor. Ethanol (or chosen solvent) was used as the extraction solvent. The extraction process was carried out until the solvent in the siphon tube became colorless. The resulting extract was concentrated using a rotary evaporator and stored for further analysis. (Azmir, 2013).

LARVICIDAL ACTIVITY

Anopheles stephensi. Larvae were collected from stagnant water pools and identified by their horizontal floating posture. Five larvae were transferred to each of six Petri plates containing 25 ml of water. Plates labeled a to e received 10 ml, 50 ml, 100 ml, 250 ml, and 500 ml of ethanol extract of *Didemnum psammatode*, respectively, while plate f served as a control without extract. The experiment was conducted in triplicate, and larval mortality was recorded hourly for 24 hours.

RESULT AND DISCUSSION

In the present investigation, the ethanolic extract of *Didemnum psammatode* was tested for its larvicidal activity against *Anopheles stephensi*. mosquito larvae. The results, presented in Table 1, Table 2, Figure 2, and Plates 5 and 6, show a dose-dependent mortality rate. The highest concentration of the extract exhibited a highly significant mortality rate. Specifically, the concentrations of 500, 250, 100, 50, and 10 μg/ml resulted in 93%, 87%, 67%, 53%, and 27% mortality, respectively. No mortality was observed in the control group.

The ethanolic extract of *Didemnum psammatode* demonstrated maximum larvicidal activity against *Anopheles stephensi*. mosquito larvae at 500 μg/ml. This finding is consistent with various studies on larvicidal agents: Silva *et al.,* (2021) attributed the activity of *Eugenia calycina* to spathulenol and

related compounds; Meenakshi *et al.* (2012) noted that *Phallusianigra* contains alkaloids and terpenoids; Deepak Kumar *et al,* (2014) linked the activity of *Cassia occidentalis* to carbohydrates and tannins; and Arumugam *et al.* (2019) found that *Didemnum bistratum* contains anthraquinones and indole spermidine alkaloids. Additionally, Thakur *et al.,* (2004) identified saponins in sea cucumbers as active compounds, while Perez *et al.,* (2020) highlighted chitosan derivatives in marine crabs. Torres *et al.* (2015) found unsaturated steroids and flavonoids in *Anacardium occidentale* extracts, Rouari *et al.* (2022) cited rutin and caffeoylquinic acid in *Oudneya Africana*, and Priya *et al.* (2016) noted phenols and flavonoids in *Eudistoma viride*. Overall, the larvicidal effects of these natural compounds are often due to their diverse bioactive constituents.

Table 1: Effect of ethanol extract of *Didemnum psammatode* against *Anopheles stephensi*. larvae

Concentration of ethanolic extract of *Didemnum psammatode*										**Control**	
500 µg/ml		**250 µg/ml**		**100 µg/ml**		**50 µg/ml**		**10 µg/ml**			
D	L	D	L	D	L	D	L	D	L	L	D
5	0	4	1	3	2	2	3	2	3	0	5
4	1	4	1	4	1	3	2	1	4	0	5
5	0	5	0	3	2	3	2	1	4	0	5

Table 2: Effect of ethanol extract of *Didemnum psammatode* on Percentage of Mortality

	I	II	III	Mean
500 µg/ml	100	80	100	93
250 µg/ml	80	80	100	87
100 µg/ml	60	80	60	67
50 µg/ml	40	60	60	53
10 µg/ml	40	20	20	27
Control	0	0	0	0

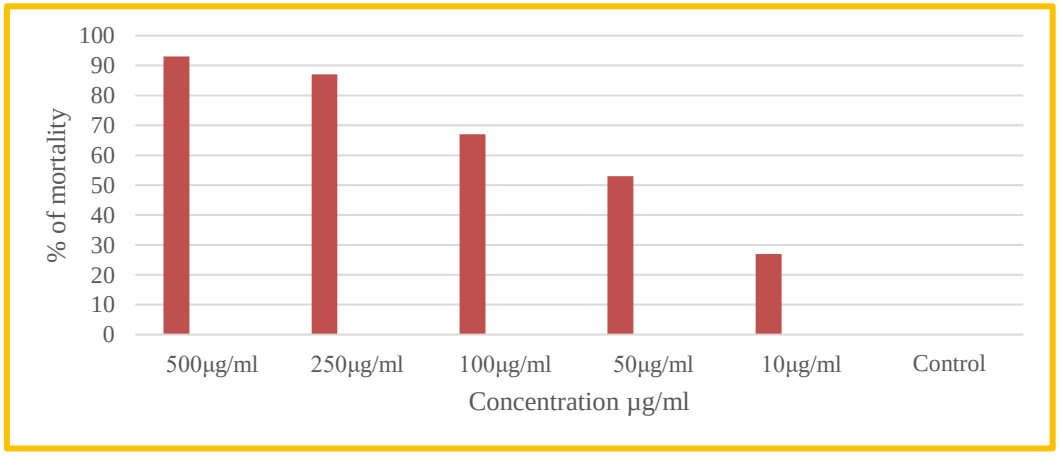


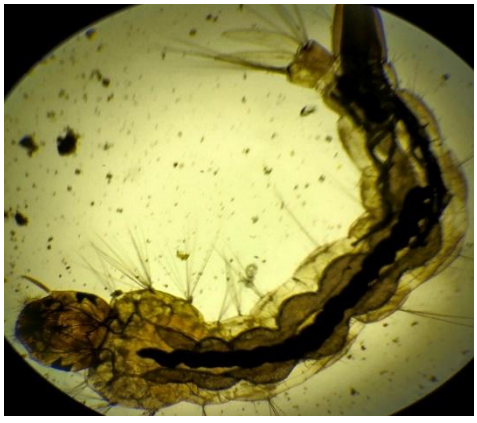
Fig 1: Effect of ethanol extract of *Didemnum psammatode* against *Anopheles stephensi*. Larvae

Plate 1: ***Didemnum psammatode***

Plate 2: Larvicidal activity of ethanolic extract of *Didemnum psammatode* against *Anopheles stephensi*.

500 µg/ml

250 µg/ml



100 µg/ml

50 µg/ml

10 µg/ml

Control

Plate 3: Larvicidal activity of ethanolic extract of *Didemnum psammatode* against *Anopheles stephensi*

CONCLUSION

The ethanolic extract of *Didemnum psammatode* exhibits significant larvicidal activity against *Anopheles stephensi* mosquito larvae, with the highest efficacy observed at 500 µg/ml. This study highlights the potential of marine-derived compounds as effective larvicides. The observed larvicidal activity aligns with findings from various studies on natural compounds, which attribute such effects to diverse bioactive substances including alkaloids, terpenoids, saponins, and phenols. The results suggest that *Didemnum psammatode* could serve as a valuable resource for developing sustainable and environmentally friendly mosquito control strategies. Further research is warranted to explore the specific compounds responsible for its larvicidal activity and their mechanisms of action.

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Chapter 8

ANTIBIOTIC USE IN POULTRY PRODUCTION

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ABSTRACT

Antibiotics have been essential in poultry production for treating bacterial infections and promoting growth. However, their widespread use has led to concerns about antibiotic resistance, posing risks to both animal and human health. Regulatory actions and research are now focused on alternatives like probiotics, prebiotics, and phytogenics to maintain productivity while reducing antibiotic reliance.

KEYWORDS: Antibiotics, Poultry, Antibiotic Resistance, Growth Promoters, Probiotics, Prebiotics, Phytogenics, Alternatives

INTRODUCTION

The use of antibiotics in poultry production has been a cornerstone of intensive farming practices since the mid-20th century. Antibiotics are employed in two primary ways: as therapeutic agents to treat bacterial infections and as growth promoters to enhance feed efficiency and overall productivity. The global demand for poultry meat and eggs has driven the widespread adoption of these practices, particularly in large-scale operations. However, the indiscriminate use of antibiotics in poultry has led to growing concerns about antibiotic resistance, prompting regulatory actions and research into alternatives.

THERAPEUTIC USE OF ANTIBIOTICS

In poultry production, antibiotics are crucial for the treatment of infectious diseases such as colibacillosis, necrotic enteritis, and respiratory infections caused by pathogenic bacteria like *Escherichia coli*, *Clostridium perfringens*, and *Mycoplasma gallisepticum*. These diseases can significantly impair flock health and lead to economic losses. Therapeutic antibiotics are administered either through feed, water, or by injection. When used properly, they control bacterial outbreaks and reduce mortality, ensuring the welfare of the flock.

SUB-THERAPEUTIC USE AND GROWTH PROMOTION

Antibiotics have also been historically used at sub-therapeutic levels to improve growth rates, feed efficiency, and overall productivity. By modulating the gut microbiota, antibiotics help the birds absorb nutrients more effectively, leading to faster weight gain. Common antibiotics used for growth promotion include tetracyclines, macrolides, and bacitracin. The low-dose, long-term use of antibiotics in this manner has contributed significantly to the productivity of the poultry industry, but it has also accelerated the development of antibiotic-resistant bacteria.

CONCERNS AND REGULATION

The excessive use of antibiotics in poultry has raised serious concerns about public health. The emergence of **antibiotic-resistant bacteria**, such as *Salmonella* and *Campylobacter*, which can be transmitted to humans through food, is a significant risk. Resistant strains can make bacterial infections in humans more difficult to treat, leading to prolonged illness and higher mortality. The growing awareness of these issues has led to strict regulations in many countries. For example, the European Union banned the use of antibiotics as growth promoters in 2006, and many countries are now following suit by enforcing stricter rules on antibiotic use in animal farming.

ALTERNATIVES TO ANTIBIOTICS IN POULTRY PRODUCTION

In response to the global push to reduce antibiotic use, several alternatives have emerged to ensure poultry health and performance without relying on antibiotics. These alternatives focus on maintaining gut health, enhancing the immune system, and preventing disease outbreaks.

1. Probiotics

Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host. In poultry, probiotics help maintain a balanced gut microbiota, inhibit the growth of harmful bacteria, and boost immune responses. Common probiotic strains used in poultry include *Lactobacillus*, *Bifidobacterium*, and *Bacillus* species. Studies have shown that probiotics can improve feed conversion ratios and overall bird health, making them a viable alternative to antibiotics for promoting growth and disease resistance.

2. Prebiotics

Prebiotics are non-digestible food ingredients that selectively stimulate the growth and activity of beneficial gut bacteria. They work by providing nutrients to probiotic bacteria, enhancing their population and activity. Prebiotics like **inulin**, **fructo oligosaccharides (FOS)**, and **mannan-oligosaccharides (MOS)** are commonly used in poultry diets. These compounds have been shown to improve gut health, enhance nutrient absorption, and reduce the need for antibiotics by minimizing the risk of bacterial infections.

3. Phytogenics

Phytogenics, or plant-derived compounds, are increasingly being explored as alternatives to antibiotics in poultry. These natural products, including essential oils, herbs, and plant extracts, have antimicrobial, anti-inflammatory, and antioxidant properties. Oregano oil, garlic extract, and thyme oil are popular phytogenics that have been shown to improve gut health and immune function in poultry. Phytogenics can serve as growth promoters and disease preventatives, contributing to better overall health in poultry flocks.

4. Organic Acids

Organic acids such as citric acid, formic acid, and butyric acid are used in poultry diets to lower gut pH, creating an unfavorable environment for pathogenic bacteria while promoting the growth of beneficial microbes. Organic acids also enhance nutrient digestion and absorption by improving enzyme activity in the gut. Studies have demonstrated that organic acids can reduce the incidence of infections like *Salmonella* and *E. coli*, making them an effective alternative to antibiotics.

5. Vaccines

Vaccination is a preventive strategy to protect poultry from bacterial and viral diseases. By inducing a targeted immune response, vaccines reduce the need for antibiotics to treat infections. Vaccines for diseases such as Newcastle disease, infectious bronchitis, and avian influenza are widely used in poultry production. Emerging vaccines targeting bacterial pathogens, such as *Clostridium* and *E. coli*, are also being developed to reduce reliance on therapeutic antibiotics.

6. Enzymes

Enzyme supplementation is another alternative that enhances feed digestibility and nutrient availability. Enzymes like xylanase, phytase, and protease break down complex molecules in feed, improving nutrient absorption and reducing gut stress. This, in turn, enhances the birds' immune system and overall health, lowering the need for antibiotics to treat gut-related issues.

7. Immunomodulators

Immunomodulators are substances that boost the immune response of poultry, making them more resistant to infections. These compounds can be derived from plants, microorganisms, or synthetic sources. For example, beta-glucans and chitosan have been shown to stimulate the immune system, helping poultry fight off bacterial and viral infections more effectively.

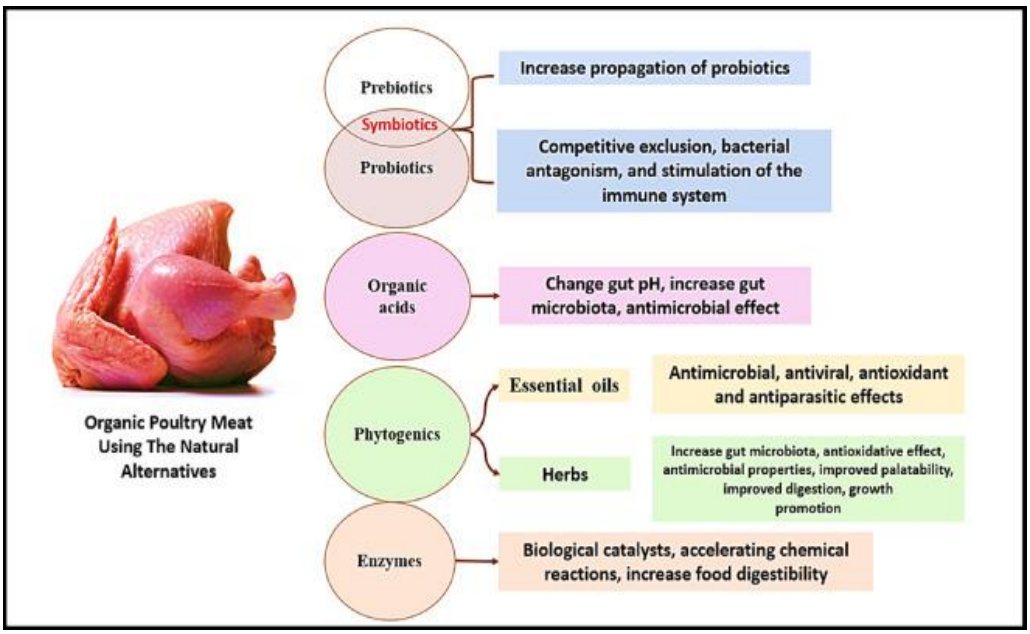

Fig 1: Source: https://www.sciencedirect.com/science/article/pii/S0032579122000013

CONCLUSION

As concerns about antibiotic resistance continue to rise, the poultry industry is under increasing pressure to reduce its reliance on antibiotics. Fortunately, there are several promising alternatives, including probiotics, prebiotics, phytogenics, organic acids, vaccines, enzymes, and immunomodulators. These alternatives not only help maintain the health and productivity of poultry but also address the growing demand for sustainable and antibiotic-free meat production. By integrating these alternatives into poultry management practices, the industry can achieve a balance between productivity and public health safety.

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Chapter 9

KELP AS A BIOSTIMULANT FOR SUSTAINABLE PLANT GROWTH

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ABSTRACT

There is an increasing interest in the use of naturally obtaining compounds as bio stimulant in plant growth. In that case seaweeds and various other seaweeds extracts have been utilized in plant growth as regulators or stimulators. The seaweed extract of brown, green, red algae are observed to have positive effect on plant growth. This paper emphasis that kelp, a seaweed extract obtained from an *Ecklonia maxima*a type of brown algae. The kelp contains essential nutrients like Amino Acids, vitamins, minerals, polysaccharides and anti-oxidants. It improves stress tolerance, high temperatures and salinity of plants. It can apply to soil by different means. It also contains plant growth hormones similar to the naturally occurring phytohormones in plants. These phytohormones stimulate germination, elongation, differentiation and shoot and root formation. This work aims to utilize kelp as abiostimulant for plant growth and development under controlled condition.

KEYWORDS: Kelp, Plant Growth, Seaweeds, Plant Growth Regulators, Bio Stimulant, Stresses Tolerance.

INTRODUCTION

PLANT GROWTH PROMOTION

Kelp contains phytohormones like auxins, cytokinins, gibberllins that promote root elongation, shoot formation, and stem elongation and flowering respectively. It also contains amino acids like proline and glutamic acid which helps in protein synthesis and enhance overall growth of the plants (Zheng, *et al*., 2016).The essential vitamins like A, B, C, E and minerals like magnesium, calcium, iodine, iron and zinc. These contribute to metabolic processes, chlorophyll synthesis. (Rengasamy, *et al*., 2005)

STRESS RESISTANCE AND TOLERANCE

Kelp, large brown algae has developed various mechanisms to resist and tolerate stress. This stress includes temperature, salinity, nutrient level and environmental stresses. Researches shows the addition of kelp for plant growth indicates enhancement of thermal tolerance (Umanzor, *et al*., 2019) and high salinity of plants.(Drira, *et al*., 2021)

NUTRIENT UPTAKE AND EFFICIENCY

Kelp contains macronutrients, micronutrients, polysaccharides, vitamins, minerals and so on. Macronutrients like sodium (Na), potassium (K), phosphorous (P) which are helpful in promoting growth in plants. Micronutrients like calcium (Ca), magnesium (Mg), iron (Fe), zinc (Zn), copper

(Cu), manganese (Mn) and traces of organic elements can increase nutrients uptake of plants. Polysaccharides in kelp acts as a chelators and bind to micro nutrients and enhance their bioavailability and uptake by plant roots. (Turan, *et al.,* 2004)

ROOT DEVELOPMENT AND SOIL HEALTH

Healthy soil is a key component to growing high quality crops. Kelp have emerged as a promising candidate in soil management seaweeds, especially kelp enhances soil health by improving the moisture-holding capacity of the plant. This allows for better moisture retention around the roots, which can lead to enhanced root growth. Kelp contains fucoidans and other polysaccharides like alginate and laminar in that are found to be improving soil structure, water retention and act as carbon source for beneficial soil microbes also it support plant root system by improving micro biome activity of the soil. (Kaur & Inderdeep, 2020)

BIOFORTIFICATION

Biofortification is increasing the nutritional value of plants by using various biological methods like agronomic practices, conventional breeding, biotechnology based methods like genetic engineering and genome editing. Using kelp for Biofortification, focuses on enhancing nutrient content, particularly Iodine, Iron, calcium, magnesium. Kelp can be applied both directly and indirectly. Kelp can be directly applied to plants that improves nutrients uptake and improve plants growth. Indirectly kelp can be supplemented in nutrient-rich feed for animal. (Panda, *et al.,* 2012)

DISEASE RESISTANCE

Sustainable Agricultural practices demands natural compounds which induce plant immunity against pathogens. Using kelp can stimulate plant immunity against disease causing microorganisms. Kelp are observed to stimulate Induced Systematic Resistance (ISR) Polysaccharides in kelp especially laminarins, acts as elicitors of ISR, which inhibits pathogens growth. Kelp also strengthens cell walls by increasing the production of lignin. (Shukla, *et al.,* 2021)

APPLICATION METHODS

Kelp can be applied to plants in various forms. As Foliar sprays, soil drench, seed treatment, Hydroponic systems. Foliar sprays can be directly applied to leaves, which allows plants efficiently absorb the nutrients and growth regulators (Zodape, *et al.*,2011).This method is particularly useful in growth stages such as flowering and fruiting (Temple, *et al.*,1989).Seed Treatment can be used to incorporate kelp into plants by treating seed with kelp extracts which exhibits improves germination rates and stronger initial growth (Mattner, *et al.,* 2013). Hydroponic Systems are systems that uses kelp-based solutions in hydroponics to stimulate plant growth in nutrient-deficient environments (Miceli, *et al.*,2021).Soil Drench where, Kelp as either solutions or extracts can be directly applied to the soil, improving soil health and enhancing root nutrient uptake.(Dmytryk, *et al.,*2015).

CONCLUSION

Kelp, as a natural product is used in wide range of crops as plant growth regulator, which enhances disease resistance, reduces need for chemical fertilizers. Kelp, with its unique combination of growth hormones, nutrients and bioactive compounds, is an excellent bio stimulant for promoting plant growth, nutrient uptake, and stress tolerance, disease resistance which makes it a valuable supplement in both organic and conventional systems.

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Chapter 10

REVIEW ON RECENT ADVANCES OF HYDROGELS FOR SMART DRUG DELIVERY

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ABSTRACT

In recent years, significant progress has been made in addressing the clinical and pharmacological limitations of hydrogel drug delivery applications. But still big problem remains. Here, we discuss recent advances in solving these problems, specifically the efficient delivery of hydrogels in vivo, the sustained release kinetics of drugs in hydrogels, and expansion of drugs that can be delivered Trans dermally, the dual responsive drugs. In this review, we discuss various mechanisms underlying the hydrogel formation, focusing on hydrogel responsive to various stimuli and hydrogel–drug interactions throughout the network. Also a detailed study of various addition agents including Nano particles is reviewed. It also presents a few diagrams of experimental release data from the literature to provide guidelines for the rational design of hydrogel for smart drug delivery systems.

KEYWORDS: Hydrogels, Drug Delivery, Therapeutics.

INTRODUCTION

Hydrogel delivery systems can take advantage of the positive therapeutical effects of drug delivery and also its demonstrated clinical applications. Hydrogels can control the site and release time of various therapeutic agents, such as small-molecule drugs, macromolecular drugs, and cells spatially and temporally.[1] Hydrogels have tunable physical properties, controllable degradability, and the ability to protect unstable drugs from degradation, and therefore have a variety of physical and chemical interactions with encapsulated drug for release [2]. In recent years, "Smart drug delivery systems "that can maintain long term doses in the affected area have been actively developed all over the world to ensure long-term controlled dose delivery [3]. There are three main aspects for drug delivery: it is an area for drug storage, a controlled release rate, and a release drive. Hydrogels do all these three functions. In addition to this, they can hide the bitter taste and unpleasant smell of medicines [4]. Therefore, hydrogels have a good potential for application for oral, nasal, buccal, rectal, vaginal, ophthalmic, injection, and other drug delivery methods. When injected or transplanted into the body, Hydrogels can maintain an effective and controlled release of the drug injected in body fluids [5]. The clinical benefits of many lipophilic drugs are limited due to various problems including poor solubility, poor dispersion, and lack of uniformity, poor dissolution, lack of bioavailability, and lack of *in vivo* stability. [6]. However, when these drugs are uploaded to a hydrogel system, the above defects can be improved to some extent, resulting in solubilization,

sustained release or controlled release effects, and enhanced stability and bioactivity [7]. Conversely, small molecule drugs that are highly soluble exhibit more advantages, including improved absorption and high bioavailability, but these properties are incompatible with sustained drug delivery effects.

Despite many of these beneficial properties, hydrogels also have some limitations. The low tensile strength of many hydrogels limits their use in load-bearing applications and can lead to the premature dissolution or flow of the hydrogel from a certain local site.[8] This limitation may not be essential in many typical drug delivery applications (such as subcutaneous injection). Perhaps, more important, is the issue related to the drug delivery properties of hydrogels. The amount and uniformity of drug loading on the hydrogels may be limited, especially for hydrophobic drugs. The high water retention ability and large pores of most hydrogels often result in relatively rapid drug release, lasting from over a few hours to a few days. Even simple applications may have problems; although some hydrogels are sufficiently deformable enough to be injectable, many are not, and require surgical implantation. Each of these issues significantly limits the actual use of hydrogel-based drug delivery therapies in the clinic. This review focuses on recent developments that address clinically relevant issues related to the use of hydrogels for drug delivery.

REVIEW OF LITERATURE

In context to available reviews an effort is made to put forward review of few latest applications of hydrogels in drug delivery.

TRANSDERMAL DRUG DELIVERY

In recent years, the development of hybrid drug delivery systems, such as hydrogels and nanoparticles, has gained considerable attention as new formulations for skin delivery.

Haojie Wei, Shuang Liu and coworkers [9] developed hydrogel based micro needles to improve the effectiveness of transdermal drug delivery in a variety of applications because of its ability to penetrate the stratum corneum of the skin's layer and their excellent biocompatibility. They experimented with natural polymers, Chitosan (CS) and Pullulan (PL) as raw materials were selected for manufacturing hydrogels. Among them two CMCS-SFP/OPL hydrogels with excellent swelling and water retention and excellent biocompatibility as a substrate to prepare Salvia miltiorrhiza loaded hydrogel-based micro needles, HFM-1 and HFM-2. Rapid drug release from HFM-1, which enables effective transdermal drug delivery, has also been demonstrated, suggesting that natural polymer-based hydrogel-based micro needles are promising devices to realize efficient, painless, and biocompatible transdermal drug delivery.

Improvisation of the overall therapeutic effect of the drug in terms of efficacy and patient compliance has led the researchers to develop a new Drug Delivery Method. The Transdermal Drug Delivery is of structural scientific interest due to its reliability, patient compliance, and painless technology that administers the drug formulation into the bloodstream through the skin at a given rate. Salonee Swain, *et al.* [10] lists pioneering knowledge about the development and mechanism of the Transdermal Drug Delivery System. They incorporated the essence of the Polymer Micro needles and Polymer Hydrogels by making the Transdermal Drug Delivery Technique the most appropriate and effective method of administering drugs over the other Drug Delivery Methods. In their review presented overall study of the Transdermal Drug Delivery Technology and the advantages of this

method over all study of drug delivery methods which ushers this method to be the Novel Drug Delivery System.

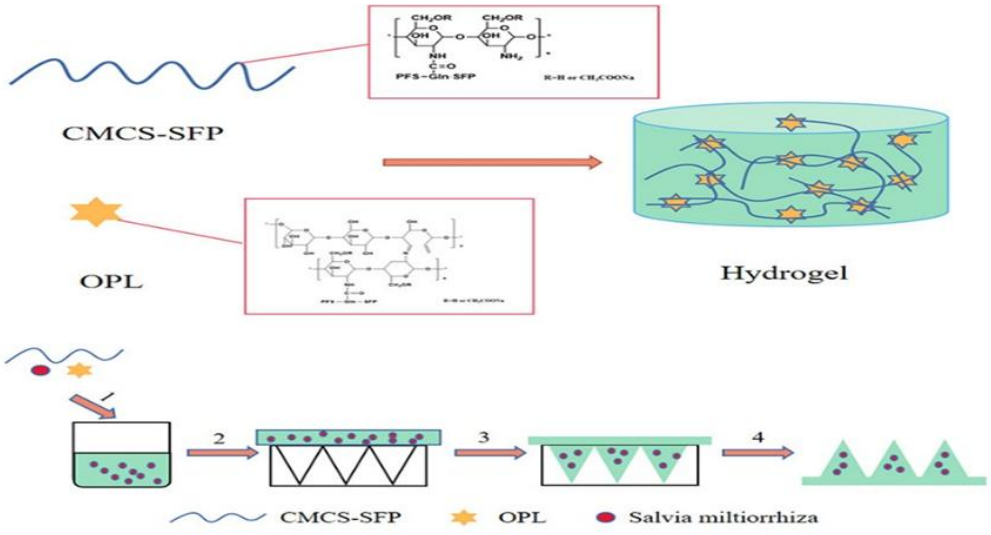

Fig 1: Schematic diagram of Preparation of hydrogel [9]

ENHANCED DRUG DELIVERY BY ADDITION OF VARIOUS AGENTS

Cyclodextrin (CD) is one of the most versatile substances produced in nature and can form supramolecular hydrogels with polymers or small molecules based on non-covalent interactions such as host-guest interaction and hydrogen bonding. CD-based host-guest supramolecular hydrogels are widely used in the field of topical drug delivery because of their their unique properties, such as excellent biocompatibility, shear-thinning nature, and stimuli responsiveness. Guihua Fang, *et al.* [11], demonstrated the formation of supramolecular hydrogels with types CD (α, β, and γ-CD) and the in vitro physicochemical properties of these hydrogels. Also elaborated the CD-based host-guest supramolecular hydrogels application in local drug delivery, ranging from intra-tumoral/peritumoral, subcutaneous, intra-articular, bone defect site, intramyocardial and ocular administration to transdermal and intra-renal administration.

Considering the pharmaceutical and pharmacodynamicuses of Azadirachta indica gum, Baljit Singh, and his team [12] grafted 2-hydroxyethyl methacrylate (HEMA) onto a polysaccharide gum in the presence of crosslinking agent to design network structure by copolymerization in the form of hydrogel for use in drug delivery carrier of methylprednisolone, an anti-inflammatory drug for colon diseases. The gum-poly(HEMA) hydrogels have been shown to biocompatible, antioxidant, and mucoadhesive and can be evaluated as drug delivery carriers of methylprednisolone for colon ailments. The neem gum-poly (HEMA) copolymeric hydrogels was porous. Drug release occurs through anon-Fickian diffusion mechanism. Drug release follows a zero-order model.

Fang Wang and his team [13] have developed two nanocomposites polysaccharide hydrogels TPP-CNC and TPP-CNF bya simple mixing method, which were constructed with multiple dynamic bonds. In addition, the hydrogels showed excellent fatigue resistance and high energy dissipation ratio during loading-unloading tests because of the sacrificial physical bonds, which also reduced the self-healing time at room temperature (about15 minutes). More importantly, the drug-loaded nanocomposites hydrogels showed sustained release, decreased burst release, increased release in acidic environments, and the drug release kinetics belonged to the Fickian

Release mechanism.

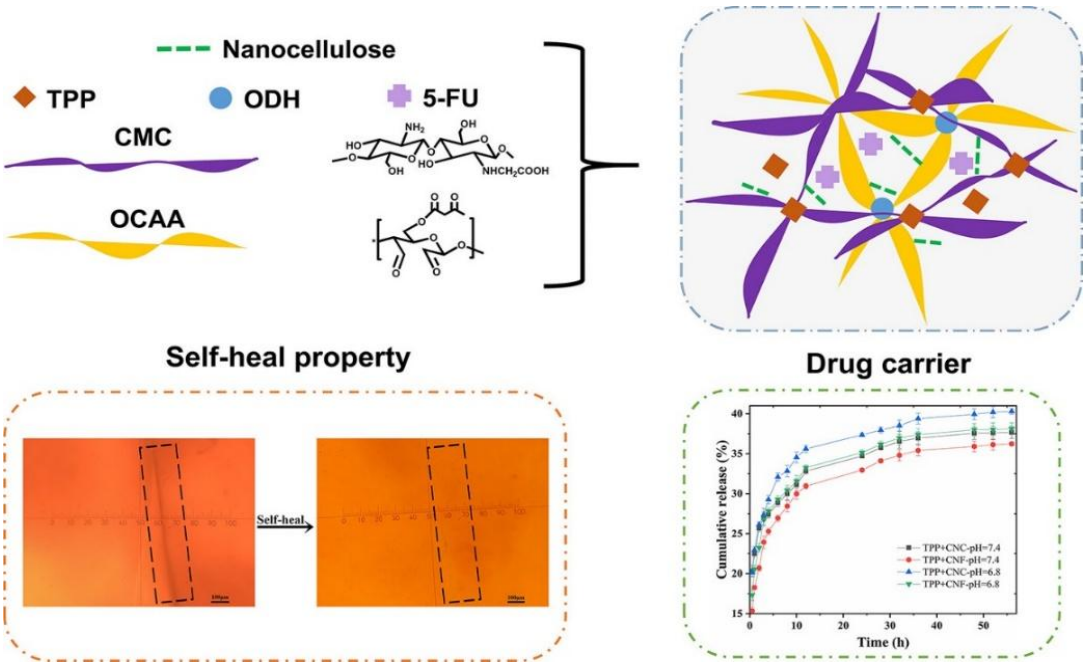

Fig 2: Schematic diagram of Nano cellulose hydrogel enhibiting self-healing property (13)

Self-assembled peptide hydrogels are widely used as carrier materials for drug delivery because they can solve the problems such as low solubility, poor selectivity, and serious side effects of conventional chemotherapeutic drugs. ShiyuZong, *et al.* [14], has developed a novel and injectable drug delivery platform for the antitumor drug doxorubicin (DOX) using a pH-responsive ionic-complementary octapeptide FOE. This octapeptide self-assemble into in a stable hydrogel under neutral conditions as it degrades into the tumour micro-environment. FOE hydrogel acts as a smart drug reservoir by local injection achieving sustained drug release and enhancing antitumor effects. This octapeptide opens up new avenues for promoting the clinical translation of anticancer drugs due to its excellent injectable properties and the economic benefits of simple and short sequence.

The synthesis of hydrogels as a device capable of maintaining the drug level in a desired range for a long and sustained period of time is a leading strategy for many researchers.

Emanuele Mauri and colleagues [15] suggested the functionalization of polyethylene glycol (PEG) chains with two different pH-sensitive linkers, ester andhydrazone, and their application as building blocks of microwave-assisted hydrogels for controlled delivery of small hydrophilic drugs the obtained release profiles were compared, underlining the opportunity to tune the release rate using the synthesized hydrogels. These linked installations make it possible to reduce the rhodamine escape to the surrounding environment compared to systems where solute's release was only driven by a pure diffusion mechanism.

The ability to provide pharmaceuticals from a single device with different release kinetics would be significant to adjust drug level according to the biomedical and therapeutic needs. In addition, the proposed microwave-assisted hydrogel synthesis replaces the problems related to small steric hindrance of hydrophilic molecules for sustained release applications, ensuring, at the same time, the production of sterile delivery systems without residue of organic solvent and byproducts that

could reduce their efficacy Ziba Gharehnazifam *et al.* [16], used silk fibroin hydrogel as a drug carrier for vincristine. They applied inverse analysis and general continuum mechanics to define material parameters and mechanical properties. vincristine-loaded silk hydrogel syringes, they were injected into PBS and enzyme solutions to monitor the drug release rate for 40 days. Results revealed deswelling behaviour and drug release rate were in good agreement with those of experimental results. Vincristine is released dramatically within the first hour from silk fibroin hydrogel and can be employed as a reliable tool for further predictions.

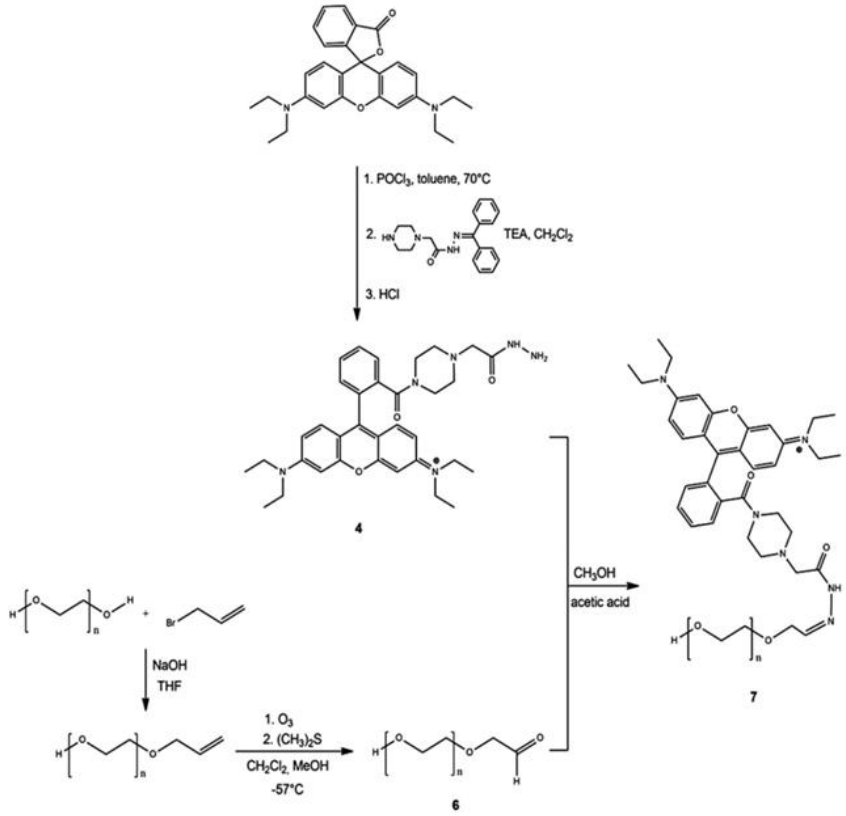

Fig 3: Synthesis of PEG Hydrozone (15)

Injectable thermo sensitive hydrogel has been regarded as an attractive drug delivery system, which displays a sol-gel phase transition upon injection in response to temperature. Recently, the thermo sensitive hydrogel has become a matter of importance in cancer therapy, providing high local drug concentration, sustained release characteristics, minimal invasiveness, and low systemic toxicities. Multiphysics simulation predicts optimal time and coordination for multi-injections.

Considering the swelling behaviour of hydrogel results in a precise prediction of drug release. This approach reveals the thermo sensitive hydrogel-based drug delivery system for cancer therapy.

Extensive application of thermo sensitive hydrogel in local cancer therapy, including chemotherapy, photo thermal therapy, photodynamic therapy, gene therapy, chemo-photo thermal combined therapy, and chemo-/immuno- combined therapy are focused.

Keeping in view the advantages of the dietary fiber almond gum in food and health care, herein this work, modification of the gum has been carried out to prepare the hydrogels for use as drug delivery systems (DDS).The almond gum-polyacrylic acid hydrogels containing hydrocortisone drug were synthesized by Baljit Singh [17] to improve the therapeutic potential of the drug to treat

colon inflammation. The in vitro drug release and various properties such as thrombogenecity, haemolytic potential, mucoadhesion test, antioxidant activity, and gel strength of hydrogels and bigels were measured. Further, during microscopic analysis, it has been found that as the content of the organogel was increased in the biphasic bigel matrix, the dimensions of the droplets (number and size) were enlarged. The results of properties indicated that bigel formation has enhanced the thrombogenecity, mucoadhesion and antioxidant activity of the hydrogel formulations. The release of hydrocortisone from DDS occurred in a slow and sustained manner with non-Fickian diffusion in colonic pH 7.4.

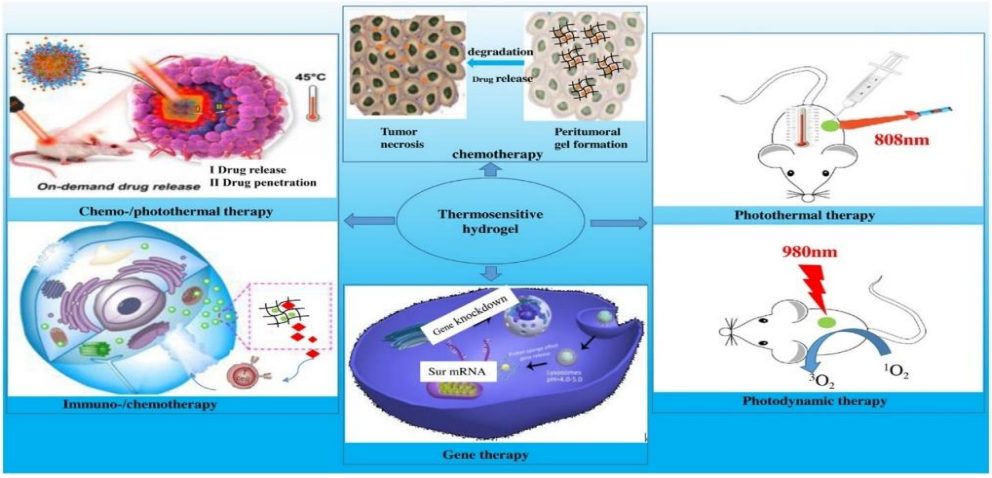

Fig 4: Various Applications of Thermo sensitive Hydrogels (16).

THERMO SENSITIVE DRUG DELIVERY

Kasula Nagaraja *et al.* [18], synthesized pH and temperature-sensitive tamarind gum (TM)-based hydrogels by free radical polymerization using a combination of acrylamide (AM), *N*-isopropyl acrylamide (NIPAM), and ethylene glycol vinyl ether (EGVE) monomers with bis (2-(methacryloyloxy) ethyl phosphate (BMEP) as a crosslinker TANEB hydrogel. Swelling studies revealed the dual responsive nature of the TANEB hydrogels and showed remarkable cytotoxicity against human colorectal adenocarcinoma cancer cells (HCT116 cells) along with good cell cycle ability. Thus, the TANEB hydrogel formulations could be used as a potential delivery system for anticancer drugs.

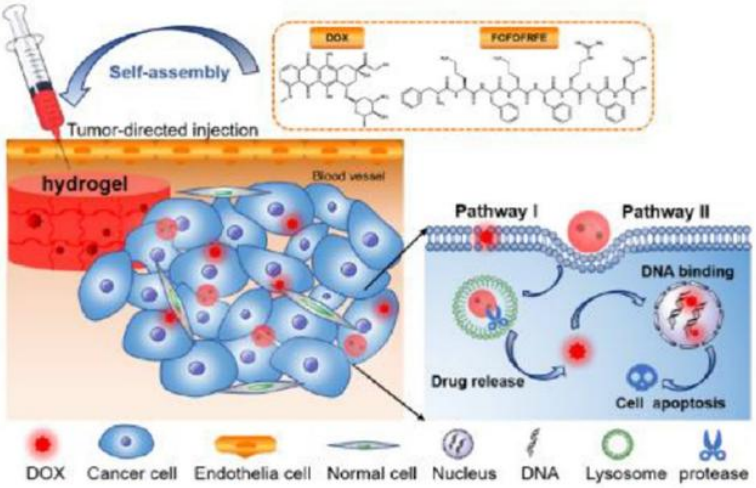

Fig 5: TANEB Hydrogel as Anticancer drugs (18).

Hossein Derakhshankhah *et al.* [19] synthesized a Folate-conjugated thermal- and pH-responsive magnetic hydrogel .A folate-conjugated pH- and thermal-sensitive magnetic hydrogel of poly(vinyl alcohol) (PVA), poly(*N*-isopropyl acrylamide) (PNIPAAm), folate-conjugated poly(acrylic acid) (PAA-FA), and Fe_3O_4 nanoparticles (NPs) was developed as a "smart" drug delivery system (DDS) for chemo/hyperthermia therapy of cancer cells. The developed DDS showed synergic cancer therapy process by combination of chemotherapy and hyperthermia approaches.

The developed magnetic hydrogel represents acceptable drug loading efficiency. A combination of chemotherapy and hyperthermia approaches exhibited synergic cancer therapy outcomes.

Magnetic thermo sensitive hydrogels stand out in the field of magnetic hyperthermia because of their dual responses of both magnetic and thermal stimulations. Zhuo Chen *et al.* [20] explored the, microfluidic technology to prepare magnetic thermo sensitive hydrogels. Two anticancer drugs, camptothecin, and doxorubicin hydrochloride were loaded in the core and shell layers of generated double emulsions to achieve the simultaneous delivery of hydrophobic and hydrophilic drugs. The results of the cellular cytotoxicity assay indicated that these combined drug-loaded hydrogels provided sufficient cytotoxicity in the cancer cell inhibition, and it was also demonstrated that poly (N-isopropyl acrylamide) (PNIPAM) could be used as a safe carrier for drug delivery systems. Magnetic thermo sensitive hydrogels are prepared using a microfluidic device. These hydrogels can respond to both magnetic and thermal stimulation and can be used as drug carriers. Drugs can be released on demand by controlling the switch of the magnetic field.

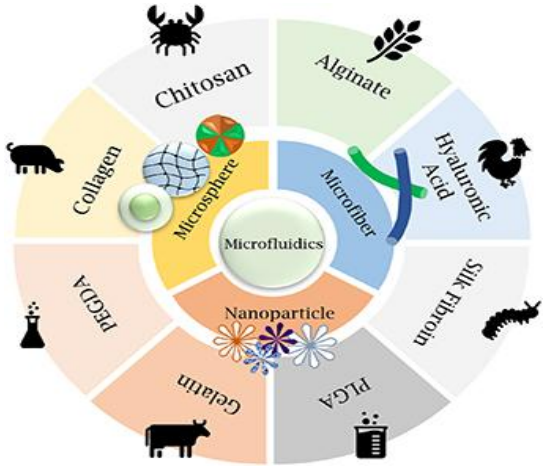

Fig 6: Schematic diagram of microfluidic carriers made of various materials.

In another studies Chih Kit Chunga and his team [21] evaluated Thermosensitive poloxamer 407 (P407) hydrogels as slow release system for optimizing CTLA-4therapy. Slow release reduces systemic antibody levels and potentially mitigates the side effects of CTLA-4therapy. Results revealed, local hydrogel delivery of anti-CTLA-4 antibodies near established tumours effectively sloweddown tumour growth, whilst significantly reduced serum anti-CTLA-4 levels. Altogether, P407 hydrogels represent promising delivery systems for the optimization of CTLA-4 blocking therapy.

The thermo-sensitive properties of poly (N-isopropyl acrylamide) (PNIPA) hydrogels are modified by the addition of hydrophilic acrylamide comonomers and an interpenetrating network of sodium alginate for drug delivery applications near 37 °C. A mathematical model is presented to describe

the mass transport kinetics during the hydrogel drug delivery process, which is accompanied by a volume change during phase transition.

G. Fu and W.O. Soboyejo [22] in their work provides a method to control the drug release process for PNIPA-based hydrogels. It is important to note here that the drug loading process described in this work, i.e. equilibrating at 53 °C for 2 days, was designed

DUAL RESPONSIVE SMART HYDROGELS

The design of the dual-network structure enables robust hydrogel. The dual-network hydrogel shows intelligent dual stimulus-response behavior. The gel as a drug-delivered carrier can precisely control the release process. The hydrogel exhibits considerable biocompatibility and antioxidant properties.

The design of multi-stimuli-responsive vehicles for the controlled and localized release of drugs is a challenging issue increasingly catching the attention of many research groups working on the advanced treatment of hard-to close wounds. RossellaLaurano *et al.* [23] synthesized a thermo- and pH-responsive hydrogel (P-CHP407) from an ad hoc amphiphilic poly (ether urethane) (CHP407) exposing a significant amount of –COOH groups (8.8 ±0.9 nmol/g polymers). Nano scale hydrogel characterization by Low Field NMR (LF-NMR) spectroscopy suggested that the presence of carboxylic groups in P-CHP407 caused the formation of bigger micelles with a thicker hydrated shell than CHP407 hydrogels, The hydrogels were found biocompatible according to ISO 10993 and able to load and release Ibuprofen: delivery kinetics of Ibuprofen enhanced by P-CHP407 hydrogels at alkaline pH, suggesting their potential to use as smart delivery systems in the treatment of chronic infected wounds.

Stimuli-responsive materials have been experiencing explosive developments, which are functionally integrated with multi-signals in response to external environment variations. Yet another group of researchers YuWang and his team [24] presented a novel dual-responsive graphene hybrid structural color film as electronic skins. The film is fabricated by adding conductive reduced graphene oxide (rGO)-poly (N-isopropyl acrylamide) (PNIPAM) filler into a poly (ethylene glycol) diacrylate (PEGDA) inverse opal scaffold. Because of the temperature response adjustability of the PNIPAM polymer, the resultant film is capable of changing volume or internal nanostructure under temperature stimuli. Based on these features, the hybrid film could not only feed electrical signals back, but also exhibit color changes visually when responding to the temperature and NIR stimuli. Furthermore, the value of the hybrid film on electro-thermal conversions has been explored which indicates that the hybrid conductive structural color films possess the promising application prospects in flexible electronics. The film showed dual-responsive performance facing the temperature and NIR stimuli.

KaiShiZhiLiu *et al.* [25] successfully prepared a dual thermo- and pH-responsive polyvinyl alcohol formaldehyde (PVF) based hydrogels were via redox grafting polymerization by incorporating respectively poly(N-isopropyl acrylamide) (PNIPAM) and poly(acrylic acid) (PAA) moieties onto PVF backbone. Their pH-responsiveness and excellent repeated absorption performance of hydrogels in water and different buffer solutions. In addition, the deswelling behaviour leads to the noticeable changes of macroscopic dimensions of hydrogels; thus anticipating potential applications in dual thermal and pH sensors.

An intelligent drug delivery platform was designed by DanShao and coworkers[26] based on the hybrids of mesoporous silica nanoparticles (MSN), sodium hyaluronate (HA), chitosan (CS). The synthesized hydrogel oxidized sodium carboxymethyl cellulose (oxCMC) can be used for dual-responsive dual-drug delivery. The results of cell viability demonstrate that the developed dual-drug encapsulated hydrogel has significantly higher efficacy of chemotherapy than that of single-drug (MTX or Cyt) encapsulated hydrogel. An intelligent drug delivery platform based on MSN/HA/CS/oxCMC is designed. The drug delivery platform has great growth inhibitory effect on HepG2 cell.

Wanyi Zhou *et al.* [27] prepared a glucose and MMP-9 dual-response temperature-sensitive shape-adaptive hydrogel (CBP@GMs/Cel&INS) for the treatment of chronic diabetic wounds.

CBP@GMs/Cel&INS composed of CS, gelatin, and PVA had excellent biocompatibility and effectively promoted cell proliferation and migration, effectively releasing insulin and celecoxib, thus exerting anti-inflammatory, hypoglycaemic, and promoting angiogenesis.. Further mechanistic studies showed that CBP@GMs/Cel&INS down-regulated the expression of inflammatory cytokines and downstream MMP9, down-regulated the expression of AGEs, and accelerated angiogenesis, thus having significant therapeutic effects on chronic diabetic wounds. These results suggest that CBP@GMs/Cel&INS is a promising wound dressing for chronic diabetic wounds.

Constructing robust hydrogels with biodegradability and dual stimuli-responsive by utilizing natural polymer as raw materials remains a sustaining challenge. Fuyu Song, and team [28] proposed an interpenetrating strategy in which N-isopropyl acrylamide (NIPAM) and acrylamide (AM) block copolymers were introduced as the second network into the carboxymethyl cellulose single network gel (CMC gel) to construct a dual-network robust hydrogel (CMC/PNIPAM-co-PAM). The dual-network design strategy effectively improves the mechanical strength of CMC gel. The hydrogel suggests intelligent dual stimuli-responsive behavior to pH and temperature. It is proved that the strong hydrogel possesses good cytocompatibility in vitro biocompatibility testing. In addition, the embedding of tetracycline makes the hydrogel excellent antioxidant performance. This dual-stimulus response integrated hydrogel is expected to play a critical role in drug delivery and targeted therapy.

Seonmok Kim and Seunho Jung, [29] synthesized Succinoglycandialdehyde (SGDA) by periodate oxidation of succinoglycan. Hydrazine-functionalized alginate (HZ-Alg) was prepared by EDC/HOBt reaction. SGDA-cross linked alginate hydrogels (SGDA/HZ-Alg) were fabricated via hydrazone linkage. SGDA/HZ-Alg and displayed biocompatibility, rheologically self-recoverability and tuneability, and pH-controllability, they would be potential biomaterials for the hydrogel-based drug delivery systems.

NANO PARTICLES INFUSED HYDROGELS

Nanoparticles provide massive advantages regarding drug targeting, delivery, and release, and with their additional potential to combine diagnosis and therapy, emerge as one of the major tools in Nano medicine. The main goals are to improve their stability in the biological environment, to mediate the bio-distribution of active compounds, improve drug loading, targeting, transport, release, and interaction with biological barriers. The cytotoxicity of nanoparticles or their

degradation products remains a major problem, and improvements in biocompatibility are the main concern of future research. [30, 31]

Xianglian Li, and his team [32] rationally designed and synthesized a nonapeptide (NapFFKKFKLKL) as an effort on a recent repors of concerning endogenous agents (*i.e.*, pyridoxal phosphate, adenosine triphosphate, adenosine monophosphate, folinic acid) that modulate the oligomerization of apoptosis-associated speck-like protein (ASC) *via* the peptide epitope of KKFKLKL. The synthesized hydrogel can co-assemble with dexamethasone sodium phosphate (Dexp) to generate a NapFFKKFKLKL/Dexpsupramolecular hydrogel for ocular drug delivery. Overall, the resulting NapFFKKFKLKL/Dexp hydrogel may be a promising drug carrier system to treat various posterior disorders (*i.e.*, uveitis).

Now a day, silver nanoparticles (AgNps) have attracted considerable attention in various biomedical applications like drug delivery, photothermal ablation of cancer, and imaging agent for cancer diagnosis. KalyaniPrusty and coworkers [33] synthesized PAM-SP@Ag hydrogels by *in situ* polymerization process. It demonstrated on the nanosilver embedded soy protein polyacrylamide (PAM-SP@Ag) nanocomposite hydrogel which is synthesized by *in situ* polymerization process for the release of ciprofloxacin drugs. The gelling actions of prepared nanocomposite hydrogels are given by the rheological study. The cytotoxicity behaviour of PAM-SP@Agnanocomposite hydrogels along with improved swellings and rheological properties are enabling the material as a suitable vehicle for the safe release of ciprofloxacin drug.

Characterization of a hybrid polymeric nanoparticle/thermosensitive hydrogel system. Development of a promising skin drug-delivery system for local anesthetic benzocaine. Such a transdermal diffusion synthetic membranes have been used by Renato Grillo*et al.* [34] to assess skin permeability to these systems, providing key insights into the relationships between drug and Nano formulations. The benzocaine-loaded poly-ε-caprolactone nanoparticles (BZC: NPs) were synthesized, characterized, and incorporated into Poloxamer 407-based hydrogel (PL407).Developed a hybrid polymeric nanoparticle/thermosensitive hydrogels system that contributed to a better understanding of the interaction between hydrogels, nanoparticles, and synthetic membrane and open perspectives for the development of new drug delivery systems for the skin.

Xianyan Qin and coworkers [35] studied an injectable triblock copolymeric micelle-crosslinked hyaluronan hydrogel hybrid offers a unique "plum–pudding" structure to deliver hydrophobic small molecules as well as bio macromolecules in a prolonged and controlled manner. Overall, this versatile injectable F127-HA hydrogel hybrid represents a neat and clinically relevant platform system to achieve localized therapy, which may further be explored to achieve concurrent loading and prolonged release of both small molecules and macromolecular therapeutics for other disease therapies.

The AAm-NaCMC-MMT hydrogel rings were successfully synthesized by Ghorbanali Sharifzadeh and his team [36], using MBA for controlled vaginal drug delivery. More importantly, the resultant AAm-NaCMC-MMT hydrogel rings were appeared to be biocompatible against HSF 1184 cells. This research highlights that the addition of MMT NPs within hydrogel rings may be promising for drug delivery applications.

Ischemia-reperfusion (I/R)-induced organ injury is a serious health problem worldwide, and poor recovery of acute phase injury leads to chronic fibrosis and further organ dysfunction. Thus, a more precise approach to enhance tissue repair is needed. By using a renal I/R model, Shuyun Liu *et al.* [37] aimed to evaluate the role of a hydrogel-based dual-drug delivery platform on promoting tissue repair. This study highlighted that SAP could sequentially deliver the two drugs to achieve anti-inflammatory and pro-proliferative effects with one injection and thus is a promising delivery platform for tissue repair.

Rana Jahanban-Esfahlan, and coworkers [38] designed and developed a magnetic natural hydrogel based on alginate (Alg), gelatin (Gel), and Fe_3O_4 magnetic nanoparticles (MNPs) as an efficient and "smart" drug delivery system (DDS) for cancer therapy. The formulated Alg-Gel/Fe_3O_4-Dox exhibited pH-dependent drug release behaviour due to the presence of carboxylic acid groups in the DDS. According to the results, the Alg-Gel/Fe_3O_4 magnetic hydrogel can be considered as an efficient and "smart" DDS for cancer therapy and diagnosis.

Near-infrared (NIR) light-responsive, injectable hydrogels are among the most promising drug delivery systems for localized anticancer therapy owing to their minimally invasive administration and remote-controlled manner. Pengfei Sun *et al.* [39] designed a novel type of dynamic-covalent hydrogel (GelPV-DOX-DBNP) with NIR light-triggered drug release behaviour for the chemo-photothermal combination treatment of tumours. In vivo results prove that GelPV-DOX-DBNP exhibited a markedly enhanced chemo-photothermal synergistic therapy for 4T1 tumour model mice, compared to chemotherapy alone or PTT. This work presents a new strategy to construct NIR light-responsive hydrogel as one alternative drug delivery system for anticancer applications.

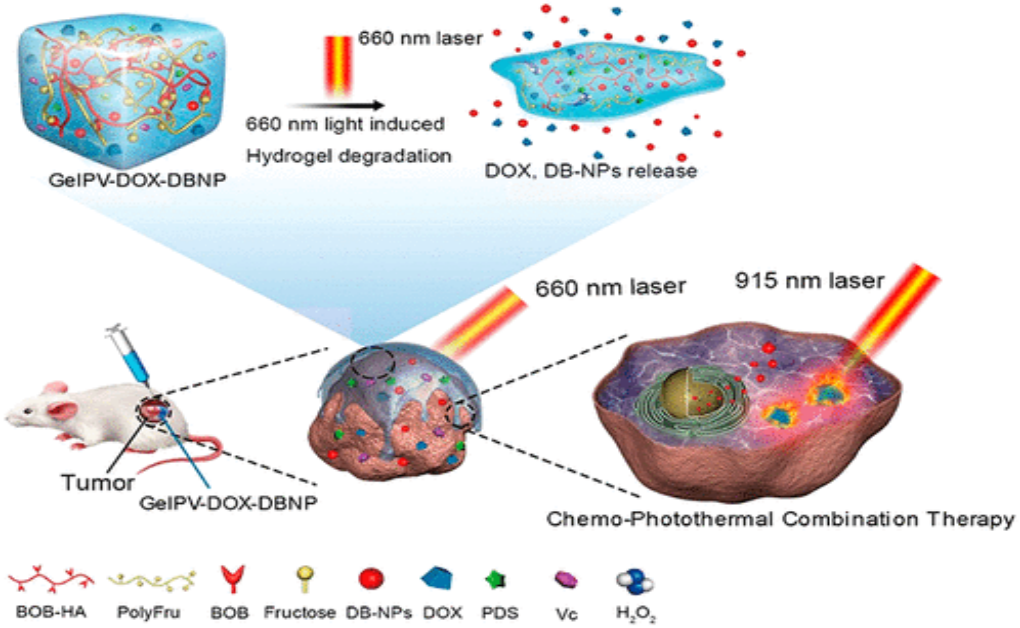

Fig 7: Schematic representation of Near Infrared (NIR) light responsive hydrogel (39)

Carboxymethyl cellulose (CMC)-based hydrogels have superabsorbent properties but low mechanical strength. Variation of other hydrogel components might improve the mechanical strength but has been occasionally seen to decrease the swelling and drug-loading capacity. To address these problems Daham Jeong, and coworkers [40] designed a dual-component system, consisting of both carboxymethyl β-Cyclodextrin (cmβCD) and CMC. They synthesized the

superabsorbent CMC-based hydrogel containing cmβCD to evaluate their intrinsic mechanical strength and swelling capacity they also showed the highest mechanical strength and the best drug release properties apart from the appreciable swelling capacity. Furthermore, cmβCD/CMC hydrogels are non-cytotoxic towards human dermal fibroblasts, suggesting their safe use as nontoxic, bio-friendly, and effective drug delivery systems.

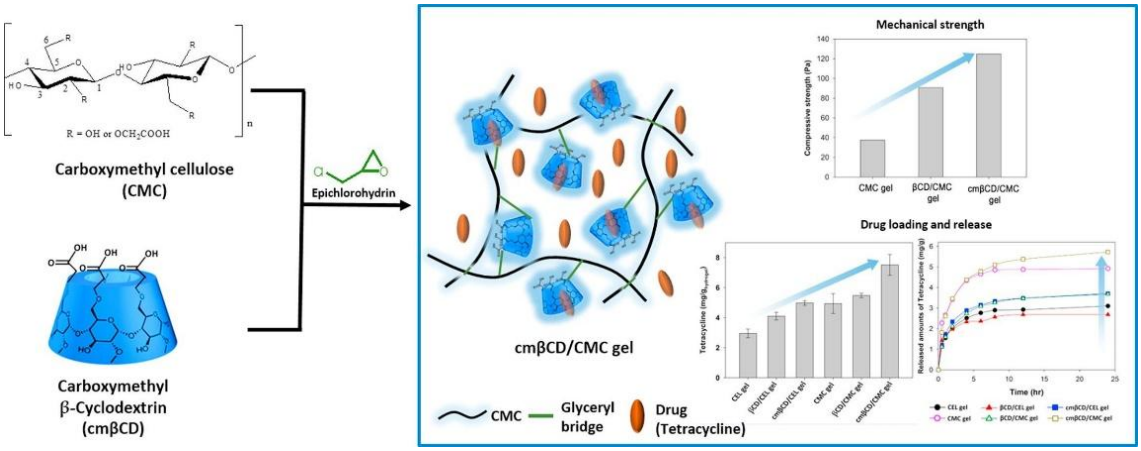

Fig 8: Functionalization of Carboxymethyl cellulose (CMC) hydrogel drug.

Shoeing Wei and coworkers [41] studied the use of a carbohydrate polymer hyaluronic acid (HLA) as a matrix to design novel transdermal Nano gel loading poorly soluble drug Nano crystals. Novel Nano crystals based hydrogel was designed by using HLA as a matrix. Baicalin nanocrystals (BCA-NC) were prepared by coupling homogenization technology and spray-drying technology. BCA-NC-gel with 1% HLA significantly improved the skin permeation of BCA. HLA-based nanogel system is a promising carrier for drug transdermal delivery. The results demonstrated that the BCA-NC could be successfully prepared in terms of trehalose after spray-drying. In conclusion, HLA based nanogel system is a promising carrier for effectively transdermal delivery of the poorly soluble drug.

CONCLUSION

The hydrogel system offers multiple advantages to conventional drug delivery systems such as: excellent biocompatibility, easier accessibility, biodegradability, and multifunctionality.

In this review, hydrogels that have been recently developed for the treatment of various disorders are discussed, with particular emphasis on their advantages for direct therapeutic delivery, opening new perspectives of drug delivery and variations in currently used methods for overcoming the limitations have been highlighted.

Dual responsive hydrogels established as an appealing alternative drug delivery strategy that could realize sufficiently high drug concentrations at a biological target (such as the brain and spinal cord) in a minimally invasive fashion and limited systemic toxicity has been covered as a major part of this review.

Thermo responsive hydrogels with number of key attributes make them suitable for drug delivery. Designed to be liquid at room temperature and progressively turn into gel at body temperature, make them readily available to be injected to create drug depots that conform to the surrounding tissue and release therapeutic payloads

A number of studies in this review highlight how the unique properties of thermo responsive hydrogels have led to positive outcomes in a variety of applications, including treatments for brain tumours, spinal cord and brain injuries, as well as neurodegenerative disorders. Moreover, even though further investigation is still required, thermo responsive hydrogels have shown encouraging results in the field of immunotherapy, which may drastically improve treatment for these invasive brain tumours. They have been employed for Chemotherapy and hyperthermia approaches of synergic cancer treatment. Dual thermo responsive, Ph responsive and stimuli responsive hydrogels development has led to totally new dimensions including electronic skins, hybrid films for NIR stimuli.

Magnetic thermo responsive hydrogels stand out as they can respond to both magnetic and thermal stimulations and important as they can be released on demand by controlling the switch of the magnetic field.

Importantly, studies that are reviewed herein highlight how different additional agents to hydrogels can enhance drug bioavailability at the target site as well as reduce the frequency of administrations, thus helping overcome the drawbacks of traditional therapeutic agents commonly used to treat disorders especially neurodegenerative. In fact, the composition of the gel can be easily tuned to achieve suitable mucoadhesive properties that allow for nose to brain delivery. This delivery route may be particularly useful for the release of drugs to less frequent administration regimens and consequent improved patient's adherence and compliance may improve therapeutic efficacy. The smart hydrogels platform designed by various agents like silica nanoparticles, chitosan, cellulose, glucose etc led to the promising wound dressing for chronic diabetic wound.

Despite all the positive preclinical research that has been shown with hydrogels for therapeutic drug delivery, their effective use for the treatment of various disorders requires further optimization in drug loading and release, improved integration with the surrounding tissue and the development of predictive tool to efficiently manage the design space. In future work, loading and release could be optimized by adopting hierarchical drug delivery systems resulting from the mixture of molecular, Nano and micro components within the hydrogels

Addition of Nano particles emerged as an extraordinary tool in drug delivery system made it a totally new era in therapeutic drug targeting, deliver and release. Nano peptide, nanosilver, hybrid polymeric Nano particles incorporation into hydrogels made assess to akin permeability. Providing key insights for drug and Nano formulations and increased a new perspective for drug delivery through skin, vaginal drug delivery, and effectively made it possible froe transdermal delivery of poorly soluble drugs. Also opened the chances of employing as the carrier to load hydrophilic and hydrophobic therapeutic agents, as an integrated system for combination therapy.

However, the application of hydrogel still faces some challenges. After local delivery, hydrogel formed in situ could perform a transformation from solution to hydrogel state in the presence of counter ions, where the gelation morphology and time are important factors affecting the treatment of diseases and the hydrogel with low mechanical strength is prone to flow to the surrounding tissues, compromising its safety and stability and might pose safety risks such as blockage of blood vessels and compression of nerves. Additionally, in the disease microenvironment, the hydrogel disassociates, and in some cases, the drug is released as a prodrug rather than a parent drug, which

might compromise the drug activity in vivo. Importantly, how to prolong the drug release over several months must be considered. Although the hydrogel extends drug release by several weeks it is far from adequate for the treatment of chronic diseases. Thus, more efforts are required to optimize these hydrogel systems before clinical translation System. Although the hydrogels have demonstrated significant therapeutic efficacy in animals, the reliable and reproducible should be rigorously evaluated in enough patients and normal humans to ensure the therapeutic efficacy and attenuating the off-target toxicity. We believe that optimized hydrogels will achieve breakthroughs in clinical applications in the foreseeable future. Progress in nanoparticles induced hydrogels will highlight new opportunities for controlled drug delivery. There have been limited attempts to date using nanoparticles for remote-controlled drug delivery.

In conclusion, advances in biomaterials have broadened the repertoire of hydrogels designed for controlled drug delivery. With an expanding arsenal of material systems, target applications, and increasing fundamental understanding, the impact of hydrogel drug delivery systems is expected to increase in importance for years to come. Hydrogel drug delivery systems are likely to further change the scale, efficacy and cost of therapeutics, and to continue to improve human healthcare.

Conflicts of Interest statement: The authors declare no conflict of interest.

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Chapter 11

EXPLORING ORGANOMETALLIC CHEMISTRY AND GRIGNARD REAGENTS

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INTRODUCTION

OVERVIEW OF ORGANOMETALLIC CHEMISTRY

The field of organometallic chemistry examines compounds featuring bonds between metals and carbon atoms. This discipline encompasses metals such as lithium, magnesium, and various transition elements. Serving as a link between organic and inorganic chemistry, organometallic chemistry has significant implications for both scientific research and industrial use. These compounds play crucial roles in catalytic processes, materials science, and the creation of organic molecules.

FUNDAMENTAL ATTRIBUTES OF ORGANOMETALLIC COMPOUNDS

1. Metal-Carbon Bond: The distinctive metal-carbon connection in these compounds results in unique reactive properties, allowing them to engage in chemical reactions often unavailable to conventional organic molecules.

2. Nucleophilic Nature: Organometallic compounds, including Grignard reagents, frequently exhibit strong nucleophilicity due to the substantial electronegativity difference between the metal and carbon. This characteristic enables them to readily interact with electrophiles, promoting the formation of carbon-carbon bonds.

3. Reaction Versatility: These compounds can participate in various chemical processes, such as nucleophilic additions, coupling reactions, and functional group modifications, making them invaluable tools in organic synthesis.

4. Catalytic Applications: Organometallic compounds are frequently utilized as catalysts in organic reactions, including polymerization and cross-coupling processes, significantly enhancing reaction efficiency and selectivity.

THE SIGNIFICANCE OF GRIGNARD REAGENTS

In the realm of organometallic compounds, those derived from lithium and magnesium, especially Grignard reagents, are considered some of the most crucial organic reagents. These compounds, first discovered by Victor Grignard in 1900, have since transformed the field of organic synthesis.

GRIGNARD REAGENTS: AN OVERVIEW

Composition and Structure

Grignard reagents are organomagnesium halides, generally expressed as R−MgX, where R represents an alkyl or aryl group and X denotes a halogen (typically Cl, Br, or I). The carbon atom linked to magnesium carries a partial negative charge, rendering it a potent nucleophile.

Preparation of Grignard Reagents

The synthesis of Grignard reagents involves the reaction between an organic halide and magnesium metal in a water-free ether solvent, such as diethyl ether or tetrahydrofuran (THF):

$$R{-}X+Mg \rightarrow R{-}MgX$$

This process must be conducted in an anhydrous environment, as Grignard reagents are extremely susceptible to water, which can cause hydrolysis, resulting in hydrocarbon formation and rendering the reagent ineffective.

Grignard Reagents: Reactivity

Grignard reagents exhibit exceptional versatility and reactivity, particularly with electrophiles. Their primary reactions can be classified into several key categories.

Interactions with Carbonyl Compounds

A major application of Grignard reagents lies in their addition to carbonyl compounds, including aldehydes and ketones.

Aldehydes: The reaction between a Grignard reagent and an aldehyde yields a secondary alcohol:

$$R{-}MgX+R'CHO \rightarrow R{-}CH(OH){-}R'+MgXOH$$

Ketones: When reacting with ketones, Grignard reagents form tertiary alcohols:

$$R{-}MgX+R''C{=}O \rightarrow R{-}C(OH)(R'){-}R''+MgXOH$$

These reactions play a crucial role in organic synthesis for producing alcohols, as they facilitate the introduction of new carbon centers.

Interactions with Esters and Acid Chlorides

Grignard reagents can interact with esters and acid chlorides to produce tertiary alcohols. For esters, this process involves a two-step mechanism:

The Grignard reagent initially attacks, creating a tetrahedral intermediate.

This intermediate then breaks down, generating a ketone that subsequently reacts with another Grignard reagent molecule to form the final tertiary alcohol.

Interaction with Carbon Dioxide

Grignard reagents and carbon dioxide react to create carboxylic acids, a valuable method for synthesizing these crucial functional groups:

$$R{-}MgX+CO2 \rightarrow R{-}COOH+MgX(OH))$$

This process offers a straightforward approach to producing carboxylic acids from inorganic materials.

Interactions with Additional Electrophiles

Grignard reagents can also interact with various other electrophiles, such as:

Nitriles: Resulting in ketones or aldehydes after hydrolysis.

Isocyanates: Producing substituted ureas.

REACTION MECHANISMS INVOLVING GRIGNARD REAGENTS

Comprehending the mechanisms of Grignard reactions is crucial for anticipating outcomes and optimizing conditions.

Nucleophilic Addition Mechanism

The primary mechanism in Grignard reactions involves nucleophilic addition:

Nucleophilic Attack: The Grignard reagent's carbon atom targets the electrophilic carbon in carbonyl compounds, forming a tetrahedral intermediate.

Protonation: The intermediate may collapse, resulting in the desired alcohol and releasing magnesium halide by-products.

Solvent Influence

Solvent selection is vital in Grignard reactions. Anhydrous ethers stabilize the Grignard reagent through coordination, enhancing nucleophilicity while preventing hydrolysis. Commonly used solvents include diethyl ether and THF, which promote Grignard reagent reactivity.

GRIGNARD REAGENT APPLICATIONS

Grignard reagents are extensively utilized in organic synthesis due to their ability to form carbon-carbon bonds and introduce various functional groups.

Alcohol Synthesis

Grignard reagents play a crucial role in synthesizing diverse alcohols:

Secondary Alcohols: Obtained from reactions with aldehydes.

Tertiary Alcohols: Produced from ketones and esters.

These alcohols serve as essential intermediates in pharmaceuticals, fragrances, and fine chemicals.

Carboxylic Acid Synthesis

By reacting with carbon dioxide, Grignard reagents enable efficient carboxylic acid production, which is important in various applications, including drug development and agrochemicals.

Carbon-Carbon Bond Formation

Grignard reagents are essential for creating carbon-carbon bonds, facilitating the synthesis of complex organic molecules. This capability is fundamental in drug discovery, where constructing intricate molecular structures is necessary.

Synthesis of Other Functional Groups

Grignard reagents can also be used to synthesize various functional groups, including:

Nitriles: Formed from reactions with isocyanates, useful for further transformations.

Amines: Resulting from reactions with alkyl halides or primary amines.

CONSTRAINTS AND CONSIDERATIONS

Despite their effectiveness, Grignard reagents have certain limitations:

Moisture Vulnerability

Grignard reagents are extremely susceptible to moisture, requiring anhydrous conditions. Even small amounts of water can neutralize the reagent and cause unintended reactions.

Interaction with Functional Groups

The broad reactivity of Grignard reagents with various functional groups, including alcohols and acids, necessitates careful synthetic route planning to prevent unwanted side reactions.

Precautionary Measures

Given their reactivity and potential risks, handling Grignard reagents demands rigorous safety protocols. Appropriate protective gear, fume hoods, and proper waste disposal methods are essential for safe laboratory use.

PRACTICAL EXAMPLES: SIGNIFICANT USES IN ORGANIC SYNTHESIS

Pharmaceutical Production

Grignard reagents are essential in pharmaceutical synthesis. For instance, they are often used in creating anti-inflammatory drugs by forming complex alcohols and carbon frameworks. Their versatility in generating diverse molecular structures makes them crucial in drug development.

Applications in Material Science

In the field of materials science, Grignard reagents are utilized to create polymers and materials with specific characteristics. Their ability to functionalize surfaces and form cross-linked networks has led to advancements in coatings, adhesives, and cutting-edge materials.

Natural Product Synthesis

Grignard reagents are frequently employed in natural product synthesis. Many intricate natural compounds, such as terpenes and alkaloids, can be constructed using Grignard chemistry, demonstrating their adaptability in creating biologically significant molecules.

CURRENT INNOVATIONS AND FUTURE PROSPECT

Creation of Novel Grignard Reagents

Current research is centered on developing new Grignard reagents with improved reactivity and selectivity. Investigating alternative metals and ligands may broaden applications and lead to innovations in synthetic methods.

Sustainable Chemistry Approaches

Efforts are underway to incorporate Grignard chemistry into sustainable chemistry frameworks. Strategies include reducing waste and using renewable resources, aligning with sustainable chemical synthesis principles.

CONCLUSION

Organometallic compounds, especially Grignard reagents, are fundamental to contemporary organic chemistry. Their distinctive reactivity and ability to facilitate carbon-carbon bond formation make them invaluable in both academic research and industrial applications. Comprehending the principles and mechanisms governing their behavior is crucial for maximizing their potential in complex organic molecule synthesis. As research advances, Grignard reagents will undoubtedly continue to be instrumental in the progression of chemical science.

Chapter
12

AN INVESTIGATION OF BIODIVERSITY AND FRESHWATER ECOSYSTEM PRESERVATION

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ABSTRACT

Freshwater ecosystems have a crucial role in providing valuable resources and benefits to human society. However, they have seen significant modifications and an excessive decline in biodiversity. Primary hazards to the variety of freshwater ecosystems include excessive exploitation, water contamination, fragmentation, habitat loss or deterioration, and the infiltration of non-indigenous species. Modifications to the natural flow patterns caused by human-made dams, changes in land use, river reservoirs, and water extraction often result in significant effects on populations living in flowing water ecosystems. Comprehending the functional relationships and processes in freshwater ecosystems is a significant obstacle for scientists, but it is essential for successful and sustained restoration. Until far, the majority of conservation efforts have focused on individual species or tactics limited to a single level. On the other hand, the suggested concept of 'Integrative Freshwater Ecology and Biodiversity Conservation' focusses on studying the qualitative and quantitative interactions between abiotic and biotic elements at various levels of organization. As a consequence, it leads to a more comprehensive understanding of biodiversity functioning and management. The main enquiries revolve on the modelling of processes occurring in crucial aquatic habitats and their usefulness. This is achieved by identifying and quantifying the variables that govern the spatial and temporal distribution of biodiversity and productivity in aquatic ecosystems. The significance and relevance of research on IFEBC is demonstrated through case studies in three key research areas: (i) assessment and restoration of aquatic habitat quality, (ii) exploration of the genetic and evolutionary capabilities of aquatic species, and (iii) identification of stress and toxic effects in aquatic ecosystems through the use of biomarkers. Ultimately, the integration of molecular and ecological techniques may significantly enhance our comprehension of the operation of aquatic ecosystems and the implementation of conservation strategies.

KEYWORDS: Freshwater Ecosystem, Biotic -Abiotic Elements, Conservations.

INTRODUCTION

This article provides an overview of the existing understanding and ideas about the arrangement of biodiversity in aquatic ecosystems, the variables that affect its spatial and temporal distribution, its significance for humanity, its present condition, and the primary dangers that are linked to human activities. A proposal is made to address the need of establishing a stronger connection between ecological theory and practical conservation. This proposal introduces a new concept called

'Integrative Freshwater Ecology and Biodiversity Conservation' and provides examples from three main study areas to show its application. Unlike conservation techniques that focus on a particular species or level, this strategy incorporates information from several levels of organisation, resulting in more comprehensive and holistic conservation strategies.

LEVELS OF AQUATIC BIODIVERSITY ORGANIZATION: CONCEPTS AND THREATS:

Since the Rio Earth Summit in 1992, the phrases 'biodiversity' or 'biological diversity' have gained popularity among the general public. Public perception often defines 'biodiversity' as the quantity of species present in a certain ecosystem or habitat, aligning with the idea of species richness as the most basic indicator of biodiversity. The global estimates of species richness vary between three and 30 million species or perhaps more, as stated by [1].The regional species pool, or β-diversity, is determined by the number of species in a particular ecosystem and how they are distributed throughout space. It is influenced by the number of species in each habitat type, known as α-diversity, as well as the turnover of species between different habitat types, referred to as γ-diversity [2]. The concept of biodiversity has evolved to encompass more complex ideas, going beyond species and including a wider range of diversities. This includes entire ecosystems, habitats, and ecotones, as well as the biological communities and species within them. It also considers the variation within species at both the phenotypic and genetic levels. While the theoretical idea of biodiversity incorporates variety, most actual conservation efforts are not integrative.

Aquatic habitats are much diversified and are considered one of the most varied kinds of ecosystems found globally. Aquatic ecosystems exhibit a wide spectrum of diversity, including chemoautotrophic black smokers seen at volcanic deep-sea ridges, as well as very oligotrophic highland lakes and streams. The variety of freshwater ecosystems includes many types of water bodies such as flowing rivers and standing lakes, as well as underground water sources. It also includes the surrounding riparian systems found in both narrow and wide floodplain areas, as well as the transitional zones between these different ecosystems. All of these components interact with each other and together contribute to the overall biodiversity of freshwater ecosystems. The variety of biological communities and species in aquatic environments is influenced by gradients in salinity, temperature, availability of light, dissolved gases, and nutrients, as well as biogeographic activities. Approximately 10% of the total animal species on Earth were predicted to be found in freshwater systems. The taxonomic category of fishes, which is believed to include a range of 25,000-40,000 species, likely represents around 30-50% of total vertebrate diversity. Community and species diversity estimations mostly focus on the macro-biological level. However, it is probable that the species richness of freshwater fungi and microbes, which play a significant role in the functional biodiversity of freshwater ecosystems, has been undervalued.

Intraspecific diversity pertains to the variability seen among populations within a given species. This variety encompasses not just morphological variability, but also encompasses variance in behaviour, physiology, and life form across populations or individual organisms of the same species. Genetic diversity, the fundamental foundation of biodiversity, may be seen as Genetic variety refers to the diversity of genes within a species or an entire ecosystem. The second interpretation

Functional biodiversity is strongly associated with the concept of 'functional biodiversity', which

refers to the variety of ecological functions and roles performed by different species within ecosystems, as well as the overall biological diversity present [3]. For example, this includes the diversity of pathways through which pollutants or organic matter is broken down in aquatic ecosystems. Functional biodiversity in river ecosystems encompasses several phenomena, including disturbance mechanisms such as the 'flood pulse', ecological succession, nitrogen cycling, energy flow, and biotic interactions [4].Currently, there is little consideration of the connections between the various levels of biodiversity in freshwater ecology and conservation.

FACTORS THAT AFFECT THE DIVERSITY OF AQUATIC LIFE

A comprehensive knowledge of the elements that determine biodiversity is crucial for the advancement of holistic ideas in aquatic ecology and conservation. Factors that affect biodiversity include ecological and evolutionary influences, such as the rate of evolution, the size of the geographic region, interactions between different species, the amount of available energy in the environment, the productivity of the ecosystem, and the level of disturbance[5]. By adhering to these principles, increased duration and accelerated progression facilitate the emergence of new species and enhance species-level biodiversity. The evolutionary speed theory posits that the pace at which evolution occurs is influenced by temperature, and that the variety of life forms is a result of evolution. Consequently, the level of biodiversity is reliant on the duration of continuous development of the biota across time [6]. An exemplary illustration of this phenomenon is Lake Baikal in Siberia (Russia), which is one of the oldest lakes in the world. In comparison to similarly sized lakes in Canada, Lake Baikal harbours a far more varied range of animal species [7]. Expansive regions with various and intricate environments provide a larger number of ecological niches. These niches, together with interactions between different species such as competition or predation, may prevent the exclusion of some species and ultimately lead to higher biodiversity. The relationship between biodiversity, ambient energy, and ecosystem productivity is apparent. This is because a smaller number of species can withstand unfavorable climatic circumstances, and the richness of species is constrained by the distribution of output or energy among them. Disturbance is a significant component that affects biodiversity. The logic for this is that mild disturbance slows down competitive exclusion. The intermediate disturbance concept seems to be invalid in stream ecosystems that experience extremely variable water flows and fluctuating water temperatures, since these circumstances may greatly reduce the variety of invertebrates. There are many instances that demonstrate how mild flooding may be essential for the diverse range of organisms in stream substratum. This habitat is necessary for the productivity and functioning of flowing water ecosystems [8]. Furthermore, it is important to acknowledge that a large number of different species and their variety, which may be attributed to non-specialized species, may have a negative association with the overall health of an ecosystem. Therefore, it is not always desirable in conservation management [9].

THE IMPORTANCE OF BIODIVERSITY FOR HUMANS

The close connection between biological diversity and ecosystem services and their significance for human well-being has been extensively studied and documented [10]. Freshwater biodiversity offers a wide range of valuable goods and services to human societies, some of which are irreplaceable. The preservation of freshwater biodiversity is of utmost importance in the field of conservation. A

key focus during the International Decade for Action 'Water for Life' – from 2005 to 2015 was prioritizing water resources [11]. Measuring the value of biodiversity solely in terms of monetary value falls short, as there are intangible factors that are equally significant. These include environmental ethics, religion, intrinsic values, responsibility and social beliefs, beauty and life-fulfilling values, and educational and scientific arguments. This text explores the significance of biodiversity and examines its effects on both individuals and society, specifically focusing on examples from aquatic environments. The understanding and recognition of the different benefits of biodiversity for humanity varies significantly across diverse cultural, ethnic, and educational backgrounds [12].

THE CURRENT SITUATION OF BIODIVERSITY LOSS AND EXTINCTION

According to [13] the fossil record indicates that the majority of species have become extinct, with over 99% of all species that have ever existed now being extinct. In this century, the rate of extinction in various taxonomic groups is approximately 100-1000 times higher than the natural background rate observed over centuries, which ranges from 0.001-0.01%. This current rate is comparable to the mega extinction events triggered by rapid climate changes, such as the Permian decline and the biodiversity loss in the Pleistocene [14]. Estimates of species extinction rates are often derived by extrapolating from a sample of 100,000 well-known species to the total number of described or estimated species [15].

The vulnerability of freshwater biodiversity is due to the various ways in which humans utilize and impact freshwater resources. These activities, such as extraction, diversion, containment, and contamination, can significantly compromise the value of freshwater as a habitat for organisms. Furthermore, it is worth noting that freshwater habitats account for a mere 0.01% of the world's water and occupy a mere 0.8% of the Earth's surface [16]. Despite their limited extent, these habitats support a remarkable 6% of all species and one third of all vertebrate species, making them distinct from any terrestrial fauna [17]. Streams and rivers are significantly impacted by the biodiversity crisis, as highlighted by Postel and Richter in 2003. Freshwater invertebrates have the highest extinction rates among all freshwater organisms. However, they are often overlooked in discussions of aquatic biodiversity conservation, despite their crucial functional roles in freshwater ecosystems. Based on careful analysis, it has been determined that the current extinction rates in freshwater mussels are estimated to be between 2-7% per century. These places those among the highest rates of extinction compared to other taxonomic groups [18]. Estimates suggest that mussel extinction rates in continental North America could exceed 6% per decade [19]. According to a study conducted by Dudgeon *et al.,* in 2006, freshwater habitats play a crucial role. The extinction rates of freshwater animals in North America, as determined by analysing data on unionid mussels, gastropods, crayfishes, fishes, and amphibians, were found to average 0.5% per decade. These rates are projected to potentially reach as high as 4% per decade, which is five times greater than the calculated losses of other species.

THREATS TO AQUATIC BIODIVERSITY

Various factors pose threats to aquatic biodiversity, especially freshwater biodiversity. These factors can be broadly categorized into five main categories: overexploitation, water pollution, habitat degradation, flow modifications, and invasions by exotic species. Global environmental changes,

such as nitrogen deposition, and climatic shifts, including temperature changes and alterations in precipitation and runoff patterns, impact all of these threat categories [20]. Freshwater ecosystems are incredibly diverse and have been heavily impacted by human activity. Furthermore, conflicts that arise from multiple users of water are compounded by the fact that freshwater ecosystems are positioned as 'receivers' and have high levels of endemism and non-substitutability [21].

Fishes are most impacted by overexploitation, with mollusks, crustaceans, and other taxonomic groups also being affected, although to a lesser degree. Species that possess significant economic value, have low reproductive rates, and reproduce later in life are especially susceptible to overexploitation. Large body size and/or aggregation during specific periods, such as spawning migrations in diadromous species, often contribute to a higher risk of overharvesting. Some examples of aquatic resources that have been heavily exploited include sturgeon species used for caviar production and various species of tuna found around the world.

Water pollution from domestic and industrial point sources has been significantly reduced in most industrialiser countries, although it continues to pose a significant challenge in many countries around the world. Despite the improvement in water quality of European rivers over the past few decades [22] the recovery of numerous endangered aquatic species, particularly those that rely on specific habitats, is not progressing as expected. Aquatic habitat degradation can manifest in different ways, including alterations in land use within catchment areas, such as deforestation. Changes in erosion and sedimentation patterns in streams and rivers can significantly affect the interstitial zone, which is a crucial habitat in these [23]. Water impoundments and dams, used for purposes such as hydropower generation, agriculture, and drinking water supply, can have significant impacts on aquatic species that rely on natural flow patterns .Habitat degradation and the construction of dams often lead to the fragmentation of aquatic habitats. This fragmentation results in decreased genetic exchange and limited opportunities for compensation migrations, population density modulations, and recolonizations.

ECOLOGICAL INTEGRITY IS CRUCIAL FOR THE PRESERVATION OF BIODIVERSITY

Integrity is the ability to sustain and uphold a cohesive and adaptable community that resembles the biological makeup and functional structure of the local natural waters. Biodiversity should not be compared to the temporary increase in species variety caused by introducing non-native plants and animals into natural ecosystems. Instead, it should prioritize the study of native biodiversity, including genetic, taxonomic, ecosystem, and ecological function levels. Deviation from natural norms suggests a decline in biodiversity.

INTEGRATIVE FRESHWATER ECOLOGY AND BIODIVERSITY CONSERVATION

AQUATIC HABITAT QUALITY AND RESTORATION ECOLOGY:

Habitat quality in aquatic ecosystems is not easily assessed due to the need to consider the specific requirements of different species at different life stages, as well as the connectivity of habitats. Therefore, IFEBC approaches should prioritise the most significant target species, which are usually keystone, indicator, umbrella, or flagship species. Additionally, they should concentrate on significant anthropogenic habitat changes, such as the construction of dams and weirs. Dams can effectively disrupt habitats by obstructing the spawning migrations of both diadromous and migratory freshwater fish species, leading to habitat fragmentation. An example that is well-known

is the lacustrine brown trout (Salmotrutta), a species that is currently endangered in the European alpine and sub-alpine regions. This species relies on migrations between habitats to successfully complete its life cycle.

Aside from the general quality of the habitat structure, the characteristics of particular crucial habitats and ecotones are of equal significance. In recent years, researchers have started to recognize the significance of stream bed quality in relation to biodiversity, ecosystem processes, and ecosystem health. Several studies have been conducted to investigate this impact [24]. The conditions and dynamics of stream beds are influenced by the flow regime, which controls erosion, sediment deposition, and remobilization. Climate and land use changes, along with flow regulation and in-stream habitat alteration, can significantly impact these delicate processes, resulting in severe consequences for the stream bed and, consequently, the overall functioning of the ecosystem [25]. Significant changes in stream bed composition and processes can have a profound impact on the distribution of species and their productivity.

STRATEGIES INVOLVING THE USE OF WATER TO CONSERVE AND SUSTAINABLY MANAGE RESOURCES

Avoid constructing additional dams in regions with significant biodiversity (refer to maps) or production. Differentiate between natural flooding that provides concrete advantages to rivers and riparian areas, and flooding caused by human activities [26]. Utilize terrestrial biological methods to address the latter issue, instead than only depending on river engineering. Employ indigenous species ecosystems wherever feasible in aquaculture and implement ecosystems-based fisheries management approaches.

CONCLUSIONS AND PERSPECTIVES

The case studies presented indicate that the most effective conservation strategies for freshwater biodiversity involve the integration of multiple levels of biological organization. Considering the dynamics of structural habitat availability, quality, and connectivity, as well as strategies for conserving the genetic basis of biodiversity and addressing environmental stressors is likely to lead to long-term success. Utilizing molecular and ecological techniques, this study aims to analyze, model, and interpret the functional processes in freshwater ecosystems. These processes are crucial for understanding the ecosystem services that are derived from freshwater biodiversity. Many ecologists and conservation biologists acknowledge the importance of comprehending the functioning of ecosystems at various levels of organization. However, it is common for them to focus on one level at a time. Therefore, it is crucial for the enhance collaboration between researchers and conservation biologists across various levels. One of the key challenges in the field is the development and optimization of predictive models for understanding the functioning of lotic ecosystems with high spatial and temporal resolution, from a scientific perspective. These models will be highly valuable for evaluating the impacts of natural and human-caused disturbances on productivity and biodiversity, particularly in relation to climate change. Studying the impact of habitats on various species, such as fish, invertebrates, and microbiota, using a 'landscape genetics' approach, or analyzing the genetic and ecological interactions of species that evolve and coexist together, can help in creating more comprehensive models and identifying areas of high biodiversity in freshwater that incorporate genetic diversity.

Evolutionary and population genetic studies have the potential to significantly contribute to the identification of conservation priorities. For optimal results in these fields, it is crucial to establish connections between the genetic makeup and important evolutionary characteristics like adaptation and variations in life history. In order to enhance the effectiveness of future research in ecotoxicology and ecotoxicogenomics, it is crucial to give more attention to the mechanistic connections between population relevant effect responses and the underlying molecular and cellular mechanisms. The understanding and conservation of aquatic ecosystems, especially in stream habitats, are areas that require further research and attention, as they are currently not well understood compared to terrestrial ecosystems.

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Chapter
13

UTILIZING ALGAE FOR SUSTAINABLE NANOPARTICLE SYNTHESIS AND APPLICATIONS

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ABSTRACT

Algae have long been used commercially and industrially as food, feed, additives, cosmetics, pharmaceuticals, and fertilisers, but the trend is now changing to algae-mediated green nanoparticle production (NPs). Algae are a rich source of secondary metabolites, are easy to produce, develop quickly, and are scalable, therefore this trend is growing by the day. Green synthesis of NPs has gotten a lot of interest recently as a safe, easy, sustainable, cost-effective, and environmentally friendly methodology. Metal precursors are reduced, capped, and stabilised by secondary metabolites in algae, resulting in metal, metal oxide, or bimetallic NPs. Depending on the site of NPs synthesis and reducing agents, NPs synthesis could be intracellular or extracellular. Brown, red, blue-green, micro and macro green algae have been the most extensively studied algae for the production of NPs. Algal biosynthesized NPs have also been researched for their biomedical uses, which include anti-bacterial, anti-fungal, anti-cancerous, anti-fouling, bioremediation, and biosensing activities, due to their biocompatibility, safety, and unique physico-chemical properties. The justification for algal-mediated production of metallic, metallic oxide, and bimetallic NPs from a variety of algae is discussed in this paper. In addition, a critical evaluation of the mechanism of biosynthesis of NPs from algae and their biomedical uses was conducted.

KEYWORDS: Algae; Green Synthesis; Nanoparticles; Biomedical Applications.

INTRODUCTION

The extraordinary physio-chemical properties of nanoparticles (NPs) and associated nano materials have spurred nanotechnology development during the last few decades. Almost every scientific field has been impacted by nanotechnology, which has made it possible to develop original answers to a number of research road blocks. Nano biotechnology was first introduced by the use of biological moieties to create Nano scale particles that could alter the physical properties of NPs. The synthesis of NPs of different sizes and shapes has generated a lot of attention because of their novel properties compared to their bulk counterparts. The consistency of a material's chemical, biological, and physicochemical properties vary significantly at the Nano scale due to the high aspect ratio of surface area to volume. Consequently, not able disparities surface. Considerations include mechanical properties, melting point, heat, optical absorption, electrical conductivity, biological activity, and catalytic

activity. Nanoparticles (NPs) are small particles that fill the space between bulk materials and atomic or molecular structures. NPs' structural configurations, size, and place of origin have all been described. Because of their unique morphological (shape, size, and charged is tribution) and physico-chemical properties, nanoparticles (NPs) are used in almost every scientific sector, including space, energy, defence, communication, medicine, and agriculture. NPs are being employed more and more in tissue engineering, medication delivery, imaging, therapy, illness detection, and cancer treatments. But NPs must be used in living things, including humans. Ideally, NPs used in biomedical applications should originate from renewable sources. The current trend in NP synthesis, which takes into account a number of factors including biocompatibility, bioavailability, bio-distribution, and most importantly, biosafety of NPs, is trending. Because algae are a rich supply of proteins, peptides, secondary metabolites, and pigments that can be utilised as nano-bio factories, algae are becoming more and more popular for green synthesis. They are also appealing candidates for the biological production of nanoparticles due to their rapid growth rate, simplicity in harvesting, and affordable scaling up. Algae are the most fundamental species on Earth; they are the main photosynthetic creatures and can be found in a variety of situations. Algae are perfect for green synthesis because of their capacity to hyper-accumulate metals and transform them into NPs. Numerous metallic and metal oxide nanoparticles (NPs) are produced from several kinds of algae, including brown (Phaeophyceae), green (Chlorophyceae), red (Rhodophyceae), blue-green (Cyanophyceae), and green (Phaeophyceae).

MECHANISM INVOLVED IN THE ALGAE-MEDIATED BIOSYNTHESIS OF NPS

Algae have a remarkable ability to transform heavy metal ions into more pliable forms and are known to hyper-accumulate these ions. These attractive characteristics have led to the anticipation of algae as model organisms for the synthesis of several kinds of nanomaterials, particularly metallic NPs. When an algae extract is added to a precursor metal solution, the biosynthesis of nanoparticles is set in motion. Algae's biological components, which include proteins, carbohydrates, lipids, oils, minerals, phycobilins, antioxidants, and other phytochemicals, help, reduce the charge of metal ions to zero valent states. The three-phase process of bio-reduction includes an activation phase that comprises metal ion reduction and nucleation as a result of the enzymes released by algal cells, which are visible from the solution’s colour shift. Nucleated metal elements combine throughout the development phase to generate thermodynamically stable nanoparticles (NPs) with a variety of sizes and forms. In the last termination phase, NPs acquire their final form. The physical properties of NPs are controlled by variables like temperature, pH, stirring, static conditions, and substrate concentration. The process involved in the biosynthesis of AuNPs by algae has been particularly covered here; it is essentially the same as the mechanism involved in the synthesis of other NPs.

Biosynthesis of NPs from algae could either be intracellular or extracellular depending on the location of NPs formed. The intracellular approach involves the dose-dependent production of NP inside the algal cell. Reducing agents include NADPH or NADPH-dependent reductase, which are produced during metabolic activities like photosynthesis, respiration, and nitrogen

fixation. Chloroauric acid was incubated with Ulvaintestinalis and *Rhizoclonium fontinale* algae at 20^0C for 72 hours, resulting in the intracellular synthesis of AuNPs. The thallus changed from green to a visibly purple colour, signifying the biosynthesis of AuNPs. Moreover, no colour change was observed when the gold metal solution was incubated with biomass, indicating that no intracellular enzymes or metabolites were connected to the bio-reduction process. In a different experiment, the chloroplasts of *Klebsormidium flaccidum* encased in silica gel solution visually changed from green to purple, indicating the cells' ability to decrease the gold precursor (chloroauric acid). TEM investigation provided additional confirmation of this, revealing dark-colored patches inside the thylakoid membrane that suggested the existence of reduced gold precursor salt produced by NADPH-dependent reductase of a similar vein, Senapati and colleagues (2012) provided evidence of the algal cell wall of *Tetraselmis kochinensis* producing AuNPs intracellularly. It was amply demonstrated by UV-visible spectroscopy that extracellular synthesis did not occur. The presence of bioactive moieties that are responsible for bio reduction is most likely the reason why the AuNPs were more densely present close to the cell wall as opposed to the cytoplasmic area.

When metal ions adhere to the surface of algal cells and are reduced there by metabolites like proteins, lipids, non-protein RNA, DNA, ions, pigments, and enzymes, this is known as the extracellular mode of production. The extracellular mode of synthesis is more practical since it is easier to purify NPs; nonetheless, there are certain necessary pre-treatments that must be done, such as washing and blending the algae biomass. The type, starting concentration, and pH of the metal and substrate, as well as other physio-chemical factors, all affect how NPs agglomerate and change in size. Increased pH strengthens the reducing ability of functional groups, which stops NPs from clumping together. By interacting with the amine groups of surface-bound proteins and their left over amino acids, basic pH aids in the capping and stabilization of NPs. The existence of a surface plasmon peak at 530 nm, which suggests the participation of proteins, enzymes, and biomolecules in algae-mediated NP synthesis, corroborated the extracellular production of AuNPs synthesized by *S. platensis* at different doses of chloroauric acid.

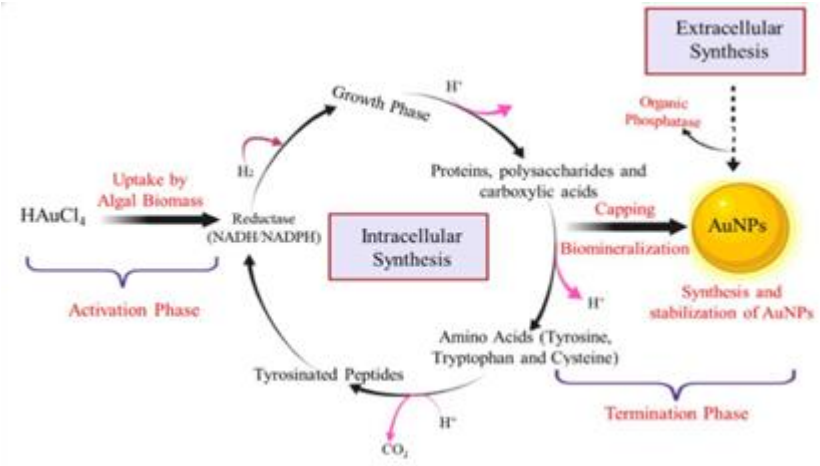

Fig 1: Schematic illustration of mechanism involved in extracellular and intracellular synthesis of algae-mediated gold nanoparticles (AuNPs)

BIOSYNTHESIS OF NPS FROM ALGAE

The classification of algae, which includes brown algae (phaeophytes), redalgae (rhodophytes), and green algae (chlorophytes), is based on the pigmentation that these eukaryotic, unicellular, and multicellular creature's release. Because they grow quickly, are simple to work with, and have a biomass growth rate that is typically ten times quicker than that of higher plants, algae are frequently utilised for the production of different metallic and metal oxide nanoparticles. To date, several algal strains have been studied for the environmentally friendly synthesis of various NPs. Here, the literature is thoroughly and critically evaluated with regard to the biosynthesis of NPs from several kinds of algae.

BROWN ALGAE-MEDIATED BIOSYNTHESIS OF NPS

The family Sargassaceae and order Fucales include brown algae. Sterols such cholesterols, fucosterols, sulfated polysaccharides, and functional groups like glucuroronic acid, muramicacid, alginicacid, and vinyl derivatives, which operate as capping and reducing agents for the formation of NPs, are the main constituents of fucales. Distinct species of brown algae have been used to create distinct metallic (such as silver and gold) and metal oxide (such as zinc oxide and titanium oxide) nanoparticles.

Among the most often produced NPs from brown algae are metallic NPs like copper (CuNPs), silver (AgNPs), and gold (AuNPs). More than half of the published data in the literature concerning various metallic NPs relate to the production of AgNPs from various strains of algae. This is because AgNPs have better physico-chemical properties than their bulk forms, which makes them particularly helpful in a variety of industries, including drug delivery, jewellery, paints, textiles, dental metals, and wound healing. Several species have been reported in the literature to be able to biosynthesize AgNPs from brown algae, including *Gelidiella acerosa, Turbinaria conoides, Desmarestia menziesii, Sargassum polycystum, Padina pavonica, and Cystophora moniliformis. T. conoides* was shown to produce spherical AgNPs (96 nm) through extracellular production, and these particles showed exceptional antibacterial activity against *Pseudomonas aeruginosa, Candida albicans, Escherichia coli, Staphylococcus aureus,* and *Staphylococcus epidermis*. It has been noted that the organic moieties, amines, polyamines, free hydroxyl, and carbonyl groups found in Turbinaria species (*T. ornate* and *T. conoides*) serve as reducing agents for the precursor silver salts used in the AgNP synthesis process.

AuNPs, a different type of NP that has been widely synthesised from brown algae strains, have demonstrated a number of bio-activities that are significant form medicine, including anti-fouling, anti-coagulant, and antibacterial properties. *T. conoides* is one of the most well-known species of brown algae among those that have been identified as being traditionally employed in the production of AuNPs. Triangular, spherical, rectangular, and polydispersed AuNPs were among the morphologies that may be produced from *T. conoides* through the extracellular pathway. The majority of the time, *T. conoides* and chloroauric acid were used to create AuNPs, which are precursors of gold ions. *Laminaria japonica*, a significant species of brown algae, has also been studied in relation to the green synthesis of AuNPs.

Bio-active substances such polyphenols, peptides, proteins, vitamins, carotenoids, and fibresare abundant in *L. japonica*. Extracellular synthesis of spherical (15–20 nm) AuNPs was carried out

from *L. japoni* causing phytochemicals and functional groups that acted as capping and reducing agents. There have also been reports of the production of AuNPs using other brown algae species, including *Fucus vesiculosus, Sargassum myriocystum, Ecklonia cava, Sargassum wightii, Stereospermum marginatum, Padina gymnospora, Dictyota bartayresianna,* and *Cystoseira baccata.* Apart from metallic nanoparticles, brown algae have also been documented to biosynthesize different types of metal oxide nanoparticles, including titanium oxide nanoparticles (TiO2NPs) and zinc oxide nanoparticles (ZnONPs). In one work, ZnONPs were created by heating dried S. muticum algal powder with distilled water until well combined, adding zinc acetate salt solution, and continuously stirring the mixture for hours until NPs were produced. The produced ZnONPs had a hexagonal form and ranged in size from 35 to 57 nm. Bioactive functional groups such as amines, sulphate, hydroxyl, and carbonyl were used to cap the particles.

RED ALGAE-MEDIATED BIOSYNTHESIS OF NPS

Red algae are members of the Rhodophyta family and are mostly consumed as food in many nations because of their distinct flavour and high protein and vitamin content. These proteins and vitamins may be the finest options for stabilisation and decrease in the manufacture of NPs mediated by algae. However, because of its self-aggregation, sluggish grow thin crystallisation, and stability problems, the synthesis of NPs from seaweed red algae is still in its early phases. Porphyravietnamensis is one of the more noticeable strains of red algae, having been reported to synthesise a variety of NPs on multiple occasions. This is because it contains a strong reducing agent, such as sulfated polysaccharides, which contain anionic disaccharides units consisting of 4-linked 3,6-anhydro-l-galactose and 6-sulfate residues flashing with 3-linked d-galactosyl residues. Numerous red algae strains, including *Kappa phycusalvarezii*, *Palmaria decipiens, Gelidiella acerosa, Gracilaria dura, Kappaphycus sp..,* and many more, have been documented in the literature for the production of AgNPs.

Comparing red algae-mediated AgNPs to the physio-chemical technique reveals that the former is less time-consuming, less expensive, and less environmentally harmful. The two most important characteristics of NPs in biomedical applications are their size and form. AgNPs synthesised from several strains of red algae are reportedly mostly spherical in shape and range in size from 20 to 60 nm. The anti-micro fouling property of these extracellularly synthesised AgNPs is very desirable in the medical domain. While the prevention of micro fouling in extracellular synthesis is a one-step procedure, micro fouling evacuation in intracellular NP synthesis necessitates multiple phases.

Comparatively speaking to AgNPs, very few investigations have been conducted on the production of AuNPs mediated by red algae. Using chloroauric acid as a precursor salt, Lemaneafluviatilis is one such marine red alga that being studied for the production of AuNPs. TEM revealed that it produced 5.9 nm-sized face-centered cubic and polydispersed crystalline AuNPs. Corallinaofficinalis has also been reported to produce spherical AuNPs extracellularly using reducing agents such as hydroxyl, phenol, and carbonyl functional groups. Numerous other red algae species, including *Kappaphycus alvarezii*, *Galaxaura elongata*, and *Chondrus crispus*, have also been reported to have simple AuNP production in addition to *L. flaviatilis* and *C.*

officinalis. The red algae strain *Gracilaria edulis* effectively biosynthesized bimetallic Ag-Au NPs in addition to monometallic NPs by utilising varying molar ratios of AgNO3 and HAuCl4 (1:1, 1:3, and 3:1). Strong anticancer effects on human breast cancer cells have been demonstrated by these artificial bimetallic nanoparticles.

BLUE-GREEN ALGAE-MEDIATED BIOSYNTHESIS OF NPS

Blue-green algae are members of the order Chroococcales, which comprises two unique families: Chroococcaceae and Entophysalidaceae. They have an unusual status in the biological world. These two families' members can be identified by the colonies they establish as their growing habitat. On damprocks, they form parenchymatous cell masses that proliferate in dense patterns. Because they use water as an electron donor and have two photo-pigments—carotene and chlorophyll a—that aid in photosynthesis, blue-green algae are photoautotrophic in nature. They are also thought of as unicellular bacteria's equivalents due to their shape. Blue-green algae, in contrast to brown and red algae, have also been extensively used for the synthesis of several kinds of NPs. *Spirulina platensis* is the primary blue-green algal source of AgNPs. The cyanobacteriumS. Platensis is a free-floating filamentous cyanobacterium with multicellular trichomes that have a left-handed helix and one open end. Additionally, 60–70% of it is composed of vegetable protein, which is high in iron, beta carotene, natural vitamins, and vital fatty acids. All of these nutrients can aid in the reduction and capping of NPs. AgNPs with a spherical form, ranging from 2 to 8 nm, have been synthesised from S. platensis and are effectively employed in the food, health, and pharmaceutical industries. AgNPs have also been synthesised from a variety of other blue-green algae species, including Plectonemaboryanum (octahedral, 200 nm), Microchaetediplosiphon (spherical, 80nm), Oscillatoriawillei (spherical, 10–25nm), and Cylindrospermumstagnale (pentagonal, 38–88 nm), in addition to S. platensis.

Similar to AgNPs, *S. platensis* as demonstrated its rolein AuNP production. The extracellular synthesis of spherical, octahedral, and cubic AuNPs mediated by *S. platensis*has been reported by several researchers, demonstrating the involvement of proteins and peptides as reducing agents. Another significant species of blue-green algae is *Phormidium valderianum*, also referred to as alkalo-tolerant Rhodococcus. By using UV-Vis spectroscopy, this species has produced intracellular mono-dispersive triangular AuNPs with an absorbance of 1.897 at a wavelength of 530 nm. Surface plasmon resonance (SPR), which is dependent on particle size, constant dielectric medium, and surface absorbed species, is responsible for the development of a single broad peak of AuNP at 530 nm. It has also been shown that *P. valderianumuses* cytoplasmic metabolites as reducing agents to synthesis espherical, hexagonal, and FCC (24 nm) AuNPs extracellularly. Additional to monometallic NPs, S. With the aid of extracellular proteins, platensish has also been documented in the production of bimetallic nanoparticles (NPs), including core shell Ag-AuNPs and magnetic crystalline-shaped silica-NPs. It has been reported that *Chlamydomonas reinhardtii*, a significant fresh water green algae species, is involved in the mediation of CdSNPs, or cadmium sulphide bimetallic nanoparticles. CdSisa semiconductor belonging to the II-VI group that has special optoelectronic properties and has been widely used in LEDs, photo-catalysis, and biosensors.

GREEN ALGAE-MEDIATED BIOSYNTHESIS OF NP

Based on their habitat, green algae are classified into two primary groups: micro and macrogreen algae. Macro green algae are multicellular sea organisms that resemble plants, whilst micro green algae are unicellular and mostly grown or inhabit fresh water. Nowadays, a lot of work is done on the biosynthesis of different metal oxide, bimetallic, and monometallic NPs from green algae. Here, we have separately discussed the macro-mediated and micro-mediated production of NPs from both kinds of green algae.

GREEN MICRO ALGAE-MEDIATED BIOSYNTHESIS OF NPS

Micro green algae, which area member of the Cladophoralesorder, are widely employed in a wide range of biotechnological, industrial, and medical applications. Alkaloids, phenols, flavonoids, carbohydrates, and functional groups that may act as both stabilising and reducing agents in the micro-mediated production of NPs are among the many vital components that they are a rich source of. AgNPs are the most widely produced monometallic NPs among other NPs from several species of microgreen algae in vitro.

More than 20 distinct species of green microalgae have been used to produce AgNPs through biosynthesis to date. When examined using several spectroscopic and microscopic techniques, including SEM, XRD, FTIR, DLS, and EDX, the AgNPs synthesised from various species display intriguing and varied physico-chemical features. The majority of the extracellularly employed micro green algae species, including Pithophoraoedogonia (cubicand hexagonal, 24–55 nm), *Chlorococcum humicola* (spherical, 16 nm), Chlorella vulgaris (triangular, 28nm), and *C. Enteromorphaflexuosa* (circular, 15nm) and *Reinhardtii* (rectangular and rounded, 1–15 nm). To date, the biosynthesis of AgNPs has been achieved through the utilisation of more than 20 different species of green microalgae. Upon analysis by a range of spectroscopic and microscopic methods, such as SEM, XRD, FTIR, DLS, and EDX, the AgNPs synthesised from different species exhibit a fascinating array of diverse physico-chemical characteristics. Pithophoraoedogonia (cubic and hexagonal, 24–55 nm), Chlorococcumhumicola (spherical, 16nm), *Chlorella vulgaris* (triangular, 28nm), *C. Enteromorphaflexuosa* (circular, 15 nm), and Reinhardtii (rectangular and rounded, 1–15nm) are the most commonly used extracellularly employed microgreen algae species.

In addition to AgNPs and AuNPs, semiconductor NPs has also been synthesised using micro green algae. A lot of work has gone into creating silicon-NPs from microgreen algae. Because silicon nanoparticles are semiconductors by nature, they are frequently employed as bio-indicators in industrial wastes to detect the presence of hazardous substances. They hold significant position in the ecological cycle as well since they are vital to the recycling of nutrients and the generation of oxygen. In order to do this, *C. vulgaris*, a green alga, was considered. Algal extract was combined with silicon alkaloids, which were utilised as a silicon precursor. The peptides and proteins in the *C. vulgaris* extract hydrolysed and poly-condensed silicon alkaloids to create silicon-NPs.

GREEN MACRO ALGAE-MEDIATED BIOSYNTHESIS OF NPS

Green macro algae, which contain a variety of useful compounds that are responsible for NP capping and reduction, are also known as bio-factories for the manufacture of metallic

nanoparticles. In addition to being engaged in the creation of nanoparticles, these chemicals show potentanti-viral, anti-tumor, anti-bacterial, and cytotoxic properties towards microorganisms. Different strains of green macro algae have been widely employed in the production of metallic nanoparticles (NPs) in recent times.

One of them ost beneficial green macro algae species, Ulvafasciata, was used to create nano-sized silver colloids, which were then put to cotton fabric both with and without citric acid totest their anti-microbial effectiveness. In a different study, the amide, carboxylic, and nitro compound-rich *Gracilaria edulis* was utilised to create spherical AgNPs and octahedral ZnONPs. Another significant species of seaweed green macro algae, *Chaetomorpha linum*, is well known for its ecological roles in controlling the availability of nutrients to its habitat. It has also been used to synthesise AgNPs by catalyzing the reduction of silver ions (Ag+) to Ag0 in the extracellular environment with the aid of peptides, flavonoids, and terpenoids. In addition to AgNPs, green macroalgal species including *Rhizoclonium fontinale* and *Prasiola crispa* have also been known to synthesise AuNPs. Due to its application in targeted medication delivery for cancer treatment, AuNPs have garnered a lot of attention in the last few years. Because AuNPs are not reproducible at the ideal size and form, synthesising the misusually difficult. However, green macro algae overcame this difficulty and produced stable, reproducible AuNPs.

CONCLUSION

Undoubtedly, algae are great options for the environmentally friendly synthesis of nanoparticles (NPs) since they are abundant in secondary metabolites, which function as capping and reducing agents. This field, nevertheless, is still in its infancy and cannot be expanded for commercial purposes. This may be the result of a number of constraints on algal-mediated NP biosynthesis, including sluggish reaction kinetics (lasting several days to weeks), low NP yield, subpar morphological properties of biosynthesized NPs, and selection of algal strain as well as inadequate synthesis condition optimisation, including adjustments to pH, temperature, contact duration, and concentration. In addition to these, there are other variables in the NP yield, and process control is one of them. Moreover, because large levels of agglomeration have been documented in some circumstances, colloidal stability is frequently a problem that requires careful consideration. The use of algae in the manufacture of NP has also been restricted by a lack of understanding of the synthesis mechanism. Therefore, more research is required to address the issues of kinetics, yield, and cell viability in order to build large-scale photo-bioreactors. Additionally, a comparative study on the physiochemical properties of NPs synthesised using conventional methods and algae represents a significant knowledge gap that the scientific community should address.

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Chapter
14

FERRITES FOR GAS SENSING TECHNOLOGIES

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ABSTRACT

In modern technology gas sensors play vital role in identification and monitoring of gases. These sensors are applicable in various sectors such as medical, industrial, environmental and smart home appliances etc. Among many other gas sensing materials spinel ferrites have gained lot of attention due to their unique structural, catalytic, magnetic and morphological properties. Their tunable properties, thermal stability, high sensitivity and selectivity make them superior as compared to other traditional sensing materials. Their cost effective and ecofriendly nature makes them suitable for large scale applications. Despite these advantages, spinel ferrites have certain limitations which need careful attention to ensure their effective use in gas sensing. This chapter begins with overview of spinel ferrites. Further it discusses the importance of gas sensors in modern technology followed by exceptional properties of ferrites. Finally, it concludes with discussion about the challenges, future directions and conclusion.

KEYWORDS: Ferrites, Gas Sensing, Morphology.

INTRODUCTION

Spinel ferrites are type of ceramic material which shows remarkable properties and have general formula MFe_2O_4. Here M represents divalent metal cation (M^{2+}) and Fe stands for iron in its trivalent state (Fe^{3+}). The specific arrangement of metal ions in the crystal structure makes them useful for applications in various field. Usually, Spinel ferrite shows cubic crystal structure which consist of two different sites namely tetrahedral and octahedral where metal cations can reside. The typical arrangement of metal ions in these sites leads to formation of different spinel configurations such as normal, inverse and mixed.

NORMAL SPINEL

For minerals with general formula AB_2O_4 normal spinel structure is very common. Here (A) represents divalent cations and (B) represents trivalent cations. In this arrangement the A and B cations occupy tetrahedral and octahedral sites respectively. The A cations occupy one-eighth of the tetrahedral voids and B cations occupy one-half of the octahedral voids. The oxygen anions occupy cubic close packed sites. Usually, the A cations are smaller than B cations and are surrounded by four oxygen neighbors in tetrahedral sites. The B cations which are at octahedral sites have six oxygen neighbors. The unit cell contains 8 A cations, 16 B cations and 32 oxygen atoms.

INVERSE SPINEL

These spinel materials have same general chemical formula AB_2O_4 as that of normal spinel, but they differ in distribution of cations. In this spinel structure arrangement of A and B cations is reversed compared to normal spinel. Here tetrahedral sites are occupied by half of the trivalent (B) cations and the octahedral sites are occupied by both divalent (A) cations and the remaining trivalent cations. Thus, the divalent cations share octahedral sites with trivalent cations. The unit cell of inverse spinel structure contains 32 oxygen atoms, 8A and 16 B cations. Inverse spinel structure has significant influence on the properties of ferrites particularly where cation distribution plays important role.

MIXED SPINEL

This structure has intermediate configuration between normal and inverse spinel structure. In mixed spinel there is no strictly defined cation distribution between tetrahedral and octahedral sites as that of normal and inverse spinel structure. The fraction of divalent and trivalent cations occupies both tetrahedral as well as octahedral sites. The degree of mixing among tetrahedral and octahedral sites varies in different mixed spinel.

This type of cations arrangement in the lattice produces profound effect on the properties of spinel ferrite. Thus, by controlling the distribution of cations in the crystal lattice, researchers can tailor the properties of spinel ferrites for various applications in the field of sensors, catalysis, magnetic storage [1-3]. Researchers can modify the chemical and physical properties of spinel ferrites through proper selection of divalent cations such as Co, Mn, Ni, Mg, Zn etc.

Spinel ferrites are promising candidates for gas sensing applications by virtue of their stability, low cost and ease of synthesis. Due to their unique properties these materials are useful in detection of various toxic and hazardous gases such as carbon monoxide, ammonia and many other volatile organic compounds. The exceptional gas-sensing ability of the spinel ferrite is mainly attributed to their ability of adsorption of gas molecules on their surface. It makes them highly sensitive even for small concentration of gases. In addition to this these materials often shows semiconducting behavior which is necessary for resistive type gas sensors. Also, doping of various metal ions in the crystal lattice results in modification of their electric properties which in turn increases their selectivity and sensitivity for specific gases. In last few years extensive research has been conducted to utilize full potential of spinel ferrite nanoparticles. Recent advancement in the field of nanotechnology has further enabled researchers to synthesize nano structured ferrites with high surface to volume ratios which increases the potential of these materials for sensing applications.

IMPORTANCE OF SENSORS IN MODERN TECHNOLOGY

HEALTHCARE

According to new research, it is observed that gas sensors are applicable in detection of certain biomarkers in breath, which could help in diagnosis of the diseases at an early stage. For example, in diagnosis of diabetes, spinel ferrites are used as sensor material to analyze the concentration of acetone in breath. These materials provide simple and faster way to diagnose diabetes by detection of acetone despite high breath humidity [4]. The spinel ferrites provide potential solution for making sensors that are comfortable and easy to use. Such devices can be used to monitor breathing patterns and sleep disorders [5]. Gas sensors can also be used in various medical devices to measure the

amount of carbon dioxide (CO_2) in the breath of a patient. In capnography one can check the respiratory condition of patient by determining the level of exhaled carbon dioxide [6]. Thus, precise monitoring of gases through sensors helps medical professionals in delivery of effective treatment by ensuring the safety of patient.

ENVIRONMENTAL MONITORING

Gas sensors can detect the presence of many harmful gases such as Carbon monoxide (CO), nitrogen oxides etc [7, 8]. Which are colorless and odorless. On exposure to high level of such pollutants can lead to various health related issues. By constantly monitoring these pollutants gas detectors can warn us about the possible health hazards. Thus, with the help of gas sensors we can identify areas that have poor air quality and can take necessary steps to reduce the pollution sources. In short by keeping eye on the air we breathe gas sensors provide the valuable information to safeguard the environment and human health.

INDUSTRIAL SAFETY

In industry gas sensors are used to detect leaks of hazardous gases [9]. These devices constantly monitor the release of dangerous gases and are able to detect even small fraction of gases in the air. Once the leak is identified they trigger an alarm to notify the workers. This notification provides sufficient time to workers for evacuation of working site and hence avoids the possibility of explosions, fire and inhalation of hazardous gases. Thus, in general, gas sensors play a vital role in ensuring the safety of peoples at working place when they are dealing with the hazardous chemicals.

SMART HOMES AND IOT

Now day's gas sensors are becoming an essential component of modern home appliances. Ferrite based gas sensors are useful in detection of various hazardous gases and volatile organic compounds. Their thermal and chemical stability makes them suitable for their long-term use even in case of temperature and humidity fluctuations. In comparison to other sensing materials their production cost is low. Spinel ferrites are nontoxic recyclable and ecofriendly material which is essential for sustainable smart home solutions. Integration of sensors with these smart devices furnishes real time data to the owners and notifies them about the possible potential threats [10].

Spinel Ferrite: Material with exceptional properties for gas sensing applications

Due to their unique combination of properties spinel ferrites have emerged as promising material for gas sensing applications.

PROPERTIES OF SPINEL FERRITES

CHEMICAL STABILITY:

Chemical stability is important factor which can affect the performance and durability of gas sensors. In gas sensing applications materials are exposed to various gases, harsh environmental conditions and even in some cases to corrosive gases. Hence it is necessary to ensure the chemical stability of the gas sensing material. The chemical stability assures the sensor can distinguish between target and non-target gas molecules without undergoing unwanted side reactions. Also, due to chemical stability active sites on the surface remain available for adsorption of gas molecules even in presence of contaminant gases. Thus, excellent chemical stability of spinel not only makes

them suitable for their use in harsh chemical environment but also it will help to operate with these materials for relatively longer period of time [11].

CATALYTIC ACTIVITY:

The catalytic activity of spinel is an important aspect which contributes towards their effectiveness in gas sensing applications. The catalytic properties of spinel material help to promote the chemisorption process which occurs when gas molecules bind to surface of material. This results in change of electric resistance when exposed to different gases. The inherent catalytic property of spinel helps in effective chemisorption process which significantly improves sensitivity of gas sensors. Thus, they can detect even very low concentration of gases. Usually, these materials show better catalytic activity at relatively low operating temperatures which is beneficial for energy efficiency. Therefore, proper understanding of this property will help researchers to develop sensors with good sensitivity, selectivity for wide range of applications [12].

HIGH SURFACE AREA AND POROSITY:

Spinel ferrites possess excellent gas adsorption and interaction capabilities for sensing applications by virtue of their high surface area and porous nature. The nanostructured ferrites with high surface area and porosity provide more reaction sites for interaction between sensing material and target gas molecules. This increases the probability of adsorption of gas molecules and leads to increase in sensitivity of sensors [13].

SEMICONDUCTING BEHAVIOR:

The semiconducting properties of spinel are important for gas sensing applications. The electrical properties of ferrite changes when gas molecules interact with the surface. This allows the device to detect and identify specific gases [14].

THERMAL STABILITY:

The exceptional thermal stability of these materials allows their use at elevated temperatures [15].

MAGNETIC PROPERTIES:

Due to their inherent magnetic properties these materials can be used for development of advanced sensors. By manipulation of their structure and composition researchers can create highly sensitive and versatile sensor devices for different applications [16].

ADVANTAGES OF SPINEL FERRITE FOR SENSING:

OPERATION AT RELATIVELY LOW TEMPERATURE:

One of the key advantages of spinel ferrite is their ability to function at relatively lower temperature compared to other gas sensing materials. These materials can significantly reduce the energy consumption by virtue of their ability to operate at low temperature. Due to lower operating temperature less, energy is required to heat the sensors. This property is important for portable devices where battery life is critical. Conducting sensing operations at lower temperature also extends the life span of sensor. Thus, with the help of spinel ferrites we can develop more cost-effective and energy- efficient sensing devices for various applications. $ZnFe_2O_4$ is a typical example of spinel-based gas sensor that can operate at relatively low temperature. Studies have shown that this sensor has high sensitivity towards ethanol within 225-300^{0}c rang [17].

ACTIVE SITES FOR ENHANCED GAS INTERACTION IN SPINEL FERRITE GAS SENSORS:

As compared to their bulk counterparts the spinel ferrite nanoparticles have higher surface area. Hence spinel ferrite nanoparticles furnish large number of active sites where gas molecules can interact with the surface of material. When the gas molecules adsorb on the surface they alter the properties of the spinel, which forms the basis of gas sensing mechanism [18].

LOW COST AND SIMPLE FABRICATION TECHNIQUES:

In order to utilize the gas sensors for widespread applications it is necessary to design fabrication techniques which are fast, cost-effective and accessible. The Spinel ferrites can be fabricated by using variety of methods such as sol-gel. Hydrothermal, Co-precipitation and spray pyrolysis.

TUNABILITY OF PROPERTIES THROUGH CATION SUBSTITUTION:

Spinel ferrites are ideal materials for sensing field due to their ability to incorporate different transition metal cations in their crystal structure. By modifying their composition researchers can tune the properties of spinel to meet the specific requirement of various sensing applications. The electric properties of these materials can be manipulated by changing the dopant and concentration of dopant ions. In comparison to traditional metal oxides these materials can improve electric response of sensor by modification of oxygen vacancies in the structure. Also, there is a vital role of dopant type and its concentration on the selectivity and sensitivity of sensors [15].

LIMITATIONS:

There is lack of clarity about the interaction of different gas molecules with spinel ferrites. This creates hindrance in designing and optimization of sensing devices based on ferrite materials [19].To increase the sensing performance of the material it is necessary to have good control over morphology of the material. Achieving this control is cumbersome procedure. Also, there is problem of limited gas detection range of the material.

FUTURE DIRECTIONS:

In order to overcome the challenges associated with these materials the researchers should focus on

a) Development of sensing material with proper understanding of the sensing mechanism.

b) Use of various dopant elements to improve selectivity and sensitivity.

c) Optimization of synthetic parameters to control morphology of the material.

CONCLUSION:

The unique properties of spinel ferrites make them a promising material for gas sensing applications. In nano dimensions these materials possess high surface area for the adsorption which helps them in detection of low concentration of gases. Their properties can be manipulated through proper structural and compositional modifications. Due to tunable properties these materials offer significant flexibility for designing of sensing devices. There are few challenges which are related to their sensing mechanism, selectivity and sensitivity. Hence in order to utilize their full potential it is necessary to work in the direction of understanding their sensing mechanism and optimization of synthetic parameters.

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Chapter

15

ANTI-INFLAMMATORY ACTIVITY OF SOME MEDICINAL PLANTS BY USING CARRAGEENAN-INDUCED PA EDEMA METHOD IN ALBINO MICE – A REVIEW

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ABSTRACT

Plants are considered as authoritative therapeutic aid. The various plants have a potential medicinal consequence. Medicinal plants have the ability to synthesize a wide verity of phytochemical compounds as secondary metabolites which shows anti-inflammatory activity. The conservative drug available in the marketplace treat inflammation produces various side effects. For conquer these problems medicinal plants play a major role to alleviate many diseases related with inflammation. Inflammation is part of the body's immune response. There can be four primary indicators of inflammation: pain, redness, heat or warmness and swelling. These reviews try to make accessible an overview of reported anti-inflammatory activities of some medicinal plants drug by using Carrageenan-Induced Paw Edema method in albino mice.

KEYWORDS: Medicinal Plants, Anti-inflammatory, Response.

INTRODUCTION

According to World Health Organization (WHO), about three-quarters of the world population depends on traditional medicines (mainly herbs) for their healthcare. Ayurveda and Chinese medicinal systems are the most suitable traditional system which has a considerable amount of research on pharmacognosy, chemistry, pharmacology and clinical therapeutics (Kiranjot, *et al.,* 2010; Ayannar and Ignacimuthu, 2011). It is evident that several plants have been used in traditional ayurvedic medicine for treatment and management of distinct inflammatory disorders and wound healing activities (Gacche, 2011). Now there is a need for the new safe, potent, nontoxic or less toxic anti-inflammatory drug. Medicinal and aromatic plants contribute to major portion of the flora. The plant materials obtained from these plants are used in the pharmaceuticals, cosmetics, and drug industries. Approximately 20% of the world flora has been tested for their pharmacological or biological activities (Suffredini *et al.*, 2004). It is estimated that 80%t of the population in developing countries relies on traditional plant-based medicines for their health requirements (WHO, 1991). Even many of the modern medicines are based on raw materials obtained from medicinal plants due

to their least side effects, low prices, and lasting curative property. Extracts of many plants possesses potent antimicrobial activities (Madiha *et al.,* 2018; Khaleeq *et al.,* 2018). Inflammation is the most basic mechanism for tissue repair after an injury, consisting of a series of cellular and micro vascular reactions that serve to remove damage and regenerate new tissue. (Arpan Kumar Tripathi, *et al.,* 2023).

INFLAMMATION

Inflammation is a contained defensive reaction of cells/tissues of the body to allergic or chemical irritation, injury etc. Inflammation may have beneficial effects such as the destruction of invading microorganisms and the walling-off of an abscess cavity to prevent spread of disease. Inflammation is typically classified according to its time course as:

- Acute inflammation -The initial and often transient series of tissue reactions to injury.
- Chronic inflammation-The successive and regularly prolonged tissue reactions following the initial response. (Asija, *et al.,* 2014)

CARRAGEENAN-INDUCED PAW EDEMA

In this model study the acute and sub-acute phases of inflammation in rodents (rat and mice). Carrageenan is a widely used irritant or inflammogen or a phlogistic agent. First of all the rats were divided into three groups of six animals. Acute inflammation was inducing by intraplantar administration of 0.1 ml of carrageenan (1% solution in normal salt). The level of paw was calculated prior to inj. of phlogistic agent (0 h) and then at a predetermined interval of 60 min up to 3 h after carrageenan injection. Volume of paw was calculated using Digital Plethysmometer. Change in the paw volume was measured and antiinflammatory activity was calculated as follows: %Inhibition of inlamma t ion = 1 − × 100 Where Vt represents the change in the paw volume in drug treated group. Vc represent the change in the volume of paw in the corresponding vehicle-treated control group. (Asija, *et al.,* 2014)

PLANT WITH ANTI-INFLAMMATORY ACTIVITY

AEGLE MARMELOS

The aqueous extract of the root bark of Bilwa was prepared and tested for anti-inflammatory activity in albino rats using Carrageenan induced paw edema model and cotton pellet induced granuloma and the standard drug was taken indomethacin and Bilwa. The result revealed that anti-inflammatory activity was expressed the inhibition (Benni, *et al.,* 2011).

TAMARIX DIOICA

Analysis of the data reveals that the tested plant showed the activity at both phases of 3 and 5 hours when tested by Carrageenan Induced Paw Edema Model. Results indicated that the inhibitory activity was time and dose dependent. Maximum anti-inflammatory activity was shown by 200mg/kg. The tested plant *Tamarix dioica* demonstrated good inhibitory activity even at low dose of 50mg/kg. (Arshad Iqbal, *et al.,* 2019).

GOMPHOCARPUS PURPURASCENS

Maximum anti-inflammatory effects by all doses of leaf extracts were observed from 2–4hr post-induction in carrageenan-induced paw edema; and all tested doses of the extract inhibited the formalin-induced inflammation significantly ($p < 0.001$, $p < 0.01$). The presence of saponins,

alkaloids, flavonoids, tannins, terpenoids, anthraquinone, steroids, and phenols might be responsible for these activities. (MeazaAdugnaAyanaw, *et al.,* 2023).

CORDIA DICHOTOMA

The ethanolic extract of the *Cordia dichotoma* significantly reduces the paw volume and shows the highest anti-inflammatory activity as compared to the petroleum ether and aqueous extract of the *Cordia dichotoma*. Carrageenan-induced edema has been commonly used as an experimental animal model for acute inflammation study and is believed to be biphasic. (Arpan Kumar Tripathi, *et al.,* 2023).

EUPHORBIA GRANULATE

Anti-inflammatory activity Aqueous methonolic extract of *Euphorbia granulate* (whole plant) calculated using Carrageenan-induced edema and in vivo study was performed in female rat specie *Rattus norvegicus.* The results revealed that significant anti-inflammatory activity was observed at dose strength of 200mg/kg. (Mohsin Ahmad Ghauri, *et al.,* 2021)

PLUMBAGO ZEYLANICA, TERMINALIA BELLARICA* AND *TERMINALIA CHEBULA

The results of the oral administration of *P. zeylanica, T. bellarica* and *T. chebulla* plant extracts showed promising anti-inflammatory activity by reducing the carrageenan induced mice paw edema volume. (Shaikh, *et al.,* 2016).

VISCUM ALBUM* AND *WITHANIA COAGULANS

Methanolic extracts of *Viscum album* and *Withaniacoagulans* showed potent anti-inflammatory activity at 500 mg/kg anti-inflammatory activity by using carrageenan induced paw edema method with albino rats. (Saima Maher, *et al.,* 2018).

GAULTHERIA FRAGRANTISSIMA* AND *BYTTNERIA HERBACEAE

The extracts of the whole plant of *Byttneriaherbaceae* and leaves of *Gaultheria fragrantissima* possess significant anti-inflammatory in rats on carrageenan induced paw edema method by 57.57% on oral administration of 400 mg/kg, respectively by 55.15% on oral administration of 200 mg/kg, compared to the untreated control group. (Narayanan, *et al.,* 2020)

SUMMARY AND CONCLUSION

Traditional plants play a very important role in the discovery of new drugs. Since ancient time's medicinal plants have been used to treat different ailments due to their accessibility, availability, inherited practice, economic feasibility, and perceived efficiency. Inflammation is a defence mechanism of the body and inflammation is a healthy process resulting from some trouble or disease. But in some conditions when negative effect of the inflammatory process is produced example, these inflammatory illnesses are rheumatoid arthritis, osteoarthritis, inflammatory bowel diseases, retinitis, multiple sclerosis, psoriasis and atherosclerosis. To overcome this problem anti - inflammatory agents are very needful. For this purpose, variety of safe and effective anti-inflammatory agents is available, with many more drugs under development. So, these agents are very helpful to reduce the inflammatory response. These agents are called anti-inflammatory agents. Now present days, inflammation is a very big challenge of mankind. So much of anti-inflammatory drugs are available, but it is believed that these drugs such as opioids and analgesia inducing drugs like NSAIDS are not useful in all cases and these drugs also produce side effects, so to overcome this problem new drugs are very requisite and in plants have many of phytoconstituents which are

helpful in inflammation and have less side effects. So in this medicinal plants on behalf of their phytoconstituents which can be helpful in inflammation (Sowjanya, *et al.,* 2017).

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Chapter
16

EGG PRODUCTION: ENHANCEMENT AND CHALLENGES

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ABSTRACT

Egg production is a vital component of the global agricultural sector, driven by rising demand for protein-rich foods. Enhancements in this field have been achieved through genetic selection, optimized nutrition, and modern housing systems. However, the industry faces challenges such as animal welfare concerns, antibiotic resistance, and environmental sustainability. Addressing these challenges requires a balance between productivity, ethical practices, and innovation for long-term success.

KEYWORDS: Egg Production, Genetic Selection, Nutritional Management, Antibiotic Resistance, Animal Welfare, Sustainability, Feed Efficiency, Poultry.

INTRODUCTION

Egg production is a critical sector of the global agricultural economy, providing a rich source of protein and other essential nutrients. Over the years, the demand for eggs has risen sharply due to population growth and dietary shifts towards protein-rich foods. To meet this demand, various strategies to enhance egg production have been employed, while several challenges continue to affect the industry's sustainability.

ENHANCEMENT OF EGG PRODUCTION

Genetic Selection and Breeding One of the most effective strategies for enhancing egg production is genetic selection and breeding. Poultry breeders have focused on selecting layers (egg-laying hens) with high productivity traits, such as earlier onset of laying, larger egg size, and longer laying periods. This selective breeding has resulted in modern layer hens that can produce significantly more eggs than their counterparts from previous generations. For example, today's commercial layer hens can produce up to 300 eggs annually under optimal conditions, compared to much lower numbers in the past.

Nutritional Management Nutrition plays a crucial role in optimizing egg production. Feed formulations are carefully designed to meet the nutritional needs of layers at different stages of their production cycle. A balanced diet rich in protein, essential amino acids, calcium, vitamins, and minerals is essential for maintaining high egg production rates. Protein and energy-rich diets help improve egg size, while sufficient calcium intake is crucial for strong eggshell formation.

Additionally, advances in feed technology have enabled the use of nutritional supplements like omega-3 fatty acids, which can improve egg quality by enriching the eggs with beneficial nutrients.

Phytogenic feed additives, enzymes, and probiotics are also used to improve digestion, gut health, and nutrient absorption, ultimately leading to better production performance.

Environmental Control and Housing Systems Modern housing systems and environmental controls have revolutionized egg production by providing hens with an environment that maximizes productivity. Climate-controlled housing with regulated temperature, humidity, and lighting is critical for maintaining hen health and ensuring consistent egg production. Light management, in particular, is an important factor; layers require around 14 to 16 hours of light per day to maintain optimal laying cycles.

Different housing systems, such as battery cages, enriched cages, and cage-free systems, have been designed to improve both productivity and animal welfare. While traditional battery cages allow for high levels of egg production, there is increasing demand for cage-free and enriched systems due to consumer concerns about animal welfare.

Disease Prevention and Biosecurity Maintaining a healthy flock is essential for high egg production. Diseases such as avian influenza, Newcastle disease, and infectious bronchitis can significantly reduce egg production and quality. Implementing strict biosecurity measures and vaccination programs helps in preventing the outbreak and spread of diseases within poultry farms. These measures include controlling farm access, disinfecting equipment and facilities, and isolating new birds before integrating them into the flock.

Additionally, routine health checks and proper management of external parasites, such as mites and lice, are crucial in keeping the flock healthy and maintaining optimal production.

Technological Advancements Technology has greatly enhanced efficiency in egg production. Automation systems are widely used in commercial poultry operations for tasks such as feed dispensing, egg collection, and environmental control. These systems reduce labor costs, improve precision in feed and water management, and minimize wastage.

Advances in genomics and biotechnology also offer new opportunities for further improving egg production. Genomic selection allows for more precise identification of productive traits, and research into gene-editing technologies holds promise for addressing challenges like disease resistance and environmental adaptation in the future.

Fig 1: Egg

CHALLENGES IN EGG PRODUCTION

Animal Welfare Concerns One of the biggest challenges facing the egg production industry is the growing concern over animal welfare. Traditional housing systems like battery cages have been criticized for restricting natural behaviors in hens, leading to physical and psychological stress. In

response to these concerns, many countries and consumers are advocating for cage-free systems that offer hens more space and freedom to move around.

Transitioning from conventional to cage-free systems presents several challenges, including higher production costs, changes in management practices, and potential impacts on productivity. Producers must find ways to balance the demands for animal welfare with the need for efficient and cost-effective production.

Antibiotic Use and Resistance the use of antibiotics in poultry production, including egg-laying hens, has come under scrutiny due to concerns about antibiotic resistance. Antibiotics are often used to prevent disease outbreaks and improve feed efficiency. However, the overuse of antibiotics can lead to the development of resistant bacteria, which pose a threat to both animal and human health.

To address this challenge, there is increasing pressure on the industry to reduce antibiotic use and find alternative strategies for maintaining flock health. These include better bio-security, vaccination, and the use of pro-biotics, prebiotics, and other natural feed additives to enhance immunity and prevent disease.

Feed Costs and Sustainability Feed represents one of the largest costs in egg production, and fluctuations in feed prices can have a significant impact on the profitability of egg producers. The poultry industry is highly dependent on soybean meal and corn as primary feed ingredients, and any disruption in the supply of these ingredients can lead to increased costs.

Sustainability is another critical issue, as there is growing pressure on the industry to reduce its environmental footprint. This includes minimizing feed wastage, reducing water and energy consumption, and finding more sustainable feed alternatives, such as insect-based protein or algal sources of essential nutrients.

Market Volatility and Consumer Preferences Egg producers must also contend with fluctuating market conditions and changing consumer preferences. The demand for organic, free-range, and antibiotic-free eggs has grown in recent years, driven by health and ethical concerns. Meeting these demands often requires significant changes in production practices, which can increase costs and create challenges for producers competing in a price-sensitive market.

Additionally, egg production is vulnerable to seasonal fluctuations and market volatility, which can impact prices and profitability. Producers need to adapt to these market dynamics while maintaining a focus on both efficiency and product quality.

Environmental Impact The environmental impact of egg production is another ongoing challenge. Poultry farming can contribute to environmental degradation through the generation of waste, including manure and emissions like ammonia. The industry must find ways to manage these by-products effectively to reduce their impact on soil, water, and air quality.

In response to this challenge, there is a growing focus on adopting more sustainable farming practices, such as manure recycling and precision feeding, to minimize environmental damage while maintaining high production levels.

CONCLUSION

Enhancing egg production is a multifaceted endeavor that requires the integration of genetic advancements, nutritional optimization, technological innovation, and effective disease management. However, the industry faces several challenges, including animal welfare concerns,

antibiotic use, feed costs, and environmental sustainability. Addressing these issues will be crucial to the long-term viability and success of egg production systems, especially in light of growing consumer awareness and regulatory demands. By balancing productivity with ethical and sustainable practices, the poultry industry can continue to meet the global demand for eggs while reducing its environmental and social footprint.

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Chapter
17

ORGANIC FARMING

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INTRODUCTION

As people become more aware of the food that their family members and relatives eat, the importance of health advantages is growing. As a result, items produced by organic farming have a degree. In the past, individuals would spend money on organic products, heart beats, and high-quality local veggies. This resulted in a long life span and a stable manner of living. An overview of the advantages, difficulties, and current state of organic farming in India is given in this study.

Increasing the productivity of the area under cultivation, lowering prices, and producing more efficient goods with little to no harm to the environment and human population should be the main goals of agricultural development policies in emerging nations (Nedumaran, 2020). Over the past 10 years, organic farming systems have gained more attention due to the perception that they provide some answers to the issues facing the agriculture industry. Benefits from organic farming could include better food quality, non-renewable resource conservation, and environmental protection (Dwivedi and Charyulu, 2016). There is a need for organic farming in society, both from the stand point of farmers and consumers.

ORGANIC FARMING

In order to generate crops, animals, and popularity, organic farming uses agricultural production systems that rely on compost, green manure, crop rotation, and biological pest management. An agricultural production system that is oriented on organic practices encourages resource cycling in order to preserve biodiversity and advance ecological balance. The main components of organic farming include the use of green manure, cover crops, animal manure, and soil rotation to increase soil fertility, disrupt the residence of pests and illnesses, and optimize the biological activity of the soil.

TYPES OF ORGANIC FARMING

PURE ORGANIC AGRICULTURE

It makes use of organic pesticides and manures that are completely free of insecticides and in organic substances.

INTEGRATED ORGANIC FARMING

Integrated nutrients are involved pest management and management. It's the farming practices that use natural resources to grow crops Materials. Additionally, possessing the full nutritional benefits and also succeeds in stopping the plant or produce. Relationships between various Farming branches

METHODS OF ORGANIC FARMING

SOIL MANAGEMENT

After cultivation of crops, the soil loses its nutrients and its quality deplete. Organic Agriculture initiates the use of bacteria that is present in animal waste. The bacteria help in making the soil nutrients more productive and fertile. The use of procedures, methods, and treatments to preserve soil and improve its functionality is known as soil management. It covers soil amendment, soil conservation, and the best possible soil health. Both organic and non-organic soils require some degree of management in agriculture to keep agricultural land from declining in productivity over many years. Because organic farming relies entirely or almost entirely on healthy soil for fertilization and pest control, it places a special emphasis on optimal soil management.

Organic farming relies more heavily on the natural break down of organic matter than the average conventional farm, using techniques like green manure and composting, to replace nutrients taken from the soil by previous crops. This biological process, driven by microorganisms such as mycorrhiza and earthworms, releases nutrients available to plants throughout the growing season. Farmers use a variety of methods to improve soil fertility, including crop rotation, cover cropping, reduced tillage, and application of compost. By reducing fuel-intensive tillage, less soil organic matter is lost to the atmosphere. This has an added benefit of carbon sequestration, which reduces greenhouse gases and helps reverse climate change. Reducing tillage may also improve soil structure and reduce the potential for soil erosion. Plants need a large number of nutrients in various quantities to flourish. Supplying enough nitrogen and particularly synchronization, so that plants get enough nitrogen at the time when they need it most, is a challenge for organic farmers. Crop rotation and green manure help to provide nitrogen through legumes mostly the family Fabaceae, which fix nitrogen from the atmosphere through symbiosis with rhizobial bacteria.

Compared to a typical conventional farm, organic farming depends more on the organic matter's natural decomposition. Green manure and composting are two methods used to replenish nutrients that previous crops have taken from the soil. Microorganisms like earth worms and my corrhiza power this biological process, which releases nutrients that plants can use all season long. Crop rotation, cover crops, decreased till age, and composting are some of the techniques farmers employ to increase soil fertility. Less soil organic matter is released into the atmosphere when fuel-intensive till age is reduced. Carbon sequestration, which lowers greenhouse gas emissions and aids in climate change reversal, is an additional advantage of this. Reducing till age may also lessen the likelihood of soil erosion and enhance soil structure.

WEED MANAGEMENT

Weed is unwanted plant that grows in agricultural fields. Organic agriculture focuses on lowering weed and not removing it completely. Weeds compete with pasture or productive crops. By contaminating harvests or interfering with animals, they can cause burrs, thorns, poisoning, or other problems that hinder the use and management of desirable plants. Crops are in competition with weeds for light, water, nutrients, and space. Larger, more vigorous seedlings are less vulnerable than smaller, slower-growing seedlings. Due to their narrow, upright stems and sluggish germination, onions are among the most vulnerable [citation needed]. Broad beans, on the other hand, yield huge seedlings and are far less affected, with the exception of times when there is a water scarcity during the critical period when the pods are filling out [citation needed].

Transplanted crops that are grown in potting compost or sterile soil have an advantage over weeds that are just starting to sprout.

CROP DIVERSITY

Monoculture is the practice used in the agriculture fields where we harvest and cultivate only type of crop in a particular place. Recently, Polyculture has come into existence. Where we harvest and cultivate kinds of crops. To meet the increasing crop demand and produce the required soil microorganism. The loss of agricultural diversity puts the world's food security at risk because fewer and fewer crop species are available to the world's population. A growing number of crops are farmed in monoculture, which means that if a single disease overcomes a variety's resistance, as it did during the Great Famine in Ireland, it might wipe out an entire harvest or, as it did with the 'Gros Michel' banana, lead to the commercial extinction of an entire variety. International organisations are attempting to maintain agricultural diversity with the aid of seed banks.

CONTROLLING OTHER ORGANISM

There are both useful and harmful organisms in the agricultural farm which affect the field, so, we need to control the growth of such organisms to protect the soil and the crops. We can do this by the use of herbicides and pesticides that contain fewer chemicals or are natural. In addition to weeds, arthropods (such as insects and mites), nematodes, fungi, and bacteria are other organisms that can cause issues on farms. Among the practices are, but are not restricted to: Little pirate bugs, big-eyed bugs, and, to lesser extent, lady bugs (which have a tendency to fly away) are examples of predatory beneficial insects that consume a variety of pests. Although they tend to fly away, lacewings are also effective. Although parasitoid wasps are often effective against their chosen prey, the wind can make them less effective outside, as is the case with all smallinsects. Other mites can be effectively controlled by predatory mites. *Bacillusthuringiensis*is one of the naturally occurring pesticides that can be used on organic farms.

LIVESTOCK

Another traditional farming activity that goes hand in hand with agriculture is the raising of livestock and birds for meat, dairy, and eggs. The goal of organic farms is to give animals 'natural food and living circumstances. Having an organic certification attests to the fact that animals are raised in compliance with USDA organic standards for the whole of their lives. One of these rules is that every animal feed needs to be organically certified. Organic animals must be pastured, their diet must be organic, and they may and must be given medication when ill, but pharmaceuticals cannot be used to encourage growth.

PROS OF ORGANIC FARMING

HIGHNUTRITIONALVALUE

Compared to traditional agricultural food items, organic food products have a higher nutritional content because they don't contain modified ingredients. They are also allowed time to flourish and the optimum natural conditions for growth, which contributes to their excellent nutritional value.

ENVIRONMENTAL SUSTAINABILITY

Every country in the world wants to achieve remarkable environmental sustainability. Organic farming can help achieve this to some extent. According to research, organic farming can offer remarkable means of promoting biodiversity, ecological harmony, and environmentally sustainable

biological cycles. For instance, the main goals of organic farming are biodiversity conservation, nutrient cycle promotion, ecological balance, and soil management and conservation.

FOOD SECURITY

Due to the consequences of climate change and subpar farming methods that result in subpar crop produce, there has always been an imbalance between the supply and demand for food. Because there is a general lack of safe and nourishing food to satisfy food preferences and dietary demands for a healthy and active life, many people worldwide are starving and lack access to enough food.

BENEFITS

ECOLOGICAL: creates healthy soil; counter acts the effects of global warming; fights erosion; improves water quality; deters algal blooms; promotes biodiversity; and benefits animals.

ECONOMIC BENEFITS: include lower production costs and higher farmer income. Increased purchasing power and access to premium organic markets increased ability to negotiate financial stability through agricultural diversification, which lowers the danger of major crop failure. Eradication of poverty

BETTER TASTE AND MORE NUTRITION:

Fruits and vegetables that are organically raised have a much better taste than other mechanically farmed ones. This is due to the fact that they are given a much longer time to develop and are not pumped with artificial things. The sugar structures in these crops have more time to mature and develop into a tasty and nutritious product. Reduces pesticide and Chemical residue in soil Organic farming minimizes the use of pesticides and chemicals there by reducing the major environmental Issues. It ensures the health of soil, water, air and flora and fauna. Also reduces the major environmental Issues like soil erosion, air pollution, water pollution etc.

PROMOTION OF BIODIVERSITY

Crop rotation to build soil fertility and raising animals naturally helps promote biodiversity, which promotes greater health across all living species. As organic farms provide safe havens to wild life.

CONSUMESLESS ENERGY

Organic farming does not rely on the use of synthetic fertilizers as opposed to conventional techniques that are generous with these external chemicals. Avoiding fertilizers contributes to a greater cause of Energy conservation. This is because manufacturing synthetic fertilizers consumes a significant amount of Energy. On average, it's safe to say that the energy usage is lower by atleast 30-50% in the organic Farming systems.

CHALLENGES INORGANIC FARMING:

SHORT AGE OF BIO MASS: Lack of Biomass Many knowledgeable farmers and specialists are unsure if organic materials can provide all the nutrients in the necessary amounts. They believe that there is more than enough biological matter to meet the needs, even if this issue can be resolved.

DISRUPTY OF SUPPLY AND DEMAND: The difference between supply and demand Fruits and vegetables cannot be moved to any area, whereas non-perishable grains can be grown anywhere. There should be willing businesses, aggregators, and farmers in the area where the demand is coming from for it to be produced locally. However, metropolitan areas that lack farm lands for the production of organic fruits and vegetables are typically the source of demand.

TIME: In fact, more engagement between a farmer and his crop is necessary for organic farming in order to observe, intervene promptly, and manage weeds, for example. A single farmer may

naturally produce more crops using industrial ways than using only organic methods.

HIGH ON MRP: It is fundamentally more labour-intensive than chemical or mechanical agriculture. It is practically a given that the outcomes would be expensive because organic farming requires such meticulous attention to detail. The majority of the space is used to sell these organic fruits and vegetables after they are sold to the market. Because of this, the majority of individuals take that action to support organic products. The market-sold goods cost half as much as non-organic ones.

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Chapter 18

THE MEDICINAL AND NUTRITIONAL BENEFITS OF EDIBLE MUSHROOMS: A COMPREHENSIVE REVIEW

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ABSTRACT

Mushrooms, classified as fungi, serve as a valuable source of nutrition and medicinal compounds. These eukaryotic organisms thrive in diverse habitats, from damp soil to decaying wood, and offer a unique nutritional profile that bridges the gap between meat and vegetables. They are rich in essential nutrients including proteins, carbohydrates, vitamins, and minerals, making them beneficial for human health, particularly for heart patients. Medicinal mushrooms, such as those from the genera *Lentinus*, *Pleurotus*, *Tremella*, *Auricularia*, *Cantharellus*, and *Trametes*, have been utilized in traditional and modern medicine for their therapeutic properties. These mushrooms exhibit a range of pharmacological activities including anti-tumor, anti-inflammatory, antioxidant, anti-diabetic, and antimicrobial effects. Key bioactive compounds found in these mushrooms, such as polysaccharides, phenolic compounds, and triterpenoids, contribute to their health benefits. However, the distinction between edible and poisonous mushrooms is critical due to the presence of toxic compounds in some species. This review highlights the medicinal and nutritional values of various mushrooms, emphasizing their potential in drug development and disease prevention.

KEYWORDS: Medicinal Mushrooms, Nutritional Benefits, Lentinus, Pleurotus, Tremella, Antioxidant Activity, Edible Mushrooms.

INTRODUCTION

Mushrooms are a valuable source of nutrition for humans. As eukaryotic organisms, they rely on other organisms for sustenance, making them parasitic in nature. Scientifically, mushrooms are classified as fungi. After devastating floods, when crop fields are destroyed, the damp soil often fosters the growth of various fungi. Among these, some are edible mushrooms, which can be seen as a mercy from nature. Mushrooms have diverse habitats; they can grow on land, above ground, on dry trees, or in damp areas. Nutritionally, mushrooms are beneficial to human health as they contain phosphorus, calcium, proteins, carbohydrates, essential salts, and vitamins. They offer a unique combination of nutrients, bridging the gap between meat and vegetables. Due to their low-calorie content and rich mineral composition, mushrooms are recommended for heart patients. Additionally, they contain compounds that may help combat cancer and other infections. Mycotoxin, a compound found in some mushrooms, plays a crucial role in determining whether a mushroom is edible or poisonous. Unfortunately, the visible differences between edible and poisonous mushrooms are often subtle, leading to confusion among the general public (Shuhaida Ismail *et al.*, 2018).

MEDICINAL MUSHROOMS AND THEIR PHYTOCHEMISTRY

Over the past few decades, medicinal mushroom extracts and essences have been widely used as alternative medicine in Korea, China, Japan, and Eastern Russia. Around 200 wild species are used for medicinal purposes, with 35 species being commercially cultivated for their nutritional and medicinal value (Lakhanpal *et al.,* 2005). Medicinal mushrooms, including Lentinus, Auricularia, Hericium, Grifola, Flammulina, Pleurotus, and Tremella, exhibit potential medicinal and functional properties. Other species, such as Ganoderma and Trametes, are known primarily for their medicinal benefits (Ganeshpurkar *et al.,* 2010). Medicinal mushrooms are not only used as food but also as dietary supplements, pharmaceuticals, and natural biocontrol agents in plant protection, displaying bactericidal, insecticidal, nematicidal, fungicidal, and herbicidal activities (Wasser*et al.,* 2010). Sufficient evidence suggests that many mushroom species contain bioactive compounds that may reduce the risk of cancer, heart disease, diabetes, and viral infections. These bioactive compounds, often associated with the mycelial cell wall, enhance immunity against carcinogens (Ramesh *et al.,* 2010). In recent years, medicinal mushroom extracts have gained importance, especially in Oriental medicine, for the prevention and treatment of various diseases (Kidd *et al.,* 2000). Bioactive molecules with anticancer and immunomodulatory properties are increasingly used to support immune function in cancer patients during radiotherapy and chemotherapy, thereby prolonging survival in certain types of cancer (Mizuno *et al.,* 1995). The historical usage and current commercial and medical acceptance of various edible and non-edible mushrooms are well documented. Notable species include *Lentinus edodes* (Shiitake), *Ganoderma lucidum* (Reishi or Ling Zhi), *Phellinus linteus*, *Porio cocos*, *Grifola frondosa* (Maiitake), *Auricularia auricula*, *Hericium erinaceus*, *Tremella fuciformis*, *Schizophyllum commune*, *Flammulina velutipes*, *Pleurotus ostreatus* (Oyster mushroom), Trametes (Coriolus) versicolor, and *Ophiocordyceps sinensis* (caterpillar fungus) (Hobbs, 1995).

GENUS LENTINUS

The genus *Lentinus* (Lentinula), belonging to the family Polyporaceae, is commercially significant, with about 40 known species worldwide. These wood-decaying species are edible, providing substantial amounts of proteins, lipids, fats, minerals, and vitamins. However, not all varieties are edible, particularly those with a tough texture (Gulati *et al.,* 2011). *Lentinula edodes*, commonly known as Shiitake, is widely distributed in temperate regions of Asia, including China and Japan. It is the second most commonly produced edible mushroom globally (Chang *et al.,* 1999). Various preparations, extracts, and active components from *L. edodes* have demonstrated remarkable therapeutic potential, including antimicrobial, antiviral, cardioprotective, antifungal, antidiabetic, hemagglutinating, antioxidative, hepatoprotective, hypolipidemic, immunomodulating, and antineoplastic activities (Biser *et al.,* 2010). One of the most significant polysaccharides isolated from *L. edodes* is Lentinan (β-1, 3-glucan), known for its antitumor and immunomodulatory effects. The dried fruiting body of *L. edodes* contains carbohydrates (58-60%), proteins (20-23%), fiber (9-10%), lipids (3-4%), and ash (4-5%) (Xiaofie *et al.,* 2014). Studies have shown that Shiitake mushrooms can lower blood pressure and free cholesterol in plasma while accelerating lipid accumulation in the liver by removing them from circulation (Kabir *et al.,* 1989). Another species, *Lentinussajor-caju*, is a white rot edible mushroom that grows naturally on fallen logs during rainy seasons. It is

increasingly recognized as a potential nutraceutical food source, exhibiting pharmacological activities such as anticoagulant, anti-inflammatory, antihypertensive, and anticancer effects (Fumio *et al.,* 2014). The ethanol extract of *L. sajor-caju* has shown toxic and teratogenic effects in the developing embryos of *Daniorerio* and may be a source of compounds for developing anticancer drugs (De Castro *et al.,* 2015). *Lentinus squarrosulus* is another edible mushroom, a white rot saprophytic fungus that grows on dead and decayed wood in forests. Its mycelia exhibit strong antioxidant activity, containing high protein (57.6%) and low fat (0.5%), along with significant amounts of magnesium (0.4%), potassium (3.8%), and vitamin B (0.2%) (Abdulah *et al.,* 2011). In vitro studies have demonstrated that the mycelium extract of *L. squarrosulus* possesses antioxidant properties with no toxic effects even at high doses. In vivo studies have shown that its mycelium extract contains absorbable antioxidants that enter circulating plasma, causing an acute increase in plasma antioxidant capacity (Abdulah *et al.,* 2015). The culture broth of submerged *L. squarrosulus* mycelium produces higher β-glucan content than the mycelium extracts and has been observed to exhibit antitumor activity (Ahmad *et al.,* 2014).

GENUS PLEUROTUS

The genus *Pleurotus* includes edible mushrooms cultivated worldwide, known for their robust growth on a variety of agroforestry substrates and their production of highly nutritious food containing biologically active compounds with therapeutic effects (Gunde *et al.,* 1999). *Pleurotus ostreatus*, or Oyster mushroom, is one of the most widely cultivated edible mushrooms. It exhibits various pharmacological activities, including antitumor, hypocholesterolemic, anti-atherogenic, and antioxidative effects (Sarangi *et al.,* 2006; Bobek *et al.,* 1999). Bioactive metabolites, such as fatty acids, phenolic compounds, nucleotides, and alkaloids, have been isolated from the fruiting bodies of *P. ostreatus*, with several new compounds identified, including indolo-3-carboxylic acid, trans-3,4-dihydro-3,4,8-trihydroxy naphthalen-1(2H)-one, uracil, 4-hydroxybenzaldehyde, and 3-formylpyrrole, which may have pharmaceutical and pharmacological applications (Papaspyridi *et al.,* 2012). Ribonucleases and polysaccharopeptides isolated from *P. ostreatus* have shown potential in neutralizing HIV by degrading viral genetic material, exhibiting immunomodulatory properties (Refaie *et al.,* 2009). *Pleurotus florida*, known for its pleasant flavor and high protein content, has yielded several bioactive compounds, including ergosterol, ergosterol peroxide, and cerevisterol. The aqueous extract of *P. florida* has demonstrated anti-hepatotoxic activity in rats, while its ethanol extract has shown antimicrobial activity against various bacteria (Rahman *et al.,* 2013). In vitro studies indicate that the methanolic extract of *P. florida* inhibits the growth of solid tumors induced by EAC cell lines in a dose-dependent manner (Jose *et al.,* 2000). *Pleurotussajor-caju*, or grey oyster mushrooms, are rich in dietary fiber, β-glucan, vitamin B, and vitamin D, exhibiting significant immunomodulatory and antioxidant activities (Verma *et al.,* 2001). Nutritional analysis of *P. sajor-caju* reveals a high content of protein, carbohydrates, crude fat, ash, and crude fiber, with an energy value of 297.5 kcal/100g dry weight. Major minerals include calcium, iron, and magnesium, with the highest levels being 505.0 mg, 109.5 mg, and 108.7 mg per 100g, respectively (Gogavekar *et al.,* 2014). Phytochemical analysis of *P. sajor-caju* indicates the presence of alkaloids, flavonoids, tannins, saponins, terpenoids, cardiac glycosides, steroids, and triterpenes. Flavonoids, polyphenols, and

tannins are responsible for the antioxidant activity of the mushroom, which is beneficial for scavenging reactive oxygen species (ROS) (Verma *et al.,* 2001).

GENUS TREMELLA

Tremella belongs to the family Tremellaceae and is widely distributed and commercially cultivated as a food source. Over 100 species of this genus are recognized globally. The mushrooms in the *Tremella* genus are known for their medicinal properties, largely due to the presence of the acidic hetero polysaccharide glucuronoxylomannan, which is found in their fruit bodies, pure mycelium cultures, and yeast-like budding haploid cultures (Sergey *et al.,* 2000).

One prominent species, *Tremella fuciformis*, also known as snow fungus, is traditionally used as a tonic herb and a beauty enhancer to improve complexion. *T. fuciformis* exhibits several pharmacological activities, including anti-tumor, immuno stimulatory, hypocholesterolemic, hepatoprotective, and anti-inflammatory effects. The species is particularly rich in polysaccharides, with glucuronoxylomannan being the principal component (Chen *et al.,* 2008). Recent in vitro studies have shown that an alkali-soluble polysaccharide (ASTP) derived from *T. fuciformis* exhibits higher antioxidant activity than polysaccharides extracted with hot water, suggesting that ASTP could be a valuable natural resource for antioxidants (Qoing *et al.,* 2011). Additionally, the aqueous extract of *T. fuciformis* (0.01-1 μg/ml) has been shown to promote neurite outgrowth in PC-12 cells in a dose-dependent manner, indicating potential for use in treating neurodegenerative disorders (Kim *et al.,* 2011). *T. fuciformis* polysaccharides have also demonstrated anti-aging effects by increasing superoxide dismutase activity in the brain and liver in vivo (Chen *et al.,* 2008).

Table 1: Family and its Botanical Name and Common Names

Botanical Name	**Common Name**	**Family**	**Bioactive Compounds**	**Reference**
Lentinula edodes	Shitake	Polyporaceae	Lentinan, LEM, LAP, EP_3, Lentinamicin, EPS_4, Lentin, Eritadenine, Lectin, JLS18	(Renuka *et al.,* 2015).
Lentinula sajor-caju	White rot	Polyporaceae	Lectins, proteoglycans	(Luo *et al.,* 2011).
Lentinula squarrosulus	White rot sapro-phytic fungus	Polyporaceae	Lectins	(Abdullah *et al.,* 2015).
Pleurotus ostreatus	Oyster	Pleurotaceae	3-formylpyrrole, trans-3,4-dihydro-3,4,8-trihydroxynapthalen-1(2H)-one, indolo-3-carboxylic acid and 4-hydroxybenzoic acid, Pleuran	(Papaspyridi *et al.,* 2012). (Carlos *et al.,* 2012).
Pleurotus florida	Oyster	Pleurotaceae	Ergosterol, ergosterol peroxide, cerevisterol, mixture of palmitic acid and stearic acid, linoleic acid oleic acid	(Consolacion *et al.,* 2015).

Pleurotus sajor-caju	Phoenix mushroom	Pleurotaceae	Exopolysaccharide (EPS), Glucan rich polysaccharide	(Kanagasabapathy*et al.*, 2012). (Zheng *et al.*, 2016).
Tremella fuciformis	Snow fungus	Tremellaceae	Glucuronoxylomannan, alkali soluble plysaccharide (ASTP)	(Chen *et al.*, 2008). (Qoing *et al.*, 2011).
Tremellamesentrica	Yellow brain mushroom	Tremellaceae	Glucuronoxylomannan (GX)	(Evgeny *et al.*, 2005).
Auricularia polytricha	Cloud ear fungus	Auriculariaceae	α,β-glucan polysaccharide	(Song *et al.*, 2012).
Cantharellus cibarius	Golden Chanterelle	Cantharellaceae	Ergosterol, cerevisterol, tuberoside, β-sitosterol glucoside, ergosterol peroxide,β-sitosterol, 7-dehydrostigmasterol	(Jeong *et al.*, 2008).
Trametes versicolor	Turkey tail	Polyporaceae	Krestin, PSP, ergosterol, ergosterol peroxide, trilinolein, ergosta-7,22-dien-3β-o1, 4-isobutoxyphenyl palmitate, N-D-2′-hydroxyheptanoic-1-O-β-D-glucopyranosyl-9-methyl1-4, 3β-linoleyloxyergosta-7-ene, betulinic acid, botulin	(Harhaji *et al.*, 2008). (Seyad *et al.*, 2015).
Trametes orientalis		Polyporaceae	TOP-2, PTOP, triterpenes	(Yong *et al.*, 2014). (Zhenga *et al.* 2015).
Ganoderma lucidum	Lingzi or Reshi	Ganodermataceae	GLPG, GLIS, PGY, GL-PS peptide, F_3	(Li *et al.*, 2005). (Wu *et al.*, 2009). (Ji*et al.*, 2007).
Ganoderma tsugae	Hemlock varnish shelf	Ganodermataceae	tsugaric acid F, palmitamide	(Lin *et al.*, 2016).

GENUS TREMELLA

Tremella, belonging to the family Tremellaceae, is globally distributed and commercially cultivated, particularly for its food and medicinal properties. The genus includes over 100 species, many of which possess health-promoting attributes due to the presence of glucuronoxylomannan, a polysaccharide found in fruit bodies, mycelium culture, and yeast-like cultures.

Tremella fuciformis, commonly known as snow fungus, is renowned for its use as a tonic herb and beauty enhancer. It exhibits a range of pharmacological activities, including anti-tumor, immunostimulatory, hypocholesterolemic, hepatoprotective, and anti-inflammatory effects. Studies have shown that the alkali-soluble polysaccharide (ASTP) from *T. fuciformis* has significant antioxidant activity, which may be harnessed for treating neurodegenerative disorders and anti-aging therapies.

Tremella mesenterica, known as the Yellow Brain mushroom, is traditionally used to treat cancer and respiratory diseases. It contains glucuronoxylomannan (GX), which has been associated with various pharmacological activities, such as immunostimulation, anti-diabetic, and hepatoprotective effects. Studies have demonstrated its potential in reducing blood glucose levels and modulating immune responses in diabetic models.

GENUS AURICULARIA

The Auricularia genus, commonly referred to as wood ear or jelly ear mushrooms, is widely cultivated for its nutritional and medicinal benefits. These mushrooms are high in protein and exhibit anti-tumor, antiviral, antibacterial, and antiparasitic activities.

Auricularia auricula-judae (wood ear) is rich in carbohydrates, minerals, and proteins and is known for its antioxidant, anti-tumor, hypoglycemic, hypolipidemic, anti-inflammatory, anticoagulant, and cardioprotective effects. Studies have identified water-soluble polysaccharides from this species that strongly inhibit tumor growth.

Auricularia polytricha (cloud ear fungus) is another widely consumed species, particularly in Asia. Its polysaccharides have shown promising antioxidant, anti-inflammatory, anti-tumor, and immunomodulatory activities. The mushroom has also demonstrated hepatoprotective effects in animal models.

GENUS CANTHARELLUS

Cantharellus cibarius, commonly known as the Golden Chanterelle, is a highly nutritious mushroom found across Europe, Asia, Africa, and North America. It contains essential nutrients such as amino acids, vitamins, and trace elements, and exhibits various medicinal properties including anti-inflammatory, antioxidant, anticancer, antimicrobial, and antiviral activities. The mushroom has been studied for its ability to chelate excessive iron, reduce oxidative stress, and inhibit the growth of harmful microorganisms.

GENUS TRAMETES

Trametes versicolor, also known as the Turkey Tail mushroom, is a staple in traditional and modern medicine. It is known for its immunomodulatory and cancer-inhibiting properties, largely due to its polysaccharopeptide compounds, PSK and PSP. These compounds have been shown to have strong anti-melanoma activity and antimicrobial effects. Other species in this genus, such as *Trametes*

pubescens and *Trametes orientalis*, also possess significant antioxidant, anti-inflammatory, antidiabetic, and antitumor activities.

GENUS GANODERMA

The Ganoderma genus includes polypore mushrooms found primarily in tropical regions. With over 400 bioactive compounds, including triterpenoids, polysaccharides, and sterols, Ganoderma species are highly valued for their medicinal properties.

Ganoderma lucidum (Reishi) is the most well-known species and is used for its anti-tumorigenic, anti-inflammatory, hypoglycemic, anti-HIV, anti-ulcer, anti-osteoporotic, and immunostimulatory effects. Recent studies have highlighted its ability to reduce oxidative stress and inhibit tumor growth.

Ganoderma tsugae, another medicinal species, is noted for its anti-inflammatory, antifibrotic, antioxidative, anticancer, and anti-autoantibody properties. Research indicates its potential in modulating cancer cell signaling pathways and protecting against oxidative stress.

POISONOUS MUSHROOMS

While many mushrooms offer medicinal benefits, some species are highly toxic due to the presence of cyclopeptide toxins. These toxins can cause severe liver and kidney damage, often leading to fatal outcomes.

Genus Amanita includes some of the most toxic mushrooms, such as *Amanita phalloides* (Death Cap) and *Amanita muscaria* (Fly Agaric). These species contain potent toxins like amatoxins and muscimol, which can cause severe poisoning and, in some cases, death. Despite their toxicity, certain compounds from these mushrooms have been studied for their antibacterial and thrombin-inhibitory activities.

Pharmacological Potential of Mushrooms

Mushrooms are recognized for their diverse pharmacological properties, with over 700 medicinal and edible species identified for their significant biological activities (Mizuno *et al.*, 1995). These properties include immune system enhancement, bioregulation, and the maintenance of homeostasis and biorhythm. They are also known for their potential to prevent and treat life-threatening diseases, including cancer, cerebral stroke, and heart diseases. Key pharmacological activities of mushrooms include:

- Antitumor
- Anti-fungal
- Anti-oxidant
- Anti-viral
- Anti-bacterial
- Hepatoprotective
- Anti-inflammatory
- Anti-diabetic
- Hypolipidemic
- Anti-thrombotic
- Hypotensive (Wasser *et al.*, 1999).

ANTI-OXIDANT ACTIVITY

Mushrooms, whether wild or cultivated, have demonstrated significant antioxidant activity across numerous studies. The anti-oxidant properties are evaluated through various in vitro assays, including:

DPPH Inhibition: Measures the ability of the mushroom extracts to scavenge free radicals.

Iron Chelation: Assesses the capacity of mushroom compounds to bind free iron, reducing oxidative damage.

Lipid Peroxidation Inhibition: Evaluates the protection against the oxidative degradation of lipids.

Biochemical Assays: Determine the overall antioxidant capacity of mushroom extracts.

Key compounds contributing to antioxidant activity in mushrooms include:

Polyphenols: Such as phenolic acids, lignin, melanin, tannins, and flavonoids.

β-Carotene: An important antioxidant carotenoid.

Ascorbic Acid: Also known as Vitamin C, a well-known antioxidant (Ferria *et al.,* 2009; Barros *et al.,* 2009).

Mushroom polysaccharides, including β-glucans, are noted for their high antioxidant capacity. These compounds can be absorbed by M cells in the Peyer's patches of the small intestine, which activates systemic immune responses and contributes to overall antioxidant defense (Batbayar *et al.,* 2012). Additionally, mushroom polysaccharides and glycol-conjugates are valuable for developing natural-based medications or dietary supplements aimed at preventing oxidative stress and associated disorders. These include:

Gastrointestinal Diseases: Such as GI cancers, peptic ulcers, and inflammatory bowel disease, where oxidative stress plays a significant role (Bhattacharya *et al.,* 2014).

Edible mushrooms are rich in bioactive compounds such as carotenoids, polyphenols, vitamins, polysaccharides, and minerals. They contain significant levels of ergothioneine, which protects mitochondrial components from oxidative damage (Maja *et al.,* 2015). Specific findings include:

Mannogalactoglucan from *Pleurotussajor-caju* demonstrates increased hydroxyl radical scavenging and reducing power (Telles *et al.,* 2011).

A low molecular weight polysaccharide from *Auriculariapolytricha* exhibits hydroxyl radical scavenging activity stronger than vitamin C (Sun *et al.,* 2010).

Lentinula edodes polysaccharides show antioxidant activity through inhibition of hydroxyl, ABTS+ radicals, and lipid peroxidation (Li *et al.,* 2012).

The polysaccharides from *Grifola frondosa* exhibit antioxidant and free radical scavenging activity with varying molecular masses (Lee *et al.,* 2003).

ANTICANCER ACTIVITY

Mushrooms have demonstrated considerable potential in cancer inhibition. Notable findings include:

***Ganoderma lucidum* (Reishi)** affects cancer cell viability in breast cancer by inhibiting invasion and disrupting cell spheroids. Ganoderic acid DM from *G. lucidum* has shown inhibitory effects on cell proliferation in MCF-7 human breast cancer cells (Martinez-Montemeyor *et al.,* 2011; Wu *et al.,* 2012).

Lentinula edodes polysaccharides, including WPLE-N-2 and WPLE-A0.5-2, have anti-tumor activity against various cancer cell lines (105).

Pleurotus ostreatus shows anti-cancer and immunomodulatory effects on HT-29 colon cancer cells. The water-soluble polysaccharide POPS-1 exhibits higher anti-tumor activity against HeLa cells (Lavi *et al.,* 2006; Tong *et al.,* 2009).

Trametesversicolor polysaccharides inhibit cancer cell multiplication with an IC50 value of 4.25 mg/L in human hepatoma cancer cells (Cai *et al.,* 2011).

ANTIMICROBIAL ACTIVITY

Mushrooms have been identified as sources of natural antibiotics, with a range of antimicrobial activities:

Lentinula edodes produces antimicrobial compounds like lentinamicin and β-ethyl phenyl alcohol (Ngai *et al.,* 2003). Its extracts are effective against certain Gram-positive bacteria but less so against others (Cintia *et al.,* 2007).

Ganoderma lucidum extracts show high inhibitory activity against Enterococcus faecalis and lower activity against Pseudomonas aeruginosa (Emre *et al.,* 2014).

Clitocybegeo tropa and ***Lentinula edodes*** extracts exhibit significant antimicrobial activity against various bacterial strains (Venturini *et al.,* 2008).

ANTI-INFLAMMATORY ACTIVITY

Mushrooms contain several bioactive compounds with anti-inflammatory properties:

Pleuran, from *Pleurotus ostreatus*, and polysaccharides from *Pleurotus pulmonarius* show significant anti-inflammatory effects (Jedinak*et al.,* 2011; Adebayo *et al.,* 2012).

Hispidin, derived from *Phellinus* species, inhibits NF-κB pathway activity by suppressing ROS (Carlos *et al.,* 2012).

Lentinan from *Lentinula edodes* has been shown to be effective in treating gut inflammatory diseases (Hong *et al.,* 2015).

CONCLUSION

Medicinal mushrooms offer a wealth of bioactive compounds with potential pharmaceutical applications. Most mushroom-derived drugs are based on high molecular weight polysaccharides, which limits their synthesis. Future research should focus on exploring low molecular weight compounds or secondary metabolites for targeted therapeutic benefits. Continued exploration of wild mushrooms for their bioactive components, molecular pathways, and nutritional values could further enhance their utility in drug discovery and development.

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Chapter
19

STEM CELLS: A NEW HOPE FOR AGE-RELATED MACULAR DEGENERATION

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ABSTRACT

Age-related macular degeneration (AMD) is a progressive eye disorder that primarily affects individuals over the age of 50, leading to significant vision loss. As such, the search for effective treatments, including the potential application of stem cell therapy, is critical to restoring vision and improving life quality for those afflicted with this debilitating condition. The exploration of stem cells in combating AMD not only represents a scientific breakthrough but also symbolizes hope for countless patients facing the impending darkness of visual deterioration. As the body of research expands and technological innovations emerge, the future of stem-cell applications in eye care appears to be increasingly optimistic, paving the way for transformative therapies that could redefine patient outcomes in the face of degenerative vision disorders.

KEYWORDS: Stem Cells, Age-Related Macular Degeneration.

INTRODUCTION

The intricate relationship between aging and vision loss has garnered significant attention in recent years, particularly in the context of age-related macular degeneration (AMD). This prevalent condition affects millions of individuals worldwide, leading to debilitating consequences that can severely impair daily activities and overall quality of life. As the population ages, the urgency to explore innovative treatment options becomes increasingly paramount. Among the most promising avenues of research is the application of stem cell technology, which offers the potential to regenerate damaged retinal cells and restore sight. The exploration of stem cells in combating AMD not only represents a scientific breakthrough but also symbolizes hope for countless patients facing the impending darkness of visual deterioration. In the following sections, this essay will delve into the mechanisms of AMD, the promise of stem cell therapy, and current advancements that may revolutionize treatment in the near future.

OVERVIEW OF AGE-RELATED MACULAR DEGENERATION (AMD) AND ITS IMPACT ON VISION AND QUALITY OF LIFE

Age-Related Macular Degeneration (AMD) is a progressive eye disorder that primarily affects individuals over the age of 50, leading to significant vision loss, particularly in the central field. This condition is categorized into two types: dry and wet AMD, each presenting unique challenges. The dry form is more common and results from the gradual breakdown of light-sensitive cells in the retina, while the wet form involves the growth of abnormal blood vessels. Both types severely impair visual acuity and contrast sensitivity, making everyday activities, such as reading or recognizing faces, increasingly difficult. Consequently, individuals with AMD often experience a decline in their overall quality of life, facing isolation and emotional distress due to their diminishing independence. As such, the search for effective treatments, including the potential application of stem cell therapy, is critical to restoring vision and improving life quality for those afflicted with this debilitating condition.

THE SCIENCE OF STEM CELLS

In understanding the science of stem cells, it is crucial to recognize their potential in regenerative medicine, particularly for conditions like age-related macular degeneration (AMD). Stem cells possess the unique ability to differentiate into various cell types, which provides a promising avenue for repairing damaged tissues in the eye. Research has highlighted the transplantation of retinal pigment epithelium (RPE) cells derived from human pluripotent stem cells as a viable strategy to prevent photoreceptor cell death, thus offering hope for AMD patients facing blindness due to RPE loss (O'Neill *et al.*, 2020). Moreover, a systematic review underscores the need for further investigation into emerging treatments, suggesting a focus on drug therapies, stem cell interventions, and novel surgical techniques as potential therapeutic paths for AMD and related retinal diseases (Waugh *et al.*, 2018). By harnessing the power of stem cells, researchers aim to transform the landscape of treatment for debilitating ocular conditions.

TYPES OF STEM CELLS AND THEIR POTENTIAL APPLICATIONS IN TREATING AMD

Within the realm of stem cell therapy for age-related macular degeneration (AMD), several types of stem cells hold promise for future treatment strategies. One significant source is induced pluripotent stem cells (iPSCs), which can be derived from adult somatic cells and reprogrammed to possess pluripotent characteristics. This capability allows iPSCs to differentiate into retinal pigment epithelial (RPE) cells, addressing damage caused by cellular dysfunction in AMD. Recent studies have shown that iPSC-derived RPE cells exhibit altered responses to oxidative stress, underscoring the intricate relationship between stem cells and disease pathology Hytti *et al.*, 2024. Another notable type includes mesenchymal stem cells (MSCs), recognized for their potential in modulating inflammation and promoting tissue repair. Exosomes released from these cells contain bioactive molecules that can enhance RPE functionality and protect against retinal degeneration, indicating possible therapeutic applications in AMD management (Gu *et al.*, 2023). As research progresses, these stem cells may pave the way for innovative treatments, providing new hope for patients facing the challenges of AMD.

CURRENT RESEARCH AND CLINICAL TRIALS

Recent advancements in clinical trials for age-related macular degeneration (AMD) highlight the transformative potential of stem-cell-based therapies. These innovative approaches aim to address the limitations of existing treatments, focusing on regenerating retinal cells and potentially reversing vision loss. Current studies, such as the AMD Ryan Initiative Study, are investigating the efficacy of induced pluripotent stem cells (iPSCs) derived from patients own cells to create retinal pigmented epithelium patches for restoring damaged tissues. The National Eye Institute has also supported collaborative efforts through initiatives like the Age-Related Eye Disease Study 2 (AREDS2), which has provided crucial insights into the genetic factors of AMD, further guiding the direction of stem-cell therapy research (Radu *et al.,* 2024). Collectively, these efforts signal a promising shift towards utilizing stem cells as a viable option for AMD treatment, although ongoing research is necessary to address challenges such as transplant integration and long-term safety (Radu *et al.,* 2024).

RECENT ADVANCEMENTS IN STEM CELL THERAPIES SPECIFICALLY TARGETING AMD

Innovative approaches in stem cell therapies have shown great promise in addressing age-related macular degeneration (AMD), particularly through the development of induced pluripotent stem cells (iPSCs) and human embryonic stem cells (hESCs). These advancements have facilitated the derivation of retinal pigment epithelial (RPE) cells, which play a crucial role in retinal health. Recent clinical trials utilizing iPSC-derived RPE have reported encouraging results, indicating not only the safety of these therapies but also potential efficacy in restoring vision for patients suffering from advanced nonneovascular AMD (Kashani 2022, Yang *et al.,* 2022). Despite these promising outcomes, researchers face significant challenges, such as managing immune responses and selecting appropriate cell types for treatment. Ongoing studies aim to refine these therapies, moving closer toward viable solutions that could significantly improve the quality of life for those affected by this sight-threatening condition.

CONCLUSION

In summary, the promising results of recent studies underscore stem cells as a viable therapeutic option for age-related macular degeneration (AMD). The investigation into embryonic stem cells (ESCs) has revealed their capacity to reverse senescence in retinal pigment epithelial cells, significantly improving cellular proliferation and reducing markers of aging such as senescence-associated galactosidase staining and mitochondrial dysfunction (Wang *et al.,* 2020). Furthermore, the Stem Cell Ophthalmology Treatment Study (SCOTS) demonstrated substantial improvements in visual acuity among patients with dry AMD after treatment with bone marrow-derived stem cells (BMSCs), with 63% of eyes showing a significant increase in vision (Weiss *et al.,* 2020). These findings not only highlight the potential of stem cells to address the underlying mechanisms of AMD but also suggest a pivotal shift in how this debilitating condition may be managed in the future, providing renewed hope for patients facing progressive vision loss.

THE FUTURE OF STEM CELL RESEARCH IN COMBATING AGE-RELATED VISION LOSS AND IMPROVING PATIENT OUTCOMES

Advancements in stem cell research hold significant promise for those suffering from age-related vision loss, particularly age-related macular degeneration (AMD), which affects millions worldwide.

Continued exploration of stem cells offers potential solutions for repairing or regenerating damaged retinal cells, thereby enhancing visual function and quality of life for patients. Researchers are investigating various stem cell types, such as induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs), to identify their capacity for neuroprotection and cellular regeneration. Clinical trials are increasingly affirming that stem cell therapies can lead to functional improvements and reduced progression of vision loss, helping to bridge the gap in existing treatment modalities. As the body of research expands and technological innovations emerge, the future of stem cell applications in eye care appears to be increasingly optimistic, paving the way for transformative therapies that could redefine patient outcomes in the face of degenerative vision disorders.

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