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CURRENT RESEARCH TRENDS IN LIFE SCIENCE

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PREFACE

The field of life sciences has witnessed remarkable advancements in recent years, driven by interdisciplinary research, technological innovations, and an ever-expanding understanding of biological systems. Current Research Trends in Life Science is an effort to bring together the latest insights from diverse domains such as molecular biology, biotechnology, genetics, microbiology, and environmental sciences, showcasing contemporary research that is shaping the future of biological sciences.

This book aims to serve as a valuable resource for researchers, academicians, and students by providing a comprehensive overview of cutting-edge developments in life sciences. The chapters included here explore novel methodologies, emerging biotechnological applications, and breakthrough discoveries that address global challenges related to health, agriculture, and environmental sustainability. By presenting a wide spectrum of topics, this volume fosters a deeper understanding of the interconnectedness of various life science disciplines and highlights the impact of scientific advancements on society.

One of the key objectives of this book is to inspire further research and collaboration among scientists and scholars. By emphasizing innovative approaches and contemporary research trends, we hope to stimulate discussions and encourage new avenues of exploration in the life sciences.

We extend our sincere gratitude to the contributing authors for their valuable research contributions and to the editorial team for their unwavering dedication in bringing this book to fruition. We also appreciate the support of our readers, whose curiosity and passion for science drive the continued progress of this dynamic field.

We believe that this book will serve as an insightful reference for anyone engaged in the study of life sciences and will contribute to the ongoing dialogue in this ever-evolving domain.

- Editors

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ECO-SUSTAINABLE SOLUTIONS FOR URBAN GREENERY: A COMPREHENSIVE REVIEW

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Abstract:

Due to rapid industrialization, population growth and heavy traffic urban air constitutes various size ranges of solid particles commonly recognized as Particulates Matter or Dust. The deposited particulate matter is a chemically heterogeneous substance of many different types such as sulphuric acid mist, sulphates, or other reactive substances like specific carcinogenic compounds in the organic fraction of particulate matter. Despite concerted efforts for controlling air pollution, the particulate matter problem still persisting in urban areas. Many studies shows that plant species have an efficient eco-sustainable filter for suspended particulate matter in surrounding urban environment. Different types of plants tend to have differences in morphological features of leaf surfaces. Some types of leaves have greater surface rigidity or roughness than other leaves, which may affect their stickiness or particle solubility. Based on this concept, the study has been undertaken to identify the plant species (herb, shrubs and trees), which have higher potential of dust capturing from environment while sustaining their well being.

Keywords: Particulate Matter, Dust Capturing Capacity, Plant Species, Eco-Sustainable Filter, Urban Environment.

Introduction:

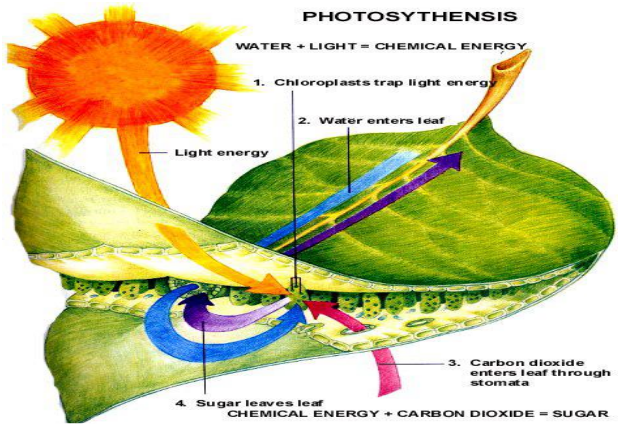
Research has shown that an urban roadside plant leaves acts as an eco-sustainable filter for removal of particulate matter. Plant leaves have microscopic pores on the underside (abaxial) of the leaf called stomata. These allow air into and out of the leaf through which the plant takes in CO_2 and lets out O_2, and allows water vapour out in the process of transpiration. As air passes through the stomata, most of the airborne particles will not pass through the stomata but will rather be eliminated on the leaf's outer surface due to available moisture. The higher the concentration of particulate matter in the area, the higher the concentration of particles on the leaf surface will be. The sizes and chemical compositions of the particles on the leaf surface are the representative of the airborne particles in the sampled area. Different types of leaves tend to have differences in several

aspects of their surfaces. Some types of leaves have greater surface rigidity or roughness than other leaves, which affect their stickiness or particle solubility. Stickier leaves would be better for collecting particles because more particles would stick to their surface and once the deposited particles are washed away, the leaves will be ready for dust capture again. Therefore, certain morphological features of leaves are more favourable for particulate capture from the surrounding environment.

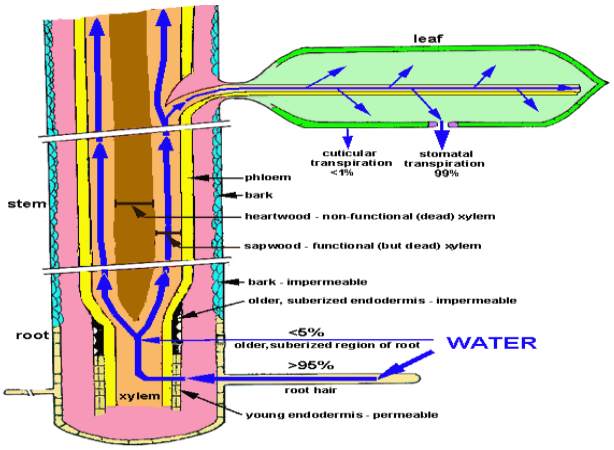
Dust Capturing Physiological Process of Plant:

The two physiological features are directly or indirectly help in efficient dust capture by plants

a. Photosynthesis (production of carbohydrates from CO_2 and H_2O using light energy)
b. Transpiration (water absorbed by the roots and transported throughout the plant evaporates into the atmosphere)



Photosynthesis



Transpiration

Dust Capturing Mechanism of plants

Stomata help in gaseous exchange as well as transpiration. As air diffuses through the stomata, most of the airborne particles will not pass through the stomata but will rather land on the leaf's surface. This is similar to a filter, where air is pulled through the filter by an air pump and the particulate matters are deposit on the filter surface. The concentration of particles on abaxial surface of the leaf normally does not observe higher than that of the top surface of the leaf (adaxial surface). There is a certain amount of force needed for particles to adhere to a surface. This amount is greater depending on the size of the particle. Because the airflow through the stomata is only passive diffusion the fine particles could stick to the bottom surface. The particles on the top surface of the leaves will mainly be from the settling of coarse particles and dust facilitated by sticky surface texture presence of fine veins on leaf surface. Particles hitting the plant surfaces may be retained on the surface, may rebound off the surface, or may be temporarily retained and subsequently removed (resuspended into air or transported to soil or other surface). Thus,

plants act as temporary retention site for atmospheric particles as many particles can be resuspended to the atmosphere be washed off by rain, or drop to the ground through leaf and twig fall. However, trees can store various trace metals (e.g. lead) in their tissue.

Factors Affecting the Dust Capturing Capacity of Plants:

a) Pollution: Pollutant uptake by plants is highly variable as it is regulated by types of pollutant and environmental forces (e.g. aviaibility of water, light intensity, wind speed, gas solubility in water, leaf size and geometry, etc.).

b) **Local Meteorological Conditions**: Pollution removal by vegetation is dependent on local meteorological conditions, the plant's inherent ability to remove the pollutant and the concentration of pollution in the atmosphere. In general, the more pollution in the air, the more the plant can remove, up to a point where the plant becomes affected by the pollutant and stomata shut, limiting the removal of gaseous pollutants. The majority of pollution removal by plants occurs inside the leaves during day time conditions, as this is the time when leaf surfaces are actively transpiring and pollution concentration can be absorbed to their maximum Individual plant size affects total removal of pollutants per tree.

c) **The Sizes and Chemical Compositions of the Particles:** The sizes and chemical compositions of the particles on the leaf surface mass indicate the source of airborne particles. Urban areas tend to have the highest concentrations of airborne particulate matter, because of traffic related activities and other human activity. This is followed by suburban areas, and then rural areas, with decreasing amounts of particulate matter (Abraham, M.E., 1998). Therefore, if leaf sampling is accurate, particle concentrations on leaves collected from sampled areas will decrease from urban to suburban and from suburban to rural.

d) **Concentration and Exposure Period to the Pollutant:** The dust capture by plant is a unique combination of concentration and exposure period to the pollutant (or pollutants), of plant species, plant age and of environmental conditions. The guidelines evolved based on the study will enable the user to determine simply and directly the factors involved in dust capturing capacity of the plant species, which if used in practice will not only increase the green cover but also simultaneously provide natural filters for reducing the particulate level in ambient air from the dense urban areas with prevailing particulate pollution problems through their dust capturing capacity.

Table 1: Particulate matter capturing capacity of different plants species during summer & winter

				Average Dust Capture	
S.No.	**Common Name**	**Botanical Name**	**Family**	**Summer Dust (gm/cm^2)**	**Winter Dust (gm/cm^2)**
Herbs					
1	Genda	*Tagetes petula*	Asteraceae	0.0008	0.002
2.	Sunflower	*Helianthus annuus*	Asteraceae	0.0083	
3.	Chaulai	*Amaranthus hypchondriceus*	Amaranthaceae		
4.	Cock'scomb	*Celosia argentea*			
Shrubs					
1.	Gurhal	*Hibiscus rosa sinensis*	Malvaceae	0.0062	0.0052
2.	Bougainvillea	*Baganvillia glavra*	Nyctaginaceae	0.0113	0.0071
3.	Chandani	*Tabernaemontana divaricata*	Apocyanaceae	0.0267	0.0333
4.	Yellow Kaner	*Thevetia peruviana*	Apocyanaceae	0.0043	0.0062
5.	Pink Kaner	*Nerium indicum*	Apocyanaceae	0.0091	0.0167
Tree					
1.	Teak	*Tectona grandis*			
2.	Mango	*Mangifera indica*	Ancardiaceae	1377.40	4664.27
3.	Banyan	*Ficus bengalensis*			
4.	Peepal	*Ficus religiosa*	Moraceae	1962.09	6813.03

5.	Sal	*Shorea robusta*	Dipterocarpaceae	472.74	309.56
6.	Babool	*Accacia nelotica*	Mimoseae	2534.36	1991.28
7.	Kanchnar	*Bauhinia varigata*			
8.	Amaltas	*Cassia fistula*			
9.	Bel	Aegle mamelos	Rutaceae	140.81	98.09
10.	Palas	Butea monosperma	Fabaceae	764.11	238.3

Table 2: Low, Moderate & High Dust Capturing Herbs, Shrubs & Trees

Dust Capture Level	**Plant Species**		
	Herbs	**Shrubs**	**Trees**
Low <10%	1.*Amaranthus hypchondriceus* (Chaulai) 2. *Gardenia jasminoides* (Crape Jasmine) 3. *Cestrum nocturmum* (Rat Ki Rani) 4. *Chrysanthamum species* (Crown Daisy	1.*Thuja species* (Moyur Pankhi) 2.*Ravuvoifia serpentine* (Serpgandha) 3.*Withania somnifera* (Ashawagandha) 4.*Acanthus species* (Acanthus)	1.*Nyctanthese arbortritis* (Harsingar) 3. *Accacia nelotica* (Babool) 4.*Holarrhena antidysentrica* (Kurchi) 5. *Clerodenrum inerme* (Glorry bower) 6. *Ficus bengalensis* (Banyan) 7.*Miliusa tomentosa* (Kari Leaves) 8.*Thespesia populania* (Ran Bhindi)
Medium 11 to 20%	1 *Lilium species* (Lily) 2.*Draceana species* 3.*Halianthus annuus* (Sunflower)	1. *Bambusa species* (Bamboo) 2. *Lagerstomia indica* (Crape Myrtle) 3. Nerium indicum (Kaner Pink)	1.*Luecena leucophloea* (Shoe Babool) 2.*Pinus gerardiana* (Chilgoja) 3.*Ficus elastica* (Indian Rubber)

	4. *Tegetes patula* (Genda) 5.*Pothus aureus* (Money Plant)	4.*Codium varigatus* (Croton) 5.*Thevetia peruviana* (Kaner Yellow) 6.*Wrightia arborea* (Dudhi) 7.*Rosa indica* (Rose) 8.*Ipomea nil* (Beshrum) 9.*Tabermaemontana divaricata* (Chandani) 10.*Acalypha hispida* (Copper leaf) 11*Plumeria acuminate* (Temple Tree)	4.*Annona squamosa* (Suger Apple) 5.*Mangifera indica* (Mango) 6.*Argyreia roxburghira* (Wooly Morning Glorry) 7.*Ficus religiosa* (Peepal) 8.*Acacia famesiana* (Vilayati Kikkar) 9. *Psidium guyava* (Amrood) 10. *Prunus comminis* (Plums) 11. *Syzygium cuminii* (Jamun) 12.*Tectona grandis*(Teak) 13.*Citrus lamina* (Lamon) 14.*Morus alba* (Mulberry) 15.*Archis sapota* (Chikoo) 16.*Anthosephalus cadamb*a (Kadam) 17.*Shorea robusta* (Sal) 18.*Delbergia sisso* (Sheasm) 19.*Delonix regiosa* (Gulmohar) 20.*Albizzia lebbek* (Siris) 21. *Artocarpus integrifolia* (Jack Fruit) 22.*Ixora parviflora* (Torch Tree) 23.*Bauhinia varigata* (Kanchnar)

			24.*Moringa olieifera* (Drum Stick) 25.*Aegle famesiana* (Beal) 26.*Pithocolobium dule* (Jangali jalabi)
High >21%	1. *Colocasia antiquorum* (Elephants Ear) 2.*Celosia argentea* (Cock'scomb)	1. *Hibiscus rosa sinensis* (Gurhal) 2.*Bougainvillea glabra* (Bougainvillea)	1.*Cassia fistula* (Amaltas) 2.*Pinus contora* (Pine) 3.*Bombax ceiba* (Samal) 4.*Butea monosperma* (Palas) 5.*Alstonia scholaris* (Satani) 6.*Azardirachta indica* (Neem) 7.*Polyalthia longifolia* (Ashoka) 8.*Callistemon citrinus* (Bottle Brush) 9.*Termanilia catappa*l (Jangal Badam) 10.*Terminalia arjuna* (Arjun) 11. *Melia azedarch* (Melia) 12.*Phoenix dactylifera* (Khjoor) 13.*Ficus infectorja* (Pilkan) 14.*Holiptelia integrifolia* (Papadi) 15.*Madhuca indica* (Mahua) 16.*Citrus maxima* (Chaktora) 17.*Populus tremuloides* (Quaking aspe

Discussion:

Multi-purpose tree plant species have a special significance to fulfill the objectives of environment as well as needs of the people. The combinations of species to address the local needs are more beneficial. The flowering Herbs & shrubs species like Crape Jasmine (*Gardeni*a *jasminoides*); Crown Daisy (*Chrysanthemum species*); Lily (*Lillium species*); Sunflower (*Helianthus annuus)*; Genda (*Tagetes patula*); Crape Myrtle (*Lagerstroemia indica*); Pink Kaner (*Nerium* indicum); Croton (*Codium variegates*); Yellow Kaner (*Thevetia peruviana*); Dudhi (*Wrightia arboriea)*; Rose (*Rosa indica)*; Beshram (*Ipomea nil)*; Chandani (*Tabernaemontana divaricata)*; Copper leaf (*Acalypha hispida)*; Temple Tree(*Plumeria acuminate)*; Gurhal (*Hibiscus rosa sinensis)* and Bougainvillea (*Bougainvillea glavra*) and trees like *Delonix regiosa* (Gulmohar), *Accacia nelotica* ((Babul), *Azadirecta indica* (Neem) *Melia azedarch* (Melia) are more valuable to fulfil these requirements apart from playing role in dust capture from environment.

Conclusion:

The interactive factors involving urban trees and air quality needs to be further investigated in order to understand the impact of urban trees on air quality. Future research should be needed to investigate the interactive relationships of pollution removal; trace gas emissions; and air temperature and building energy use effects of urban trees on overall air quality. The particulate level at various urban areas are moderate to critical level therefore critical level, cost effective particulate control technology will be necessarily required for controlling fugitive emissions. The plant species constituting Green Belt of Effective Dust capturing plant species should be developed around residential areas/ industrial area, as the trees can act as efficient biological filters, removing significant amounts of particulate pollution from urban atmospheres. This is a cost effective technology for controlling particulate and gaseous emission generated due to vehicular movement, domestic emission and even industrial emissions.

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ADVANCED TECHNOLOGIES IN EARLY DIAGNOSIS AND MANAGEMENT OF BOVINE MASTITIS

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Abstract:

In the dairy sector, mastitis poses a serious financial and health risk since it lowers milk yield, degrades milk quality, and raises veterinarian expenses. Conventional diagnostic techniques rely on bacterial culture, the California Mastitis Test (CMT), and somatic cell count (SCC), all of which have drawbacks in terms of early diagnosis, sensitivity, and specificity. By measuring udder surface temperature variations, infrared thermography (IRT) has become a non-invasive, quick, and accurate method for detecting subclinical mastitis. Other diagnostic techniques, molecular-based detection methods, and the use of artificial intelligence in identifying subclinical cases are also being considered. This chapter examines the fundamentals of cutting-edge technologies for the early detection and treatment of bovine mastitis, their integration with machine learning for precision diagnostics, and upcoming developments in the management of diseases on dairy farms. Additionally, it covers cutting-edge management techniques that use technologically advanced methods to prevent and control mastitis, eventually enhancing dairy productivity and animal welfare.

Keywords: Bovine Mastitis, Infrared Thermography (IRT), Molecular Diagnostics, Artificial Intelligence (AI), Precision Dairy Farming.

Introduction:

One of the most expensive illnesses in dairy production globally is mastitis, an infection of the mammary gland (Fessha *et al.,* 2021; Zigo *et al.,* 2021). Microbial infections, primarily caused by bacterial pathogens including Escherichia coli, Streptococcus agalactiae, and Staphylococcus aureus, are the cause of it (Tiwari *et al.,* 2024). Both clinical and subclinical manifestations of the disease might appear. Subclinical mastitis goes undiagnosed without diagnostic testing, resulting in long-term financial losses, whereas clinical mastitis exhibits obvious symptoms. Developments in diagnostic techniques are an essential component of dairy science since early and precise diagnosis is essential to the effective management of mastitis. Non-invasive diagnostic techniques like IRT present

promising answers to the growing demand for precision cattle production (Kittur *et al.,* 2024).

Currently, invasive detection techniques including the examination of milk, tissue, or blood samples (Zhang, Kang, *et al.,* 2020) and the implantation of touch sensors in the vagina or rectum (Chung *et al.,* 2021) are the most widely used methods to assess the health status of cattle on farms. However, invasive techniques can result in incorrect data and stress reactions in animals. Furthermore, it takes a lot of effort and money to figure out the necessary parameters for intrusive techniques. The growing size of farms makes it impractical to use intrusive techniques to identify issues in a large number of animals.

In order to develop treatment protocols and preventative and control measures, it is essential to comprehend the frequency of mastitis and the dispersion of the germs that cause it. A critical first step in enhancing disease control during cow udder infections is identifying the causative bacterial pathogen. According to research, the main mastitogens in most nations, including India, are Staphylococcus aureus, Streptococcus agalactiae, Strep. dysgalactiae, and Escherichia coli (Hedge *et al.,* 2013). The bacterial species that cause subclinical mastitis change the chemical characteristics and content of milk (Panchal *et al.,* 2021). Winter time had numerically larger levels of milk protein, fat, and SNF than summer time. Seasonal differences were observed in the relative abundances of Streptococcaceae and Microbacteriaceae (summer-winter) (Nguyen1 *et al.,* 2020).

This immune response in the mammary gland is characterized by vasodilation, increased blood flow, activation of skin pain receptors, and a strong inflammatory response, which ultimately raises the surface temperature of the skin in the inflammatory regions (Ezzat Alnakip *et al.,* 2014; Zaborski *et al.,* 2022). Mammary infections are among the many clinical and physiological disorders that cattle and buffaloes can be diagnosed with infrared thermal imaging (IRT) (Machado *et al.,* 2021; Cai *et al.,* 2023). In native dairy cows and buffaloes, the subclinical mastitis group (SCM) can be identified by measuring the udder skin surface temperature using IRT imaging (Satheesan *et al.,* 2024; Kittur *et al.,* 2024).

IRT is based on the Stefan-Boltzmann formula, which states that variations in the udder's infrared emission can be used to identify temperature changes brought there by inflammation. This chapter offers a thorough analysis of the ways in which IRT is revolutionizing the detection of mastitis, as well as its drawbacks and prospects.

Conventional Diagnostic Techniques The diagnosis of mastitis has traditionally depended on:

1. **Somatic Cell Count (SCC):** One of the main markers of mastitis is an increase in SCC. Although automated cell counters yield quick findings, each virus has a varied sensitivity (Ranjan *et al.,* 2010).
2. **California Mastitis Test (CMT):** This cow-side test uses a visible gel reaction to identify elevated SCC in milk. It is still a popular and economical approach (Kandeel *et al.,* 2019).
3. **Bacterial culture:** Used to identify the microorganisms causing the problem and assess antibiotic susceptibility. Nevertheless, it takes a lot of time and needs lab space.

New Developments in Molecular and Technological Science High-precision diagnostic methods have been adopted as a result of recent developments (Dahesa *et al.,* 2023).

1. **Infrared Thermography (IRT):** This non-invasive method measures changes in the surface temperature of the udder to identify subclinical mastitis.
2. **qPCR and Polymerase Chain Reaction (PCR):** These molecular-based techniques offer quick and extremely accurate pathogen identification.
3. **MALDI-TOF:** Matrix-assisted laser desorption/ionization time-of-flight Mass spectrometry provides highly accurate and exact microbiological identification.
4. **Biosensors and Nanotechnology:** New biosensor-based methods that provide quick on-site diagnosis include colorimetric tests and magnetic nanoparticles.

Fundamentals of Dairy Farming Using Infrared Thermography:

IRT is a passive, remote sensing method that produces thermographic images by capturing the infrared light that an object emits. The udder region's temperature fluctuations aid in the early detection of inflammation before any outward signs show up. Infrared radiation is detected and measured by IRT cameras, which then transform it into a thermal image. Healthy udders exhibit a uniform temperature distribution, whereas mastitic quarters exhibit localized temperature elevations. The integration of AI and machine learning improves IRT accuracy in distinguishing between normal thermal variations and mastitis.

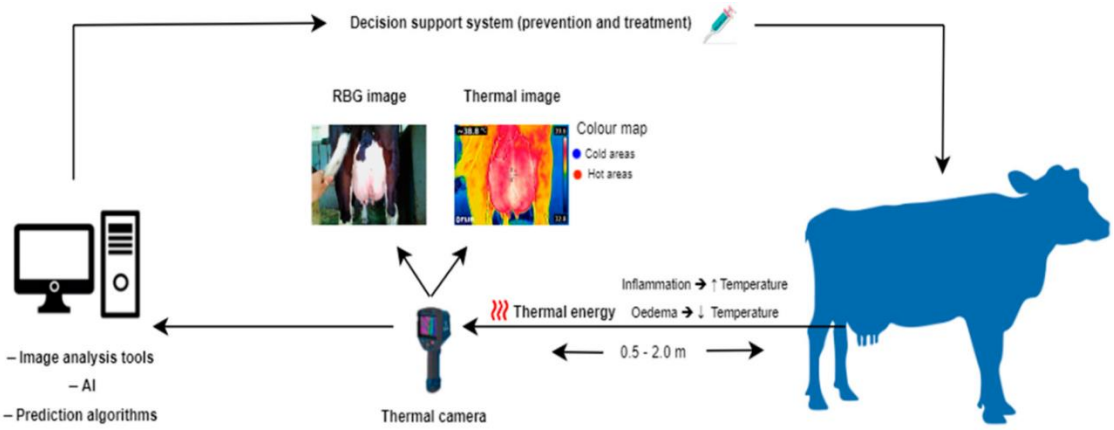

Fig. 1: Depicting use of IRT for thermography of udder for detection of mastitis (Korelidou *et al.*, 2024)

Advantages of IRT over Conventional Methods

Feature	IRT	Traditional Methods (SCC, CMT, Culture)
Non-invasiveness	✅	❌ (Milk sample required)
Early Detection	✅ (Before clinical signs)	❌ (Post-infection detection)
Time Efficiency	✅ (Instant results)	❌ (Lab-dependent)
Stress on Animals	✅ (Minimal handling)	❌ (Physical restraint needed)

IRT's Use in the Identification of Bovine Mastitis

1. **Correlation between Udder Surface Temperature and Mastitis**
    - According to research, the temperature of infected udders is noticeably greater than that of healthy ones.
    - Mastitis in machine-milked cows is indicated by temperature thresholds above 34°C.
2. **The Role of IRT in Subclinical Mastitis Prediction**
    - IRT models with machine learning enhancements have detected subclinical mastitis with an accuracy of >85%.
    - Combining IRT and SCC analysis increases the accuracy of detection.
3. **Environmental Factors' Effect on IRT Readings**
    - Under regulated conditions, IRT is effective; adjustments for humidity, wind speed, and ambient temperature may be needed.
    - Temperature-Humidity Index (THI) models enhance IRT reliability across climates.

4. **Using AI and Machine Learning to Diagnose Mastitis Using IRT**

   For automated, real-time mastitis detection, thermographic pictures are analyzed using machine learning methods like support vector machines (SVMs) and convolutional neural networks (CNNs). AI-Powered IRT Mechanisms • AI algorithms analyze thermal data and differentiate between temperature variations that are inflammatory and those that are not. • AI-IRT systems for automated farm monitoring enhance herd health management.

Examples of AI-Integrated IRT Case Studies

Study 1: An AI-enhanced IRT model outperformed SCC and CMT techniques, detecting 92% of subclinical mastitis cases.

Study 2: Over a two-year period, a real-time farm IRT system decreased losses associated with mastitis by 30%.

Implementing IRT Presents Challenges:

- Lack of generally recognized temperature thresholds for mastitis detection is a standardization issue.
- Cost considerations: Small-scale farmers may find high-end thermal cameras prohibitively pricey.
- Environmental Sensitivity: Farm circumstances impact temperature readings, necessitating sophisticated calibration methods.

2. Polymerase Chain Reaction (PCR) and Quantitative PCR (qPCR):

The quick and extremely precise detection of pathogens made possible by Polymerase Chain Reaction (PCR) and its quantitative cousin, qPCR, has completely changed the diagnostics of mastitis. Even while they work well, traditional culture techniques take a lot of time and could miss organisms that are picky or develop slowly. On the other hand, PCR-based methods enable the quick identification of pathogens in milk samples by amplifying particular DNA sequences of those pathogens (Chakraborty *et al.,* 2019).

Real-time PCR, or qPCR, measures DNA amplification in real-time and provides pathogen load detection and quantification. This feature is very useful for determining the extent of infection and tracking the effectiveness of treatment. For example, one study illustrated the sensitivity and specificity of qPCR by showing how it may be used to detect Staphylococcus aureus in bovine mastitic milk. Early intervention, individualized treatment plans, and better herd health management are made possible by the use of PCR and qPCR

into regular mastitis diagnosis. These molecular methods have the potential to improve the precision and effectiveness of mastitis detection in dairy cattle as they develop.

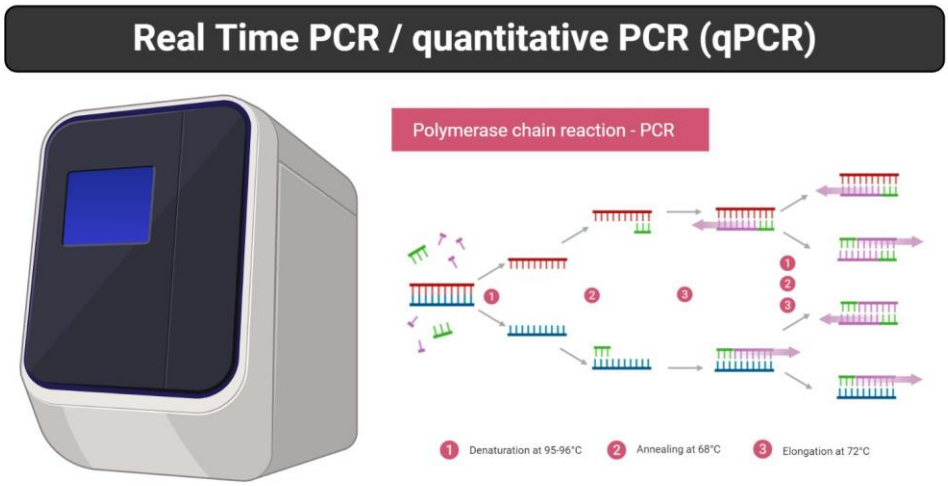

Fig. 2: Depicting qPCR for detection and quantification of pathogen load in mastitis milk

3. Matrix-Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF): Mass Spectrometry

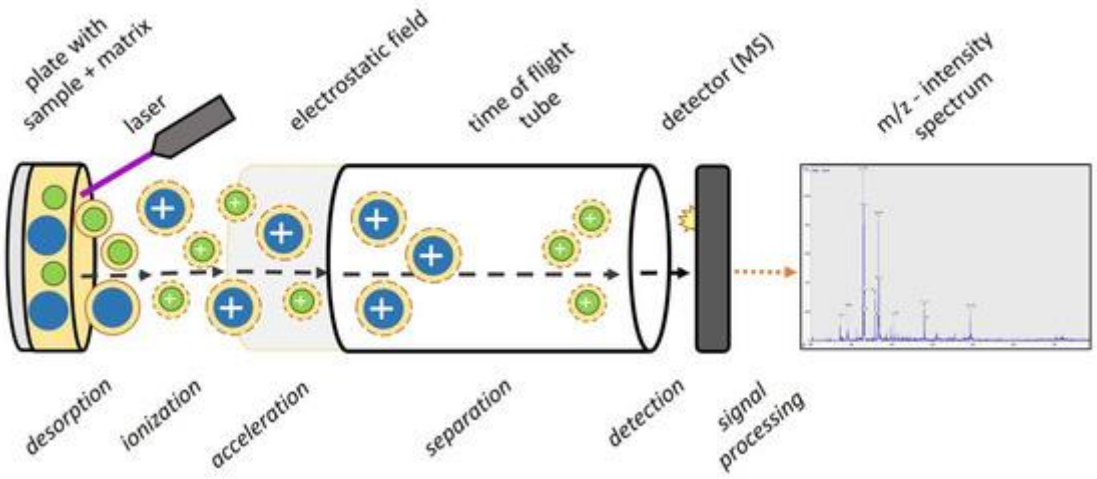

Fig. 3: An outline of the course of the study. Laser irradiation ionizes and evaporates the sample–matrix combination. In an electric field, the ions accelerate, and in a vacuum, they drift in a field-free direction. A separation between low-mass and high-mass ions takes place during flight. The length of the flight route, the mass and energy of the ions, and the charges all affect how long the journey takes. (Haider *et al.*, 2023)

A crucial tool for the quick and precise identification of the microorganisms causing cow mastitis is MALDI-TOF mass spectrometry. This method allows for accurate microbial identification by analyzing the distinct protein "fingerprints" of bacteria. A study showed how well MALDI-TOF MS works as a culture-independent diagnostic method for detecting mastitis-causing bacteria straight from milk samples. Another study shown how useful MALDI-TOF MS is for identifying subclinical mastitis pathogens in dairy farms, highlighting the importance of early diagnosis and treatment. Reduced analysis time and high-throughput capabilities are two benefits of integrating MALDI-TOF MS into mastitis diagnoses, which makes it an invaluable tool in contemporary dairy herd health management.

4. Biosensors and Nanotechnology:

Rapid on-site diagnoses of cow mastitis have been made possible by developments in biosensor and nanotechnology, which provide notable advantages over conventional laboratory-based techniques. .

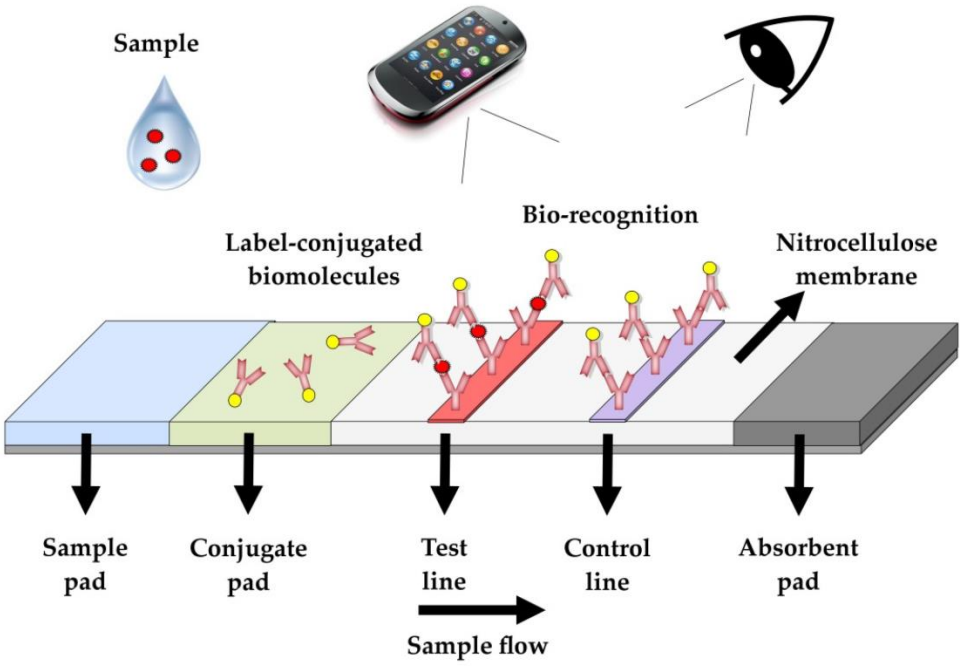

Fig. 4: Biosensors are analytical devices for the detection of specific pathogens or biomarkers associated with mastitis (Manessis *et al.*, 2022)

Biosensor-Based Techniques:

Biosensors are analytical tools that enable the identification of particular infections or biomarkers linked to mastitis by combining a biological recognition element with a physicochemical detector. These devices offer high sensitivity and specificity, allowing for

the early detection of infections. For example, lab-on-a-chip technology has been created to detect mastitis germs straight from milk samples, allowing for prompt and precise diagnosis on the farm.

Nanotechnology Applications:

By creating nanoparticles that improve detection capacities, nanotechnology offers new methods for diagnosing mastitis. For instance, it is possible to functionalize magnetic nanoparticles to bind particular bacterial antigens, facilitating their quick isolation and identification. Gold nanoparticle-based colorimetric assays have also been developed to visually detect the presence of bacteria that cause mastitis, offering a simple and affordable diagnostic method. By enabling quick and accurate infection identification, the incorporation of biosensors and nanotechnology into mastitis diagnostics has the potential to revolutionize herd health management, lowering financial losses and enhancing animal welfare.

The Function of AI in the Diagnosis of Mastitis:

AI-driven models and machine learning are being developed to enhance the management and prediction of mastitis. These algorithms provide real-time disease projections by analyzing big datasets and combining environmental factors, SCC trends, and changes in milk composition. AI-driven automation in milking parlors can further boost early detection and improve herd health monitoring

IRT Solutions Based on Portable Smartphones: Small-scale farmers can use reasonably priced mobile applications.

AI-Powered Disease Prediction Models:

Combining AI and Internet of Things sensors to monitor health in real time. Automated Farm Robotics: IRT-equipped drones and robots for ongoing herd monitoring.

Creative Techniques for Controlling Mastitis Precision Dairy Farming:

By combining automated milking systems with wearable biosensors, udder health indicators may be continuously monitored. By focusing just on affected quarters, Selective Dry Cow Therapy (SDCT) addresses the issue of antibiotic resistance while reducing the need of antibiotics. Immunotherapy and probiotics: Research is moving closer to employing good bacteria to boost immune responses and outcompete infections. • Genomic Selection: Mastitis-resistant dairy calves are becoming easier to produce thanks to developments in genetic screening.

The Function of AI in the Diagnosis of Mastitis AI-driven models and machine learning are being developed to enhance the management and prediction of mastitis. These algorithms provide real-time disease projections by analyzing big datasets and combining environmental factors, SCC trends, and changes in milk composition. AI-driven automation in milking parlors can further boost early detection and improve herd health monitoring.

Prospects and Difficulties for the Future:

Notwithstanding notable progress, obstacles still exist in guaranteeing the economical and farmer-friendly implementation of novel diagnostic instruments. Future studies should concentrate on improving diagnostics' price, field usability, and interaction with automated farm management systems

Conclusion:

The dairy business is undergoing a transformation thanks to developments in mastitis detection, such as precision dairy technologies, AI integration, and molecular diagnostics. Sustainable dairy farming methods will be promoted and the financial burden of mastitis will be lessened with further study and innovation in this area. The early detection of mastitis has been transformed by infrared thermography, which provides dairy farmers with a non-invasive, immediate, and effective substitute for traditional techniques. IRT-based solutions can improve precision livestock husbandry even further with the use of AI. Future studies should concentrate on standardizing IRT techniques and incorporating them with smart farming technologies to improve dairy herd health management.

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ADVANCES IN NEUROPHARMACOLOGY: EMERGING THERAPIES FOR ALZHEIMER'S AND PARKINSON'S DISEASE

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Abstract:

Neurodegenerative diseases like Alzheimer's (AD) and Parkinson's (PD) present major challenges due to their progressive nature and the absence of curative treatments. AD is marked by the accumulation of beta-amyloid plaques and tau protein tangles, which contribute to cognitive decline, while PD is primarily caused by the degeneration of dopaminergic neurons, leading to motor dysfunction. Existing medications mainly alleviate symptoms without altering the course of the disease. However, advancements in neuropharmacology have paved the way for potential disease-modifying treatments, such as monoclonal antibodies (e.g., aducanumab, lecanemab), gene therapy, and stem cell-based interventions. Researchers are also exploring immunotherapy to address neuroinflammation, small-molecule neuroprotective compounds, and precision medicine approaches. Additionally, artificial intelligence is transforming drug discovery by providing innovative therapeutic insights. Future treatment strategies may incorporate regenerative medicine, biomarker-driven approaches, and neurostimulation techniques to slow or potentially reverse disease progression. This chapter highlights emerging pharmacological and technological developments aimed at enhancing the management and prognosis of AD and PD, bringing hope for more effective therapeutic options.

Keywords: Neurodegenerative Diseases, Alzheimer's Disease, Parkinson's Disease, Neuropharmacology, Disease-Modifying Therapies

Introduction:

Neurodegenerative disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD) pose a significant challenge to global healthcare due to their progressive nature and the absence of definitive cures. These conditions primarily impact neurons, resulting in cognitive and motor impairments that progressively worsen. With an increasing prevalence, especially among aging populations, there is a pressing need for innovative pharmacological treatments. Neuropharmacology, which focuses on how drugs

interact with the nervous system, plays a crucial role in developing therapies aimed at slowing disease progression and managing symptoms.

Alzheimer's disease is the most prevalent form of dementia, characterized by the buildup of beta-amyloid plaques and neurofibrillary tangles composed of tau protein. These abnormalities contribute to neuronal dysfunction, synaptic loss, and ultimately, cognitive decline and memory impairment. In contrast, Parkinson's disease is primarily a movement disorder caused by the degeneration of dopaminergic neurons in the substantia nigra. The resulting dopamine deficiency in the basal ganglia leads to key symptoms such as bradykinesia, muscle rigidity, resting tremors, and postural instability [1].

Despite significant research efforts, current treatments for Alzheimer's disease (AD) and Parkinson's disease (PD) primarily focus on symptom management rather than addressing the root causes. Common pharmacological treatments include cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) and N-methyl-D-aspartate (NMDA) receptor antagonists (memantine) for AD, while PD is commonly treated with dopamine replacement therapies such as levodopa, dopamine agonists, and MAO-B inhibitors. Although these medications offer symptomatic relief, they do not slow or stop disease progression. This has led researchers to explore innovative disease-modifying therapies, including monoclonal antibodies, gene therapy, stem cell therapy, and neuroprotective agents.

Recent advancements in neuropharmacology have focused on targeting the molecular mechanisms responsible for neurodegeneration. One promising strategy involves monoclonal antibodies designed to eliminate harmful protein aggregates. For example, aducanumab, a monoclonal antibody approved for AD, binds to beta-amyloid plaques to reduce their buildup. Additionally, experimental therapies targeting tau protein aggregation, such as anti-tau antibodies, show potential in altering disease progression. In the case of PD, gene therapy aims to enhance dopamine production by introducing genes responsible for dopamine synthesis directly into the brain [2].

Neuroinflammation has been identified as a key contributor to the progression of neurodegenerative disorders. Glial cells, particularly microglia and astrocytes, play a significant role in inflammation and disease pathology. Researchers are investigating pharmacological approaches that target inflammatory pathways, including inhibitors of pro-inflammatory cytokines and immune-modulating drugs, as potential treatments for Alzheimer's disease (AD) and Parkinson's disease (PD). Additionally, small-molecule

neuroprotective compounds, such as antioxidants and mitochondrial stabilizers, are being explored for their ability to prevent neuronal damage and promote cell survival.

Stem cell therapy is also emerging as a promising field in neuropharmacology. Induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs) have the potential to replace damaged neurons and restore neural function. In PD, researchers are examining the use of stem cell-derived dopaminergic neurons to replenish dopamine levels and improve motor function. Although obstacles such as immune rejection and ethical concerns remain, stem cell-based therapies offer hope for regenerative treatments in neurodegenerative diseases.

An exciting advancement in neuropharmacology is precision medicine, which leverages genetic and biomarker analysis to customize treatments for each patient. Developments in pharmacogenomics enable a more personalized approach to selecting and adjusting medications, reducing adverse effects while enhancing therapeutic effectiveness. Additionally, artificial intelligence and machine learning are being integrated into drug discovery processes, helping to identify potential treatments and predict patient-specific responses more efficiently.

In summary, neuropharmacology continues to progress with innovative strategies aimed at slowing disease progression, restoring neuronal function, and enhancing the quality of life for individuals affected by Alzheimer's disease (AD) and Parkinson's disease (PD). Despite challenges such as overcoming the blood-brain barrier for effective drug delivery, ongoing research is driving the development of groundbreaking therapies. The incorporation of cutting-edge technologies, including gene therapy, monoclonal antibodies, stem cell-based treatments, and precision medicine, holds significant promise for the future of neurodegenerative disease management [3].

Advances in Treating Neurodegenerative Diseases like Alzheimer's

Neurodegenerative disorders like Alzheimer's disease (AD) pose a significant challenge in modern healthcare. AD is a progressive condition that leads to cognitive decline and memory impairment, impacting millions globally. The disease is mainly linked to the buildup of beta-amyloid plaques and tau protein tangles, which contribute to neuronal damage and synaptic dysfunction. Although AD remains a complex disorder, recent advancements in treatment approaches have shown promise in improving disease management and potentially altering its progression.

1. Monoclonal Antibodies Targeting Beta-Amyloid

A significant advancement in Alzheimer's treatment is the development of monoclonal antibodies designed to target beta-amyloid plaques. Aducanumab, an anti-amyloid antibody approved by the FDA, works by reducing amyloid buildup in the brain, which may help slow cognitive decline in individuals with early-stage Alzheimer's. Additionally, other monoclonal antibodies, including lecanemab and donanemab, are undergoing advanced clinical trials and have demonstrated potential in lowering amyloid accumulation and enhancing cognitive function. Unlike traditional treatments that focus solely on symptom management, these therapies aim to modify the progression of the disease [4].

2. Targeting Tau Protein Aggregation

Besides beta-amyloid accumulation, the aggregation of tau proteins is a key factor in the progression of Alzheimer's disease. New treatment strategies are being developed to prevent tau phosphorylation and aggregation, which are linked to neuronal dysfunction. Monoclonal antibodies like gosuranemab and semorinemab are being studied for their potential to neutralize harmful tau proteins. Additionally, researchers are exploring small-molecule inhibitors that target tau kinases, as well as tau aggregation inhibitors, as potential therapies aimed at modifying the course of the disease.

3. Cholinergic and Synaptic Modulation

Conventional drug therapies for Alzheimer's disease primarily aim to enhance cholinergic neurotransmission. Medications such as donepezil, rivastigmine, and galantamine, which are acetylcholinesterase inhibitors, function by boosting acetylcholine levels in the brain, leading to improved cognitive abilities. Additionally, NMDA receptor antagonists like memantine help regulate glutamatergic neurotransmission, protecting neurons from excitotoxic damage. While these treatments do not stop the progression of the disease, they offer symptomatic relief and contribute to a better quality of life for patients [5].

4. Neuroinflammation and Immunotherapy

Persistent neuroinflammation is a key factor in the progression of Alzheimer's disease. Glial cells, particularly microglia and astrocytes, are crucial in regulating inflammatory responses within the brain. Recent studies have focused on developing anti-inflammatory and immune-modulating therapies to control excessive inflammation. Drugs designed to inhibit pro-inflammatory cytokines like IL-1β, TNF-α, and IL-6 are being investigated for their potential neuroprotective benefits. Additionally, treatments that

regulate microglial activity, such as CSF1R inhibitors, are showing promise in minimizing inflammation-related neuronal damage.

5. Gene Therapy and CRISPR Applications

Innovative approaches like gene therapy and genome-editing techniques, including CRISPR, are being explored as potential treatments for Alzheimer's disease at the genetic level. Scientists are working on correcting genetic mutations linked to familial Alzheimer's, specifically mutations in the APP, PSEN1, and PSEN2 genes. Additionally, CRISPR technology holds promise for regulating gene expression, such as inhibiting beta-secretase (BACE1) activity to decrease amyloid production, potentially slowing disease progression [6].

6. Stem Cell Therapy and Regenerative Medicine

Stem cell therapy is emerging as a promising regenerative treatment for neurodegenerative disorders. Researchers are investigating the use of induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs) to replace damaged neurons and improve cognitive function. Preliminary studies suggest that neurons derived from stem cells can integrate into existing neural networks, offering the potential to reverse neurodegeneration. However, obstacles such as immune rejection and ethical concerns need to be resolved before these therapies can be widely implemented in clinical settings [7].

7. Lifestyle and Non-Pharmacological Interventions

Beyond medication, lifestyle changes have proven to be essential in managing Alzheimer's disease. Engaging in regular physical exercise, cognitive training, and maintaining a nutritious diet, such as the Mediterranean or MIND diet, have been linked to a slower rate of cognitive decline. Additionally, emerging therapies like transcranial magnetic stimulation (TMS) and deep brain stimulation (DBS) are being studied for their potential to protect neural function and support brain health.

8. Artificial Intelligence and Drug Discovery

Artificial intelligence (AI) and machine learning are transforming the process of drug discovery for Alzheimer's disease. AI-powered algorithms analyse extensive datasets to identify promising drug candidates, assess their potential effectiveness, and streamline clinical trials. Computational modelling further enhances researchers' understanding of disease mechanisms at a molecular level, facilitating the development of more precise treatments.

The landscape of Alzheimer's treatment is rapidly advancing, with significant progress in disease-modifying therapies, neuroprotective drugs, and regenerative medicine. Although a cure has yet to be found, continued research into monoclonal antibodies, gene therapy, stem cell treatments, and AI-driven drug development provides hope for future breakthroughs. A comprehensive approach that integrates both pharmacological and non-pharmacological strategies will be crucial in improving patient care and ultimately discovering a cure for this debilitating condition [8].

Advances in Treating Neurodegenerative Diseases like Parkinson's

Parkinson's disease (PD) is a progressive neurological disorder that primarily impacts motor function due to the gradual degeneration of dopaminergic neurons in the substantia nigra. Common symptoms include tremors, muscle stiffness, slowed movements, and balance impairments. Additionally, non-motor symptoms such as cognitive decline, mood disturbances, and autonomic dysfunction add complexity to disease management. While current treatments focus on symptom relief, no cure has been found, leading to ongoing research into therapies that can slow disease progression and protect neurons. Advances in neuropharmacology and innovative treatment approaches are offering new possibilities for better management and potential disease-modifying therapies.

1. Dopaminergic Therapies and Novel Drug Formulations

The primary approach to treating Parkinson's disease (PD) involves increasing dopamine levels in the brain. Levodopa remains the most effective treatment and is often combined with carbidopa to improve its absorption and reduce side effects. However, prolonged use of levodopa can lead to motor complications, including fluctuations in symptom control and involuntary movements (dyskinesias).

To overcome these issues, advanced levodopa formulations such as extended-release capsules (Rytary) and continuous subcutaneous infusion systems (ND0612) are being developed to maintain stable dopamine levels. Additionally, dopamine agonists like pramipexole and rotigotine, along with MAO-B inhibitors such as safinamide, are being refined to provide prolonged symptom relief while minimizing long-term side effects [9].

2. Gene Therapy and Neuroprotective Strategies

Gene therapy is being explored as a promising strategy to alter the progression of Parkinson's disease (PD) by addressing its underlying molecular mechanisms. Several experimental gene therapy approaches are under investigation:

- **Glutamic Acid Decarboxylase (GAD) Gene Therapy:** Designed to enhance GABAergic inhibition in the subthalamic nucleus, helping to restore motor function.

- **Neurotrophic Factor Therapy:** Aims to deliver neurotrophic factors that support the survival and regeneration of dopaminergic neurons.
- **AADC Gene Therapy:** Focuses on increasing the activity of aromatic L-amino acid decarboxylase (AADC), an enzyme essential for converting levodopa into dopamine, thereby improving treatment efficacy.

Furthermore, CRISPR-based gene editing is being researched to correct genetic mutations linked to inherited forms of PD, such as LRRK2 and SNCA mutations [10].

3. Stem Cell Therapy and Regenerative Approaches

Stem cell therapy offers a promising approach for replacing lost dopaminergic neurons and restoring brain function in Parkinson's disease. Researchers are exploring the potential of induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs) to develop into functional dopaminergic neurons and successfully integrate into neural networks.

Preliminary clinical studies have shown positive outcomes, demonstrating improvements in motor function and neuroprotection. However, challenges such as immune system rejection, ethical concerns, and long-term safety issues must be addressed through further research before stem cell therapy can be widely adopted as a standard treatment.

4. Immunotherapy and Targeting Alpha-Synuclein Aggregation

A hallmark of Parkinson's disease (PD) is the buildup of alpha-synuclein protein aggregates, known as Lewy bodies, which contribute to neuronal damage. To address this, immunotherapy approaches are being developed to reduce alpha-synuclein accumulation and slow disease progression.

- **Monoclonal Antibodies:** Investigational treatments like prasinezumab and cinpanemab are designed to target and aid in the clearance of alpha-synuclein aggregates.
- **Small Molecule Inhibitors:** Researchers are working on compounds that prevent alpha-synuclein from misfolding and forming toxic aggregates, potentially altering the course of the disease [11].

5. Deep Brain Stimulation (DBS) and Neuromodulation Techniques

Deep brain stimulation (DBS) is a well-established surgical treatment for individuals with advanced Parkinson's disease (PD) who experience motor fluctuations and medication-related dyskinesias. The procedure involves implanting electrodes in specific

brain areas, such as the subthalamic nucleus or globus pallidus, to regulate abnormal neural activity and enhance motor function.

Beyond DBS, emerging neuromodulation techniques like focused ultrasound (FUS) and transcranial magnetic stimulation (TMS) are being investigated as less invasive alternatives. These approaches aim to modulate impaired neural circuits and relieve symptoms without requiring surgical implantation [12].

6. Anti-Inflammatory and Mitochondrial-Targeted Therapies

Neuroinflammation and mitochondrial dysfunction play significant roles in the progression of Parkinson's disease (PD). Researchers are exploring various therapeutic approaches to target these underlying mechanisms:

- **Anti-Inflammatory Agents:** Studies are evaluating the neuroprotective potential of drugs that modulate inflammatory pathways, including NLRP3 inflammasome inhibitors and cytokine blockers.
- **Mitochondrial Protective Compounds:** Substances such as coenzyme Q10 and nicotinamide riboside are being investigated for their ability to enhance cellular energy production and reduce oxidative stress, helping to safeguard neurons from degeneration.

7. Gut Microbiota and Parkinson's Disease

Recent research indicates that the gut microbiome may play a significant role in the development of Parkinson's disease (PD). Gastrointestinal issues, such as constipation, often appear years before motor symptoms, suggesting a connection between gut health and neurodegeneration.

To address this, therapeutic approaches targeting gut microbiota, including probiotics, dietary changes, and fecal microbiota transplantation (FMT), are being investigated for their potential to impact disease progression and help manage symptoms [13].

8. Precision Medicine and Artificial Intelligence in Drug Development

The integration of precision medicine and artificial intelligence (AI) is transforming Parkinson's disease (PD) treatment development. Pharmacogenomic research is uncovering genetic variations that influence individual drug responses, enabling more personalized treatment strategies.

AI-driven drug discovery is advancing the identification of new therapeutic targets, refining drug development, and predicting treatment effectiveness. These innovations have the potential to enhance treatment success while minimizing side effects.

Ongoing advancements in neuropharmacology are leading to groundbreaking therapeutic approaches for PD. Researchers are making significant progress in modifying disease progression through gene therapy, stem cell treatments, immunotherapy, and neuromodulation. Additionally, personalized medicine, AI-assisted drug discovery, and gut microbiome research are opening new possibilities for treatment. Although challenges persist, continuous research offers hope for more effective and transformative therapies for individuals living with PD [14].

Neuropharmacology and Future Therapeutics: Innovations in Treating Neurodegenerative Disorders like Parkinson's and Alzheimer's

Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily impairs motor function due to the gradual degeneration of dopaminergic neurons in the substantia nigra. It is characterized by symptoms such as tremors, muscle stiffness, slowed movement, and balance issues. In addition to motor impairments, non-motor symptoms, including cognitive decline, mood disturbances, and autonomic dysfunction, add complexity to disease management. While current treatments help manage symptoms, there is no known cure, driving continuous research into therapies that can slow disease progression and protect neurons. Advances in neuropharmacology and innovative treatment approaches are opening new possibilities for better PD management and potential disease-modifying therapies.

1. Dopaminergic Therapies and Novel Drug Formulations

Current treatments for Parkinson's disease (PD) primarily aim to replenish dopamine levels in the brain. Levodopa remains the most effective therapy and is often combined with carbidopa to improve absorption and reduce side effects. However, prolonged use of levodopa can lead to motor complications, including fluctuations in symptom control and involuntary movements (dyskinesias).

To overcome these limitations, advanced levodopa formulations such as extended-release capsules (Rytary) and continuous subcutaneous infusion systems (ND0612) are being developed to ensure more stable dopamine levels. Additionally, dopamine agonists like pramipexole and rotigotine, along with MAO-B inhibitors such as safinamide, are being refined to prolong symptom relief and minimize long-term side effects [15].

2. Gene Therapy and Neuroprotective Strategies

Gene therapy is emerging as a promising approach to altering the progression of Parkinson's disease (PD) by targeting its underlying molecular mechanisms. Several gene therapy strategies currently under investigation include:

- **Glutamic Acid Decarboxylase (GAD) Gene Therapy:** Designed to enhance GABAergic inhibition in the subthalamic nucleus, helping to improve motor function.
- **Neurturin Gene Therapy:** Focuses on delivering neurotrophic factors that support the survival and regeneration of dopaminergic neurons.
- **AADC Gene Therapy:** Aims to boost the activity of aromatic L-amino acid decarboxylase (AADC), an enzyme essential for converting levodopa into dopamine, thereby enhancing treatment effectiveness.

Additionally, CRISPR-based gene editing is being studied as a potential method to correct genetic mutations linked to inherited forms of PD, such as those in the LRRK2 and SNCA genes [16].

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Precision medicine and artificial intelligence (AI) are transforming the development of treatments for Parkinson's disease (PD). Pharmacogenomic research is uncovering genetic variations that affect individual responses to medications, enabling the creation of personalized treatment approaches.

AI-powered drug discovery is expediting the identification of new therapeutic targets, improving drug design, and predicting treatment effectiveness. These innovations hold great potential for enhancing treatment outcomes while minimizing side effects [19].

Future Perspectives

The future of neuropharmacology is set to evolve through the integration of advanced technologies and multidisciplinary research, transforming treatments for neurodegenerative conditions such as Alzheimer's and Parkinson's disease. Innovations in nanomedicine could enable precise drug delivery, minimizing side effects while improving therapeutic effectiveness. Additionally, the combination of neuropharmacology and regenerative medicine may lead to personalized, cell-based therapies.

Another promising avenue is the development of biomarker-driven treatments, which could facilitate early disease detection and individualized treatment strategies. Furthermore, brain-computer interfaces and adaptive neurostimulation techniques have the potential to provide real-time symptom management and neuroprotection. The collaboration of artificial intelligence, big data analytics, and pharmacology is expected to accelerate drug discovery and enhance precision medicine approaches.

Ultimately, the future of neurodegenerative disease treatment will likely be shaped by the convergence of neuropharmacology, genetics, regenerative medicine, and digital health technologies, paving the way for groundbreaking therapies that may slow, stop, or even reverse disease progression [20].

Conclusion:

The continuous progress in neuropharmacology is driving the development of innovative therapeutic strategies for Parkinson's and Alzheimer's disease. While challenges remain, ongoing research and technological advancements provide hope for more effective and transformative therapies for individuals affected by neurodegenerative disorders.

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ECTODERMAL DYSPLASIA: GENETIC INSIGHTS, CLINICAL FEATURES, AND EMERGING THERAPIES

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Abstract:

Ectodermal dysplasia is a rare condition that is estimated to occur in approximately one in every 100,000 live births. This disorder can be associated with early morbidity and mortality. The first documented case of this condition was reported by Thurnman in 1843. It is characterized by a diverse array of anomalies, primarily affecting organs and tissues derived from ectodermal layers. The structures most commonly impacted include the eccrine glands, which can lead to conditions such as hypohidrosis or anhidrosis, as well as the hair, nails, and teeth, which may be fewer in number and exhibit a conical shape. The EDA, EDAR, and EDARADD genes provide the necessary instructions for producing ectodysplasin A, a protein that plays a crucial role in embryonic development. Diagnosis of ectodermal dysplasia may be considered when unexplained episodes of hyperpyrexia arise, although other symptoms can complicate the diagnostic process. Treatment options for hypotrichosis include topical minoxidil and wigs, while dysphagia may require dietary modifications or the placement of feeding tubes, such as a percutaneous endoscopic gastrostomy (PEG) tube or a nasogastric tube.

Keywords: Hyperpyrexia, Hypotrichosis, Hypohidrosis, Anhidrosis

Introduction to Ectodermal Dysplasia:

Ectodermal Dysplasia (ED) encompasses a collection of rare genetic disorders that disrupt the development of ectodermal structures such as skin, hair, nails, teeth, and sweat glands. These conditions arise from mutations in genes responsible for the formation and functionality of these tissues during the early stages of embryonic development. Individuals affected by ED may present with symptoms including thinning hair, irregular or absent teeth, dry skin, fragile nails, and reduced sweating, which can complicate the regulation of body temperature. The degree of severity and specific symptoms can differ based on the type of ED, with hypohidrotic ectodermal dysplasia (HED) being the most prevalent variant. While there is currently no cure for ED, treatment strategies are aimed at

alleviating symptoms through dental care, skin treatments, and the use of prosthetics or supportive measures to enhance the quality of life. Ongoing advancements in genetic research are also paving the way for a deeper understanding of the disorder and the development of potential future therapies.[1]

Historical Background and Discovery of Ectodermal Dysplasia

The notion of ectodermal dysplasia (ED) has been acknowledged for more than a hundred years, with initial accounts emphasizing individuals with irregularities in their skin, hair, teeth, nails, and sweat glands. [2]

Early Observations (19th Century)

- In 1848, Charles Darwin noted cases of families with absent teeth and limited hair growth, observing the hereditary aspects of these features.
- The late 19th century marked the first detailed medical descriptions of conditions akin to ectodermal dysplasia, as physicians reported cases of hypodontia (missing teeth) and anhidrosis (lack of sweating). Formal Classification and Naming (20th Century)
- In 1929, Christ, Siemens, and Touraine characterized Hypohidrotic Ectodermal Dysplasia (HED), also known as Christ-Siemens-Touraine Syndrome, which represented the first well-defined subtype of ED.
- In 1971, Freire-Maia and Pinheiro proposed a classification system for ectodermal dysplasias, categorizing them based on the affected structures, such as hair, teeth, nails, and sweat glands.

The late 20th and early 21st centuries have witnessed remarkable genetic and molecular breakthroughs. In the 1990s, the EDA (Ectodysplasin-A) gene was identified as the primary gene linked to X-linked hypohidrotic ectodermal dysplasia (XLHED). Further investigations connected mutations in the EDAR, EDARADD, and WNT10A genes to various types of ectodermal dysplasia. Recent developments in gene therapy and molecular medicine have introduced promising treatment options, including prenatal EDA protein therapy, as seen in the EDELIFE trial. Today, ectodermal dysplasia is acknowledged as a genetic condition with over 100 recognized subtypes, and ongoing research is dedicated to finding curative solutions.[3]

Etiology of Ectodermal Dysplasia

Ectodermal dysplasia (ED) is fundamentally a genetic condition arising from mutations in genes that govern the development and functionality of ectodermal

structures. [4] This disorder can be passed down through various inheritance patterns, including X-linked, autosomal dominant, and autosomal recessive.

Genetic Causes

1. **X-linked Recessive Inheritance**
    - Hypohidrotic Ectodermal Dysplasia (HED), the most common variant, is attributed to mutations in the EDA gene, which encodes the protein ectodysplasin-A, essential for ectodermal development.
    - This condition primarily impacts males, while females may exhibit milder symptoms due to the inactivation of one X chromosome.
2. **Autosomal Dominant and Recessive Inheritance**
    - Variations of ectodermal dysplasia can arise from mutations in genes such as EDAR, EDARADD, WNT10A, and TP63.
    - In autosomal dominant inheritance, a single mutated copy of a gene is sufficient to manifest the disorder, whereas autosomal recessive inheritance necessitates mutations in both copies of the gene.[5]

Epidemiology of Ectodermal Dysplasia

Ectodermal dysplasia (ED) is a rare genetic condition, with its frequency differing according to the specific subtype: [5]

Global Prevalence

The most prevalent variant, Hypohidrotic Ectodermal Dysplasia (HED), is found in approximately 1 in 10,000 to 1 in 100,000 live births globally.

Other types of ED are even less common, and there is limited epidemiological data due to the condition's variability.

Sex Distribution

X-linked Hypohidrotic Ectodermal Dysplasia (XLHED) predominantly affects males, who possess only one X chromosome.

Females with the mutation may experience milder symptoms as a result of X-chromosome inactivation.

Ethnic and Geographic Variation

ED has been documented across various ethnicities and populations worldwide, yet no specific geographic or racial predisposition has been established.

Familial vs. Sporadic Cases

While many instances of ED are inherited, sporadic mutations can arise without any family history. Due to its rarity, numerous cases remain undiagnosed, leading to an underestimation of its actual prevalence. However, advancements in genetic screening and awareness initiatives are enhancing early detection and management. [6]

Pathophysiology of Ectodermal Dysplasia

Ectodermal dysplasia (ED) arises from mutations in genes that regulate the development and interaction of ectodermal and mesodermal tissues during embryogenesis. These mutations disrupt normal signaling pathways, leading to defective development of structures derived from the ectoderm, including skin, hair, nails, teeth, and sweat glands.[7]

Key Molecular Pathways Affected

1. **EDA/EDAR/EDARADD Signaling Pathway**

   The Ectodysplasin-A (EDA) protein, in conjunction with its receptor (EDAR) and adaptor (EDARADD), is essential for the development of ectodermal structures. Genetic mutations in these components disrupt epithelial-mesenchymal interactions, leading to abnormalities in the organogenesis of hair follicles, teeth, and sweat glands.

2. **WNT and TP63 Pathways**

Mutations in WNT10A are associated with impaired odontogenesis, which affects tooth formation. Additionally, mutations in TP63 have a significant impact on the development of limbs and skin, particularly evident in syndromic presentations of ectodermal dysplasia.

Effects on Specific Tissues

1. **Sweat Glands**

   Hypohidrosis, characterized by diminished sweating, arises from underdeveloped or absent sweat glands. This condition can result in heat intolerance and hyperthermia, particularly in warmer environments.

2. **Hair Follicles**

   Deficiencies in hair follicle development led to hair that is sparse, thin, and brittle.

3. **Teeth**

   Abnormalities in the process of odontogenesis can lead to conditions such as hypodontia (missing teeth), anodontia (complete absence of teeth), and conical-shaped teeth. - These dental conditions can adversely affect chewing, speech, and facial aesthetics.

4. **Nails and Skin**

- Individuals may experience thin, brittle nails that grow slowly.
- Additionally, dry skin (xerosis) can occur due to decreased function of sebaceous and sweat glands.

Insights into these molecular and developmental irregularities have paved the way for potential gene-based therapies and early intervention methods to effectively manage symptoms associated with this condition.[8]

Clinical Classification of Ectodermal Dysplasia

Ectodermal Dysplasia (ED) is categorized based on the specific structures that are affected and the genetic mutations that underlie the condition. The primary classification systems are determined by functional involvement and inheritance patterns. [9]

1. Classification Based on Clinical Features

ED is divided into two types:

- **Hypohidrotic Ectodermal Dysplasia (HED) / Christ-Siemens-Touraine Syndrome**
  - The most prevalent form, typically inherited in an X-linked manner.
  - Characteristics include hypohidrosis (decreased sweating), hypodontia (absence of teeth), and hypotrichosis (reduced hair).
  - This condition is marked by conical teeth, dry skin, and an inability to tolerate heat due to the absence or underdevelopment of sweat glands.
- **Hidrotic Ectodermal Dysplasia (HED2) / Clouston Syndrome**
  - Inherited in an autosomal dominant fashion.
  - While sweat gland function remains normal, it impacts hair, nails, and skin.
  - Individuals may experience thickened nails (onychodystrophy), fragile hair, and palmoplantar keratoderma (thickened skin on the palms and soles).

2. The classification of ectodermal dysplasia (ED) according to the Freire-Maia system divides the condition into four key subtypes based on the ectodermal structures that are affected:

1. **Hair Dysplasia (Atrichia/Hypotrichosis)** – Defined by sparse, brittle, or completely absent hair.

2. **Dental Abnormalities (Hypodontia/Anodontia)** – Characterized by the absence or malformation of teeth.

3. **Nail Dystrophy (Onychodysplasia)** – Involves nails that are thick, brittle, and grow slowly.

4. **Sweat Gland Dysfunction (Hypohidrosis/Anhidrosis)** – Refers to the absence or underdevelopment of sweat glands, leading to difficulties with heat regulation.

Some syndromic forms of ED may also present with additional craniofacial defects, limb abnormalities, and immune dysfunction. The field is witnessing advancements in genetic and molecular classification, which are crucial for early diagnosis and the development of targeted treatment strategies.

Classification of Ectodermal Dysplasia

As of now, there exist roughly 150 varieties of ectodermal dysplasias. To aid in their classification, various subgroups have been created according to the presence or absence of the four key ectodermal dysplasia (ED) defects:

- ED1: Trichodysplasia (hair growth disorders)
- ED2: Dental dysplasia
- ED3: Onychodysplasia (nail growth disorders)
- ED4: Dyshidrosis (sweat gland disorders)

Diagnosis of Ectodermal Dyplasia

Identification of ectodermal dysplasia may be considered when unexplained episodes of hyperpyrexia arise; however, the presence of additional symptoms can complicate the physician's ability to reach an accurate diagnosis. Respiratory infections may lead to suspicions of cystic fibrosis, and the inclusion of hypothyroidism can further obscure the diagnostic process. Moreover, individuals with idiopathic hypoparathyroidism may also present with ectodermal conditions. According to Martini *et al.,* ozena was identified as the initial indicator of hypohidrotic ectodermal dysplasia in two young females. Early diagnosis is crucial due to the potential severity of the condition. Various diagnostic methods are available, which will be summarized below. Typically, the diagnosis hinges on the functionality of sweat glands, with the palms and soles containing the highest concentration of these glands. Consequently, assessing the quantity and maturity of glands in these areas can provide a more accurate diagnosis of anhidrotic ectodermal dysplasia. Although more invasive, prenatal diagnostic techniques allow for the possibility of therapeutic abortion. Molecular analysis is particularly beneficial for assessing the risk of transmission in affected individuals and carriers with normal phenotypes. It can also be utilized alongside chorionic villus sampling to diagnose high-risk male fetuses prenatally.

[10]. Gene mapping remains the most reliable method for confirming an antenatal diagnosis of ectodermal dysplasia, while skin samples obtained during fetoscopy are no longer recommended. Additionally, clinicians must verify that the hypohidrotic (anhidrotic) variant of ectodermal dysplasia being treated is the X-linked form.

Moreover, skin biopsies are no longer recommended for the confirmation of postnatal diagnoses in both adults and children. Previous methods such as imprinting and skin staining have been overtaken by a safer, non-invasive alternative that involves using an ophthalmoscope to directly view the sweat pores. Additionally, an ionization technique that measures chloride concentration in sweat may be applied to evaluate sweating rates. This method is known for its sensitivity, but it also has several limitations that could result in unclear outcomes.

Management

1. Hypotrichosis can be managed with topical treatments containing 3% Minoxidil and the use of wigs to address hair loss.

2. For hypohidrosis, maintaining a cool environment is essential. This can be achieved through air conditioning, using a water spray bottle, or wearing cool-vent vests. Staying hydrated with water bottles during hot weather is crucial. Additionally, skincare products such as lanolin-based emollients, liquid paraffin for dry skin, moisturizing creams for eczema, and antihistamine-infused calamine lotions for eczema-related rashes can be beneficial. Engaging in outdoor activities like swimming is also recommended.

3. In cases of hypodontia, particularly with mandibular implant assistance, various prosthetic rehabilitation options are available based on the extent of tooth loss—whether partial (hypodontia or oligodontia) or complete (anodontia). These options include overdentures, full dentures, telescopic dentures for the upper jaw, implant-retained overdentures, and All-on-four implants. Additional dental treatments may involve orthodontic adjustments for misaligned teeth, bonding for conical teeth, and denture fabrication. Simple denture repairs can be performed as early as 1.5 to 2 years, while more complex denture solutions can be developed for individuals over 16. Bonding conical teeth not only improves aesthetics but also enhances chewing efficiency. Dental implants have shown success in children over seven years old in the front mandibular arch. Due to the impact of ectodermal dysplasia on jaw development, children with hydrotic ectodermal dysplasia require dental prostheses to be replaced every 2.5 years, as these cannot adapt to

growing edentulous spaces. For adults, dental implants can improve both occlusion and mastication, in addition to enhancing appearance.

4. Hyposalivation - Treatment options include the use of artificial saliva substitutes containing carboxymethyl cellulose, which help maintain oral moisture, protect dry mucosal surfaces, and reduce the risk of dental caries.

5. Dysphagia - Management strategies may involve dietary modifications, the insertion of feeding tubes, or the use of a percutaneous endoscopic gastrostomy (PEG) tube for direct access to the stomach, as well as nasogastric tubes that are inserted through the nose into the stomach. **6. Dry eyes** - The application of ophthalmic lubricants, specifically eye drops that contain carboxymethyl cellulose, is recommended to alleviate dryness.

7. Respiratory manifestations - Symptoms such as recurrent fever may arise from respiratory illnesses like pneumonia. It is advisable for children to receive body washes using cotton towels soaked in warm water, along with the application of damp cotton towels to the forehead. Additionally, individuals with ectodermal dysplasia may experience asthma-related breathing difficulties, which can be managed with nebulizers containing salbutamol, a bronchodilator. Referral to a pulmonologist or allergist is also recommended.

8. Solidified cerumen (ear wax) - To address ear wax buildup, administer five to ten drops into each ear canal and seal the canal with a cotton plug. After one hour to a day, remove the cotton plugs that have been soaked in Soliwax Eardrops. This procedure, which aids in the removal of ear wax, should be repeated twice daily for a week. Soliwax Ear drops by NuLife Pharmaceuticals contain antioxidants such as butylated hydroxyanisole (B.H.A.), along with 2.0% w/w paradichlorobenzene, 2.7% w/v benzocaine, 5.0% w/v chlorbutol, and 15.0% w/v turpentine oil. A referral to an ENT specialist is advised.[11]

Gene Therapy and Emerging Treatments for Ectodermal Dysplasia

Recent developments in gene therapy and regenerative medicine have demonstrated significant potential for addressing ectodermal dysplasia (ED), particularly in rectifying genetic defects and enhancing clinical outcomes. [12]

1. Gene Therapy Strategies

• Prenatal EDA1 Replacement Therapy (EDELIFE Trial)

o This innovative clinical trial is evaluating the use of recombinant ectodysplasin-A1 (EDA1) protein in fetuses diagnosed with X-linked hypohidrotic ectodermal dysplasia (XLHED).

o Preliminary findings suggest that in utero intervention can restore sweat gland functionality, enhance dental development, and alleviate heat intolerance.

• CRISPR Gene Editing o Research is underway to utilize CRISPR-Cas9 technology to rectify mutations in EDA, EDAR, and WNT10A, potentially offering a lasting solution.

• Stem Cell Therapies

o Investigations are focusing on mesenchymal stem cells (MSCs) for their regenerative capabilities in skin, sweat glands, and salivary glands for ED patients.

o Additionally, advancements in 3D bioprinting and tissue engineering are paving the way for the creation of bioengineered teeth and dental implants.

2. Pharmacological and Supportive Interventions

• Targeted Biologic Therapies that employ growth factors and peptides to promote hair growth, enhance skin hydration, and facilitate tissue repair.

• Innovative Dental Solutions, featuring customized CAD/CAM dental implants and prosthetics, offer improved functionality and aesthetic appeal. These state-of-the-art treatments, when combined with early genetic screening and precision medicine, present a promising future for enhancing the quality of life for individuals with ED.

Role of Multidisciplinary Care in Ectodermal Dysplasia

The management of ectodermal dysplasia necessitates a collaborative approach involving a multidisciplinary team to effectively address the diverse symptoms that impact the skin, hair, nails, teeth, and sweat glands. The primary specialists engaged in this process include: [13]

1. **Dermatologists**
   - Responsible for diagnosing and treating skin dryness, eczema, and hair disorders.
   - Prescribe moisturizers, emollients, and treatments for the scalp to enhance skin and hair health.
2. **Dentists and Orthodontists**
   - Provide solutions like dental prosthetics, implants, and braces for conditions like hypodontia or anodontia.
   - Conduct early dental interventions to aid in chewing, speech, and proper facial development.
3. **Geneticists**
   - Perform genetic testing and provide counseling for individuals and their families affected by the condition.

- Advise patients on inheritance patterns and available prenatal diagnostic options.

4. Paediatricians and Primary Care Physicians

- Track the growth, development, and nutritional needs of children diagnosed with ectodermal dysplasia (ED).
- Address challenges such as heat sensitivity, recurring infections, and general health.

5. Psychologists and Social Workers

- Offer emotional and psychological assistance to patients facing challenges related to appearance and social interactions.
- Facilitate connections between families and advocacy groups or support networks.

A collaborative, patient-focused strategy guarantees thorough care, timely interventions, and enhanced quality of life for those affected by ectodermal dysplasia.

Role of a Pharmacist in the Management of Ectodermal Dysplasia

Pharmacists are essential in the care, education, and support of individuals with ectodermal dysplasia (ED). Their expertise aids in medication management, symptom alleviation, genetic counselling, and enhancing the overall quality of life for those impacted. [14]

1. Medication Management and Symptom Control

- Skin and Hair Care: Suggest the use of moisturizers, emollients, and medicated shampoos to address issues related to dry skin and scalp.
- Pain Management: Offer analgesics to alleviate dental discomfort resulting from malformed or absent teeth.
- Antibiotics and Antifungals: Aid in the management of recurrent infections, such as respiratory and skin infections, stemming from glandular dysfunction.
- Artificial Tear and Saliva Products: Recommend lubricating agents for individuals experiencing dry eyes or dry mouth.

2. Genetic Counselling and Patient Education

- Inform patients and their caregivers about the genetic underpinnings, inheritance patterns, and the options available for genetic testing.
- Advise families on the importance of early diagnosis, preventive measures, and strategies for long-term management.

3. Dental and Prosthetic Care Support

- Assist in the selection of dental prosthetics, fluoride treatments, and oral hygiene products to promote better dental health.

- Educate on specialized oral care techniques to help prevent cavities and gum disease.

4. Heat Intolerance and Hydration Counselling

- Provide recommendations on cooling methods, hydration practices, and temperature management to avert hyperthermia in individuals with non-functional sweat glands.
- Suggest the use of cooling vests, hydration supplements, and electrolyte drinks during periods of high temperatures.

5. Psychological and Social Support

- Deliver advice on coping mechanisms for both children and adults dealing with social and psychological issues stemming from appearance differences associated with ectodermal dysplasia.
- Direct patients to support groups and advocacy organizations for further help and resources.

Pharmacists play a vital role in a multidisciplinary team, working alongside dermatologists, dentists, geneticists, and other healthcare professionals to provide holistic care for those affected by ectodermal dysplasia.

Recent Advances in Ectodermal Dysplasia Research and Treatment

Ongoing investigations in the fields of genetics, regenerative medicine, and targeted therapies are driving notable advancements in the diagnosis and treatment of ectodermal dysplasia (ED). Key recent developments encompass: [15]

1. Gene Therapy and Molecular Treatments

- The EDELIFE Clinical Trial (2023–2024) is investigating a prenatal gene therapy that involves replacing ectodysplasin-A1 (EDA1) for X-linked hypohidrotic ectodermal dysplasia (XLHED). Preliminary results indicate that administering EDA1 protein before birth may facilitate the development of sweat glands and enhance other ectodermal structures.
- Innovations in CRISPR gene editing are being utilized to rectify mutations in genes such as EDA, EDAR, and WNT10A.

2. Stem Cell Therapy and Tissue Engineering

- Researchers are exploring the use of mesenchymal stem cell (MSC) therapy to regenerate ectodermal tissues, including skin, hair follicles, and salivary glands.
- Techniques in 3D bioprinting and tissue engineering are being investigated for the creation of personalized dental implants and prosthetic skin substitutes.

3. Advanced Dental and Prosthetic Solutions

- Experimental models have shown promise for bioengineered teeth derived from stem cells, potentially providing a lasting solution for conditions like hypodontia and anodontia.
- The use of CAD/CAM (computer-aided design and manufacturing) technology enables the production of customized and more functional dental prosthetics for patients with ED.

4. Enhanced Genetic Testing and Early Diagnosis

- Recent advancements in whole-genome sequencing (WGS) and whole-exome sequencing (WES) facilitate earlier and more accurate identification of ectodermal dysplasia (ED) subtypes.
- Prenatal screening and non-invasive genetic testing allow for the identification of pregnancies at risk, enabling timely interventions.

5. Customized Treatment Approaches

- The emergence of targeted biologics aims to address skin, hair, and immune-related issues associated with syndromic forms of ectodermal dysplasia.
- Innovative formulations of topical growth factors and peptides are being developed to promote hair growth and improve skin hydration.

Conclusion:

Ectodermal dysplasia (ED) is an uncommon genetic disorder that influences the development of ectodermal structures, such as skin, hair, nails, teeth, and sweat glands. While a definitive cure is not yet available, advancements in genetic research, gene therapy, and regenerative medicine are creating pathways for improved treatment options and early interventions. Supportive care, which encompasses dental prosthetics, skin care, hydration management, and genetic counseling, is critical for enhancing the quality of life for individuals affected by this condition. The roles of pharmacists and healthcare professionals are crucial in managing symptoms and educating patients. With the continuation of clinical trials and the emergence of innovative gene therapies, the future looks promising for more tailored and potentially curative treatments for ectodermal dysplasia.

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A NOTE ON NOMENCLATURE

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Introduction:

Nomenclature is a system of giving distinct and specific scientific names to organisms for their identification. It is an important part of organism's classification. Naming an organism is very important for communication in order to specify the organism. The term Nomenclature is derived from Latin words "nomen" means "name" and "calore" means "to call". (Nomen + calore = to call by name). The system of nomenclature allows scientists and biologists to identify, categorize and classify organisms based on distinguished characteristics. The numbers of species of various organisms present on Earth ranges from 2 million to 1 trillion, but the expected estimated is around 11 million species or fewer. In the year 2018. 1.74 million Species of living organisms were recorded in database and near about 80% have not yet been described. Among the discovered species, if each one did not have a specific, unique and separate name, then it would be impossible to refer the huge number of taxa. The system of nomenclature allows having a universal way of identifying organisms as well as it allows to track and count current number of specific species.

The names can be of two types i.e., Vernacular (Common) name and scientific name. Vernacular names are based on normal language of day-to-day life. They often have local distribution and vary greatly between geographical regions, different cultures and from language to language. The same organism can have several common names in a single area and they may change according to particular language and region of the world. For example, butterfly is called titli in Hindi, fulpakharu in Marathi, prajapati in Bangla and vannathu in Tamil. Common names can cause confusion and for this reason they can't be used or avoided in communication amongst scientists from different regions of the World. On the other hand, scientific names are given by biologists and are known to represent a particular organism in every part of the world. Scientific names are specific, distinct and have particular spelling that is not changed. Nomenclature provides labels for taxa at all levels of classification to ease communication amongst biologists. The scientific names

form a communication system fulfills the basic requirement as any other language. Hence International Code of Nomenclature for organisms has been framed.

There are different codes of Nomenclature. ICZN stands for International Code of Zoological Nomenclature. It deals with nomenclature of animals. ICNafp stands for International Code of Nomenclature for Algae, Fungi and Plants. It deals with the nomenclature of algae, fungi and plants. ICNP stands for International Code of Nomenclature of Prokaryotes. It is concerned with the nomenclature of prokaryotes including Archaea. ICTV stands for International Committee on Taxonomy of Viruses. ICNCP stands for International Code of Nomenclature of Cultivated Plants.

Binomial and Binominal are two distinct terms and do not mean the same. In botany, the term binomial is used. It means two-word nomenclature which state that while naming a plant, two separate words for genus and species should be used. Whereas in Zoology, the term binominal is used. It means to follow two name patterns for naming the animals. This allows to use single word for generic as well as species name (Tautonym). For example, *Catla catla, Gorilla gorilla, Naja naja, etc.* Hence, the term binomial is correct for botanical nomenclature and binominal is correct for zoological nomenclature. Tautonym is only used for zoological nomenclature and not for botanical nomenclature.

Binominal Nomenclature:

Carolus Linnaeus was a Swedish naturalist who proposed the scientific system of naming organisms. This system is known as binominal system of nomenclature. Linnaeus described 5900 plant species in his book 'Species Plantarum' in 1753 and 4326 animal species in the 10th edition of his book 'Systema Nature' in 1758. The technical names recognized internationally are the ones given by Linnaeus in these books. Linnaeus also gave some common rules for nomenclature of species. According to the rules, every species of plant or animal must be given one name consisting of two separate words, one id generic and other is specific name. The generic name should be written first and is followed by species name. The first letter of generic name should be capitalized and first letter of species name should be small. The names should always be written in Latinized form because Latin is a dead language and it will not change in form or spelling with passage of time. The binominal names should be printed in italics. If handwritten, both the words should be separately underlined. In the running text, the scientific name may be repeated many times. In such condition, the generic name is written in full for the first time at the

starting of the text and then after it is written only by its first capital letter. For example, *Panthera tigris* is written at the starting of the text and then it can be written as *P. tigris.*

Trinomial Nomenclature

Huxley and Strickland proposed trinomial nomenclature system. When members if any species have a large variation, then trinomial nomenclature is used. It refers to three name patterns for naming an organism where the first word is the name of genus, second word is the name of species and the third word represents subspecies. For example, *Elephas maximus indicus* is the scientific name of Asian elephant. Here the first word is name of genus, second word is name of species and third word is name of subspecies. All the words are typeset in italics and if handwritten, all the words are separately underlined. All the words are latinized and only the first letter of genus is capitalized. In the running text where scientific name may be repeated many times, in such condition, the generic and specific name is written in full for the first time at the starting of the text and then after it is written only by its first capital letter. For example, *Gorilla gorilla diehli* is written at the starting of the text and then it can be written as *G. g. diehli.*

In many cases, species name is followed by the name of person who reported it for the first time. For example, *Homo sapiens (Linnaeus).* Here Linnaeus is the name of the biologist who first described it the species *Homo sapiens.* It can be written in full or in abbreviated form. In zoological nomenclature, if the author's name is taken from indirect source other than any original publication, then it is written in square bracket.

Advantages of Scientific Nomenclature

- Every organism known to science has been given a scientific name.
- The nomenclature system provides uniqueness, stability and universality to the scientific names.
- The letters for nomenclature are derived from Latin language, hence there is no possibility of any change in their form and spellings.
- The scientific names are of universal application for all languages and countries and thus avoid any kind of confusion among scientists from any corner of the world.
- The relationship of one species with other species present in the same genus is also indicated.
- Scientific names are descriptive and easy to recollect.
- The important characteristics of an organism can be easily indicated by scientific names.

- A wrong name can easily be corrected.
- A newly discovered organism can be easily described and provided with new scientific name.

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FERROPTOSIS: A NEW FRONTIER IN CANCER THERAPY

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Abstract:

Ferroptosis is an iron-dependent, regulated form of cell death characterized by the accumulation of lipid peroxides and reactive oxygen species (ROS), resulting from impaired glutathione metabolism and the failure of glutathione peroxidase 4 (GPX4). Unlike apoptosis, necrosis, and autophagy, ferroptosis is triggered by oxidative stress and membrane lipid damage, ultimately leading to cell death. This distinct pathway has garnered significant interest as a therapeutic strategy, particularly in overcoming resistance in therapy-refractory cancers. Small-molecule ferroptosis inducers, such as erastin and RSL3, have shown promising results by selectively targeting cancer cells with impaired antioxidant defense systems. Ferroptosis has been implicated in various malignancies, including pancreatic cancer, glioblastoma, lung cancer, and hepatocellular carcinoma, where conventional treatments often prove ineffective. The potential of ferroptosis to enhance the efficacy of existing therapies and overcome drug resistance highlights its therapeutic importance. However, challenges such as ferroptosis resistance, off-target toxicity, and the identification of reliable biomarkers must be addressed to optimize its clinical application. Recent drug development efforts and ongoing clinical trials are investigating ferroptosis-inducing agents, combination therapies, and personalized approaches to maximize their therapeutic potential. As research advances, ferroptosis emerges as a promising frontier capable of transforming cancer treatment by offering novel strategies to target therapy-resistant tumors and improve patient outcomes.

Introduction:

Cancer remains one of the leading causes of mortality worldwide, with an urgent need for novel therapeutic strategies to overcome resistance to traditional treatments such as chemotherapy, radiotherapy, and immunotherapy. Ferroptosis, first described in 2012 by Dixon *et al.,* represents a unique, non-apoptotic cell death mechanism that has attracted significant attention in oncology research [1]. Unlike apoptosis, ferroptosis is primarily regulated by iron accumulation and lipid peroxidation, making it distinct in its molecular characteristics and execution pathways.

Ferroptosis has shown promise in selectively targeting cancer cells, particularly those resistant to apoptosis. Many aggressive tumors, including glioblastoma, pancreatic cancer, and drug-resistant lung cancers, exhibit heightened susceptibility to ferroptosis due to their reliance on iron metabolism and oxidative stress pathways [2]. Understanding and harnessing ferroptosis in cancer therapy could open new avenues for overcoming treatment resistance and improving patient outcomes.

Ferroptosis is tightly regulated by several key molecular pathways, with glutathione peroxidase 4 (GPX4) playing a pivotal role in preventing lipid peroxidation and maintaining cellular redox balance. When GPX4 activity is inhibited or depleted, toxic lipid peroxides accumulate, triggering ferroptotic cell death [3]. Additionally, system Xc-, a cystine-glutamate antiporter, is responsible for maintaining intracellular glutathione levels, and its inhibition further sensitizes cancer cells to ferroptosis [4]. Targeting these critical regulators has emerged as a promising approach to induce ferroptosis in therapy-resistant cancer cells.

Emerging evidence suggests that ferroptosis can synergize with existing treatment modalities to enhance anticancer efficacy. For instance, combining ferroptosis inducers such as erastin or RSL3 with chemotherapy or immunotherapy has been shown to overcome resistance in multiple tumor types [5]. Moreover, radiotherapy-induced oxidative stress can amplify ferroptosis, creating a favorable therapeutic window to eradicate resistant cancer cells [6]. This combinatorial approach could potentially improve treatment outcomes by exploiting the vulnerabilities of cancer cells through multiple mechanisms.

Despite its therapeutic potential, the clinical translation of ferroptosis-inducing strategies remains challenging due to the complex regulatory network and context-dependent effects observed in different cancer types. Further preclinical and clinical studies are needed to optimize ferroptosis-based therapies and minimize potential toxicities. Identifying reliable biomarkers for ferroptosis sensitivity and resistance will also be critical in guiding personalized treatment approaches [7]. Overall, harnessing ferroptosis as a therapeutic modality holds great promise in addressing treatment resistance and improving prognosis in cancer patients.

Molecular Mechanisms of Ferroptosis

Ferroptosis is primarily driven by iron-dependent lipid peroxidation and regulated by interconnected molecular pathways, including glutathione metabolism, lipid oxidation, and iron homeostasis. Iron plays a critical role in ferroptosis by participating in the Fenton

reaction, which generates hydroxyl radicals (•OH) that promote the oxidation of polyunsaturated fatty acids (PUFAs) in cellular membranes, leading to membrane damage and cell death [8]. Cancer cells often exhibit dysregulated iron metabolism, characterized by increased iron uptake and storage, which enhances susceptibility to ferroptosis. Key regulators of iron homeostasis include transferrin receptor 1 (TFR1), which facilitates iron import, ferritin, which stores excess iron to prevent toxicity, and ferroportin, which exports iron from cells. Elevated iron levels in tumor cells exacerbate oxidative stress and lipid peroxidation, creating a favorable environment for ferroptosis induction [9].

Lipid peroxidation is a hallmark of ferroptosis and occurs when PUFAs undergo oxidation, leading to cellular membrane damage and eventual cell death. Glutathione peroxidase 4 (GPX4) is a crucial enzyme that prevents lipid peroxidation by reducing lipid hydroperoxides to non-toxic alcohols, thereby protecting cells from ferroptosis. However, inhibition of GPX4 using agents such as RSL3 results in the accumulation of lipid peroxides, driving ferroptotic cell death [10]. Since many cancer cells exhibit heightened oxidative stress and impaired antioxidant defenses, GPX4 suppression has emerged as an attractive therapeutic target for enhancing ferroptosis in resistant tumors.

System Xc^-, a cystine-glutamate antiporter, maintains intracellular glutathione (GSH) levels, which are essential for GPX4 activity and protection against lipid peroxidation. Inhibiting System Xc^-, for example, using erastin, disrupts cystine uptake, depletes intracellular GSH, and impairs GPX4 function, ultimately triggering ferroptosis [11]. This dual approach—targeting both GPX4 and System Xc^-—has shown great potential in selectively inducing ferroptosis in apoptosis-resistant cancer cells. Leveraging these pathways offers an opportunity to target aggressive tumors that evade conventional treatments by exploiting their vulnerability to oxidative stress and iron dysregulation [12].

Role of Ferroptosis in Cancer Therapy

Ferroptosis has emerged as a promising therapeutic strategy in cancer treatment due to its ability to selectively target tumor cells while sparing normal cells. Its unique mechanism of action, driven by iron-dependent lipid peroxidation, makes it particularly effective in addressing tumors that exhibit resistance to conventional therapies. Ferroptosis is advantageous because it targets metabolic vulnerabilities that are often exploited by cancer cells, allowing for a multifaceted approach to eliminating malignant cells that evade apoptosis [13].

- **Overcoming Apoptosis Resistance**

Many cancers evade apoptosis by mutating key regulators, such as p53 and Bcl-2, resulting in resistance to programmed cell death. Ferroptosis provides an alternative pathway to eliminate these resistant cells. Studies have shown that tumor cells with defective apoptotic machinery often remain vulnerable to ferroptosis, presenting a valuable therapeutic target in refractory cancers. For instance, mutant p53, commonly found in various tumors, can inhibit apoptosis but may inadvertently sensitize cells to ferroptosis by altering lipid metabolism and iron homeostasis [14]. Therefore, inducing ferroptosis in apoptosis-resistant cancers holds significant potential for overcoming treatment failure in aggressive malignancies.

- **Targeting Metabolic Vulnerabilities**

Cancer cells often exhibit altered iron metabolism and increased oxidative stress, making them highly susceptible to ferroptosis. The metabolic reprogramming observed in tumor cells includes increased iron uptake through transferrin receptor 1 (TFR1), reduced iron export via ferroportin, and dysregulated ferritinophagy, leading to iron accumulation and oxidative damage [15]. Furthermore, cancer cells frequently have a diminished antioxidant capacity due to impaired glutathione synthesis and increased reactive oxygen species (ROS) production. These metabolic vulnerabilities create a favorable environment for inducing ferroptosis selectively in malignant cells without affecting normal tissues. Exploiting these metabolic alterations can enhance the therapeutic efficacy of ferroptosis-inducing agents.

- **Enhancing Chemotherapy and Immunotherapy**

Ferroptosis inducers can also potentiate the efficacy of existing cancer treatments, including chemotherapy and immunotherapy. Combining ferroptosis inducers with chemotherapeutic agents, such as cisplatin or sorafenib, has been shown to overcome drug resistance by inducing oxidative stress and lipid peroxidation in tumor cells [16]. This synergistic approach enhances cancer cell death and reduces the likelihood of relapse. Additionally, ferroptosis can improve immunotherapy outcomes by increasing tumor immunogenicity and promoting anti-tumor immune responses. Ferroptotic cell death releases damage-associated molecular patterns (DAMPs), which stimulate dendritic cells and enhance T-cell activation, thereby amplifying immune-mediated tumor clearance [17]. Integrating ferroptosis-based strategies with current treatment modalities offers a powerful approach to improving therapeutic outcomes in resistant and hard-to-treat cancers

Ferroptosis Inducers and Therapeutic Strategies

Several ferroptosis-inducing agents have been identified, offering new therapeutic avenues in cancer treatment. These agents include small-molecule inducers, iron-modulating agents, and combination therapies that synergistically enhance treatment efficacy. By targeting key pathways involved in ferroptosis, such as glutathione metabolism, GPX4 inhibition, and iron homeostasis, these agents selectively induce cell death in cancer cells, making them promising candidates for overcoming drug resistance in refractory tumors [21].

- **Small-Molecule Ferroptosis Inducers**

Small-molecule ferroptosis inducers have shown great potential in triggering ferroptosis by targeting crucial pathways. Erastin, a well-established ferroptosis inducer, inhibits System Xc^-, a cystine-glutamate antiporter responsible for maintaining intracellular glutathione (GSH) levels. By blocking cystine uptake, erastin depletes GSH, impairing GPX4 activity and inducing ferroptotic cell death [22]. Another prominent small molecule, RSL3, directly inhibits GPX4, leading to the accumulation of toxic lipid peroxides and subsequent ferroptosis. Furthermore, FIN56 exerts its ferroptosis-inducing effects through a dual mechanism by degrading GPX4 and promoting lipid peroxidation, making it a potent candidate for therapeutic intervention in cancer cells [23].

- **Iron-Modulating Agents**

Iron-modulating agents play a critical role in ferroptosis induction by exploiting the iron-dependent nature of this cell death pathway. Artemisinin derivatives utilize the high iron content found in cancer cells to generate reactive oxygen species (ROS) through the Fenton reaction, leading to oxidative stress and ferroptotic cell death [24]. Similarly, iron nanoparticles have been developed to selectively deliver iron to tumor cells, enhancing oxidative stress and promoting lipid peroxidation. These nanoparticles not only improve the efficacy of ferroptosis inducers but also increase the specificity of treatment, minimizing damage to normal tissues [25].

- **Combination Therapies**

Combination therapies involving ferroptosis inducers and conventional cancer treatments have shown remarkable potential in overcoming therapeutic resistance. Combining ferroptosis inducers with chemotherapy agents, such as cisplatin and sorafenib, sensitizes resistant tumor cells to oxidative stress and lipid peroxidation, enhancing cell death [26]. This synergistic approach not only improves the cytotoxic effects of chemotherapy but also reduces the likelihood of tumor recurrence. Additionally,

ferroptosis can boost immunotherapy by increasing tumor antigenicity and promoting the release of damage-associated molecular patterns (DAMPs), which activate dendritic cells and enhance T-cell-mediated immune responses. This mechanism amplifies the effects of immune checkpoint inhibitors and other immunotherapeutic approaches, leading to improved tumor eradication and prolonged survival [27].

Ferroptosis in Different Cancer Types

Ferroptosis has emerged as a promising therapeutic strategy across multiple cancer types, including glioblastoma, pancreatic cancer, and lung cancer. Many malignancies exhibit increased susceptibility to ferroptosis due to their inherent metabolic vulnerabilities, such as heightened iron accumulation, oxidative stress, and dysregulated antioxidant defenses. Exploring ferroptosis in different cancer types offers new opportunities to target treatment-resistant tumors and improve clinical outcomes [28].

- **Glioblastoma**

Glioblastoma, one of the most aggressive and treatment-resistant brain tumors, is characterized by a high iron content and elevated oxidative stress, making it highly sensitive to ferroptosis induction. Ferroptosis inducers such as RSL3 and FIN56 have shown significant efficacy in inducing ferroptosis by inhibiting GPX4, thereby disrupting the antioxidant defense system and promoting lipid peroxidation in glioblastoma cells. Additionally, GPX4 suppression leads to the accumulation of toxic lipid peroxides, ultimately triggering ferroptotic cell death. Recent studies have demonstrated that ferroptosis induction not only enhances glioblastoma cell death but also sensitizes glioblastoma to conventional therapies, including radiotherapy and temozolomide, by increasing oxidative damage and overcoming therapeutic resistance [29].

- **Pancreatic Cancer**

Pancreatic cancer remains one of the most lethal malignancies due to its resistance to conventional therapies, including chemotherapy and targeted treatments. However, recent evidence suggests that pancreatic cancer cells are highly vulnerable to ferroptosis. Ferroptosis inducers such as erastin and RSL3 have demonstrated the ability to inhibit System Xc^- and GPX4, leading to glutathione depletion and lipid peroxidation, which effectively induces ferroptosis in pancreatic cancer models. Preclinical studies have shown that combining ferroptosis inducers with chemotherapy agents like gemcitabine significantly enhances therapeutic efficacy and reduces tumor growth by exploiting the metabolic weaknesses of pancreatic cancer cells. This combination strategy holds promise

for improving the survival rates of pancreatic cancer patients who do not respond well to conventional therapies [30].

- **Lung Cancer**

Drug-resistant lung cancers, particularly non-small cell lung cancer (NSCLC), have demonstrated increased susceptibility to ferroptosis when treated with ferroptosis inducers in combination with standard therapies. NSCLC cells often exhibit high iron metabolism and elevated oxidative stress, making them prime candidates for ferroptosis induction. Targeting GPX4 and modulating iron homeostasis have proven to be effective in overcoming drug resistance in lung cancer cells. Recent studies have shown that ferroptosis inducers, when combined with tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors, can significantly enhance the efficacy of standard treatments and suppress tumor growth. Ferroptosis induction in lung cancer not only promotes tumor cell death but also improves immune responses, leading to better long-term control of metastatic and drug-resistant disease [31].

- **Current Clinical Trials and Drug Repurposing**

Ongoing clinical trials are exploring the potential of ferroptosis-inducing drugs in cancer therapy. Researchers are evaluating the efficacy of repurposed drugs that exhibit ferroptosis-inducing properties, either alone or in combination with conventional therapies, to improve outcomes in treatment-resistant cancers.

- **Sulfasalazine**

Sulfasalazine, traditionally used to treat inflammatory conditions like rheumatoid arthritis and inflammatory bowel disease, has shown promise in inducing ferroptosis by inhibiting System Xc^-, a key regulator of cystine-glutamate exchange. By blocking cystine uptake, sulfasalazine depletes intracellular glutathione, leading to oxidative stress and ferroptosis in cancer cells. Preclinical studies have demonstrated that sulfasalazine effectively induces ferroptosis in various cancer models, including glioblastoma and pancreatic cancer, paving the way for its clinical evaluation in combination with conventional anticancer therapies [32].

- **Statins**

Statins, commonly used to lower cholesterol levels by inhibiting the mevalonate pathway, have also been identified as potential ferroptosis inducers. Statins indirectly sensitize cancer cells to ferroptosis by reducing the synthesis of coenzyme Q10 (CoQ10), a critical antioxidant that protects cells from lipid peroxidation. Preclinical studies have shown that statins enhance ferroptosis and improve the efficacy of chemotherapy and

targeted therapies in multiple cancer models. Clinical trials are currently investigating the repurposing of statins as adjuvants to standard treatments to enhance ferroptosis and improve treatment outcomes in resistant cancers [33].

The integration of ferroptosis-inducing agents with existing cancer therapies holds immense promise for overcoming resistance and improving survival rates in patients with refractory cancers. Ongoing clinical trials aim to validate the safety and efficacy of ferroptosis-based combination therapies, providing a strong rationale for incorporating ferroptosis inducers into standard treatment regimens. As research advances, identifying novel ferroptosis targets and optimizing therapeutic combinations will be critical to maximizing the clinical impact of ferroptosis in cancer therapy

Challenges and Future Directions

Despite the growing interest in ferroptosis as a therapeutic strategy, several challenges must be addressed before its full clinical potential can be realized. One of the primary challenges is the heterogeneity in ferroptosis sensitivity across different tumor types. Not all cancers respond equally to ferroptosis induction due to variations in iron metabolism, antioxidant capacity, and genetic profiles. Some tumors exhibit robust antioxidant defenses through elevated glutathione (GSH) levels or increased expression of GPX4, making them less susceptible to ferroptosis. Additionally, mutations in tumor suppressor genes such as TP53 or alterations in metabolic pathways can further modulate ferroptosis sensitivity, resulting in variable responses among patients. Understanding these differences and identifying cancer subtypes that are more vulnerable to ferroptosis will be critical for the development of personalized therapeutic strategies [34].

Another significant concern is the potential toxicity associated with ferroptosis induction in normal tissues. Since ferroptosis is driven by oxidative stress and lipid peroxidation, non-cancerous cells with high iron content or compromised antioxidant defenses may also be susceptible to ferroptotic damage. This off-target toxicity poses a challenge for the safe application of ferroptosis-based therapies. Therefore, selective targeting of cancer cells while sparing normal tissues is essential to minimize adverse effects. One promising approach involves the use of tumor-specific delivery systems, such as nanoparticle-based carriers, that enhance the selective accumulation of ferroptosis inducers in malignant tissues. Additionally, exploring combination therapies that fine-tune ferroptosis induction may reduce toxicity by lowering the required dose of ferroptosis inducers [35].

A further challenge lies in the identification and validation of reliable biomarkers that can predict ferroptosis sensitivity in tumors. Biomarkers are essential for patient stratification, allowing clinicians to identify individuals who are most likely to benefit from ferroptosis-based therapies. Potential biomarkers include indicators of iron metabolism, lipid peroxidation levels, and expression levels of ferroptosis regulators such as GPX4 and SLC7A11. Recent research has suggested that lipid peroxidation signatures and iron homeostasis markers could serve as potential predictors of ferroptosis sensitivity in different cancer types. Developing validated, reproducible biomarkers will not only improve patient selection but also enhance the monitoring of treatment responses and enable timely modifications to therapeutic regimens [36].

Looking ahead, future research should focus on elucidating the molecular mechanisms underlying ferroptosis resistance and exploring novel strategies to enhance ferroptosis sensitivity in resistant tumors. Additionally, expanding the scope of clinical trials to evaluate the safety and efficacy of ferroptosis-inducing agents in diverse cancer populations will be essential for advancing ferroptosis from the laboratory to the clinic. Combining ferroptosis inducers with immunotherapy, chemotherapy, and radiotherapy holds promise for improving treatment outcomes and overcoming resistance in aggressive cancers. As our understanding of ferroptosis biology deepens, it is likely that ferroptosis-based therapies will become an integral part of precision oncology, offering new hope for patients with treatment-resistant malignancies [37]

Conclusion:

Ferroptosis has emerged as a promising therapeutic approach, especially for overcoming resistance in aggressive and drug-resistant cancers. Unlike traditional therapies, ferroptosis targets cancer cells by disrupting iron metabolism, inducing lipid peroxidation, and disturbing redox homeostasis, making it effective against apoptosis-resistant tumors. The ability of ferroptosis inducers to selectively eliminate tumor cells while potentially enhancing the efficacy of chemotherapy and immunotherapy highlights their clinical relevance. Additionally, combining ferroptosis with other treatment modalities may provide synergistic effects, improving outcomes for patients with refractory malignancies.

However, despite its potential, several challenges must be addressed before ferroptosis can be fully integrated into clinical practice. Tumor heterogeneity, with variations in ferroptosis sensitivity, requires a better understanding of cancer-specific vulnerabilities. Moreover, the risk of off-target toxicity in normal tissues necessitates the

development of selective delivery systems and safer therapeutic strategies. The identification of reliable biomarkers to predict ferroptosis sensitivity and monitor treatment responses will be critical for patient selection and treatment optimization. Ongoing research and well-designed clinical trials will help to refine ferroptosis-based therapies and unlock their full potential, paving the way for more effective and personalized cancer treatment strategies in the future.

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INTEGRATING NUTRITION AND DECISION SCIENCE: A COMPUTATIONAL APPROACH TO CANCER PREVENTION

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Abstract:

Poor dietary habits have been recognized as a significant risk factor for cancer in numerous epidemiological studies. Maintaining a nutritious and well-balanced diet is essential for minimizing cancer risk. Effective cancer prevention meal plans should include appropriate proportions of macronutrients, micronutrients, and lean proteins. Regular consumption of balanced meals supports the body's nutritional requirements, enhances overall health, and aids in essential growth and repair processes. A well-rounded diet helps prevent nutrient deficiencies and lowers the likelihood of chronic diseases linked to unhealthy eating patterns. In this study, we utilize the DDC method to gather data that fosters health and well-being. By employing the Linear Programming Problem approach, researchers can formulate strategies to optimize nutritional interventions, ensuring individuals have access to nutrient-rich and well-balanced diets that may help reduce cancer risk. This interdisciplinary approach has the potential to improve public health outcomes and deepen our understanding of the connection between nutrition and disease prevention.

Keywords: Cancer Prevention, Nutritional Analysis, Balanced Diet, Dietary Habits, Public Health.

1. Introduction:

The decision-making process indeed revolves around evaluating various options and choosing the one that is most effective in achieving specific goals and objectives. This process can be influenced by a range of factors such as available resources, constraints, preferences, and potential outcomes. [1]. Because decision making is a daily task in our everyday routines, effective tools should be used to analyze all aspects of decision making problems. Multi-Criteria Decision Making (MCDM) is a well-structured and multidimensional process developed to tackle decision-making problems in different fields and search for the most attractive alternative with consideration of all relevant criteria.

Due to its powerful tools, it analyzes complex decision-making problems in different fields. This method improves the quality of decision-making to become more rational and efficient [2]. Numerous methods have been used to make a decision according to an analysis model. Several tools have been developed to solve multi-criteria decision-making (MCDM) problems effectively Undoubtedly, MCDM has grown recently and been utilized in different fields such as sustainable energy [2,3], maintenance management [4,5], construction management [6], tourism management [7], machine selection [8], material selection [9], supply chain management [10], aviation [11,12] and risk management [13].
Nutritional science principally distinguishes two different classes among its classifications: macronutrients and micronutrients [14].

Macronutrients can be considered as the main components of different tissues, and they constitute the total amount of the caloric intake, meaning the principal energy source of the human body; they are mainly distinguished in carbohydrates, proteins and lipids [15].

Although 1 in 5 men and 1 in 6 women worldwide develop some type of cancer during their lifetime, those diagnosed are living longer than ever, thanks to screening and early detection, vaccinations, and improvements in treatment. However, even for cancers with effective treatment options, prevention has the greatest potential to reduce the burden of cancer in the general population. [16] According to the World Health Organization (WHO), a 30-40% cancer burden can be attributed to lifestyle risk factors such as tobacco smoking, alcohol consumption, a diet low in fruit and vegetables, overweight and obesity, and physical inactivity. [17]

Estimated by the American Institute for Cancer Research and the World Cancer Research Fund that 30–40 percent of all cancers can be prevented by appropriate diets, physical activity, and maintenance of appropriate body weight [18].

Wheat is a well-known cereal grain that grows on arable land and is responsible for sustaining commercial food production worldwide. Wheat cereal is a rich source of dietary fiber. The latter is a major factor playing pivotal roles in regulation of normal function of gastrointestinal tract. Evidence of reduced colorectal cancer risk after intake of dietary fiber has shown heterogenous results.[19]

Eggs also contain choline, a B-complex vitamin, which plays a key role in the normal functioning of cells, irrespective of age and gender and also lowers your risk of breast cancer [20]

Nuts consumption could also have a chemopreventive effect, especially on colorectal and prostate cancer (21, 22).

According to the 2012 World Health Organization data on cancer incidence in the global population, more than 14 million cases were diagnosed compared to 12.7 million in 2008 and 8.2 million deaths were recorded compared to 7.6 million in 2008 (23, 24). More worryingly, it has been predicted that cancer cases will increase to more than 19 million a year by 2025.

Linear programming Problem (LPP) is indeed a powerful optimization technique used in various fields, including operations research, economics, engineering, and management. By formulating a problem as an LPP, you can find the best solution that maximizes or minimizes an objective function while satisfying a set of linear constraints. This method is particularly useful when dealing with resource allocation, production planning, transportation logistics, and many other real-world problems.

2. Preliminaries:

2.1 LPP:

Linear Programming is a mathematical technique which is used to determine the optimal (maximum or minimum) value of a linear function.

2.2 Decision Variables:

Variables you want to determine to achieve the optimal solution.

2.3 Objective Function:

Mathematical equation that represents the goal we want to achieve.

2.4 Constraints:

Limitations or restrictions that your decision variables must follow.

2.5 Non-Negativity Restrictions:

In some real-world scenarios, decision variables cannot be negative:

2.6 Decisions:

Decisions are different based on the type of problem that can include Carbohydrates, Protein, and fat in the optimized food plans. we collected the prices of these foods from the local market.

2.7 Macronutrient:

Macronutrients are nutrients that people regularly require in large quantities to provide their body with energy to perform bodily functions and daily activities.

2.8 Micronutrients:

Micronutrients are essential in small amounts. They include vitamins and minerals.

3. Proposed Method:

Linear programming is an excellent tool for optimizing resource allocation, such as in the case of maximizing health benefits while minimizing costs. By assigning variables to different types of food and their respective nutritional components (carbohydrates, protein, calcium, fat), we can set up constraints based on recommended daily intake values and cost limitations. Then, using an objective function representing health benefits (perhaps measured in terms of meeting recommended daily allowances for each nutrient), we can solve for the optimal combination of foods that achieve the maximum benefit at the minimum cost. This approach allows us to make informed decisions about dietary choices, ensuring that nutritional needs are met efficiently and economically.

Table 1: **Carbohydrate (CHO), protein, and fat content of nuts (g/100 g of raw and roasted product [25]**

Nuts	Raw			Roasted		
	CHO	Protein	Fat	CHO	Protein	Fat
Almonds	19.9	21.9	50.6	17.7	21.2	55.2
Cashews	30.2	18.2	46.4	29.9	16.8	47.8
Peanuts	16.1	25.8	49.2	18.9	26.4	49.3
Pistachios	28.0	20.6	44.4	26.8	21.4	46.0
Walnuts	9.9	26.1	65.2	-	-	-

Mathemataical form of an LPP:

The Objective function:

Max.z = $\sum_{i=1}^{n} C_i X_i$

Subject to the constraints a11x1+a12x2+…..a1nxn ≤ b1, a21x1+a22x2+…..a2nxn ≤ b2, ……

am1x1+am2x2+…..amnxn ≤ bm, Non negativity Constraints $x_1, x_2, \ldots x_n \geq 0$ This paper we have taken

x_j: Quantity of food *j* consumed per day, C_j: Price of food j per 100g

a_{ij}: Amount of nutrient i present in 100g of food j, b_i: Required daily intake of nutrient i

This study explores the impact of various nutrient combinations in reducing cancer cell growth. Each combination consists of a unique set of foods:

- **Set 1**: Egg, roasted almond, wheat
- **Set 2**: Peanut, milk, potato
- **Set 3**: Rice, moong dal (green gram), oats

To optimize nutritional benefits while minimizing costs, we apply **Linear Programming (LP)** using the following approach:

1. **Define Decision Variables** – Representing the quantity of each food item to be consumed.
2. **Formulate the Objective Function** – Aiming to minimize cost while meeting nutritional requirements.
3. **Set Constraints** – Ensuring that daily nutrient intake meets recommended levels.
4. **Solve the Linear Programming Problem** – Using optimization techniques to determine the best dietary combination.

This structured approach enables the formulation of cost-effective and nutritionally balanced meal plans that may contribute to cancer prevention.

Caculation part for Set A:

Table 1: Max Z = $10x_1 + 75x_2 + 5x_3$, subject to Constraint: $1.4x_1 + 17.7x_2 + 74.48x_3 \leq 65$, $12.2x_1 + 21.2x_2 + 9.61x_3 \leq 35$, $9.9x_1 + 52.2x_2 + 1.95x_3 \leq 35$ and $x_1, x_2, x_3 \geq 0$

Solution: (X_1:Egg, X_2: Roasted Almond, X_3:Wheat)

Iteration 1:

		C_j	10	75	5	0	0	0	XB/Xj
B	CB	XB	X1	X_2	X3	S_1	S_2	S3	Ratio
S_1	0	65	1.4	17.7	74.48	1	0	0	3.67
S_2	0	35	12.2	21.2	9.61	0	1	0	1.65
S_3	0	35	9.9	52.2	1.95	0	0	1	0.67→
		Zj	0	0	0	0	0	0	
		Zj – Cj	-10	-75	-5	0	0	0	

↑

$Z_j - C_j < 0$, X_2 enters and S_3 leave the basis.

Iteration 2:

		C_j	10	75	5	0	0	0	XB/Xj
B	CB	XB	X1	X_2	X3	S_1	S_2	S3	Ratio
S_1	0	53.13	-1.95	0	73.81	1	0	-0.33	0.71→
S_2	0	20.78	8.17	0	8.81	0	1	-0.40	2.35
X_2	75	0.67	0.18	1	0.03	0	0	0.01	17.94
		Zj	14.22	75	2.80	0	0	1.43	
		Zj – Cj	4.22	0	-2.19	0	0	1.43	

$Z_j - C_j < 0$, X_3 enters and X_2 leave the basis.

Iteration 3:

		C_j	10	75	5	0	0	0	XB/Xj
B	CB	XB	X1	X_2	X3	S_1	S_2	S3	Ratio
X_3	5	0.71	-0.02	0	1	0.01	0	-0.04	
S_2	0	14.43	8.41	0	0	-0.11	1	-0.36	
X_2	75	0.64	0.19	1	0	-0.05	0	0.01	
		Zj	14.16	75	5	0.02	0	1.42	
		Zj – Cj	4.16	0	0	0.02	0	1.42	

$Z_j - C_j > 0$ .Hence, optimal solution is arrived with value of variables as: X_1=0, X_2=0.6436, X_3=0.7198

Max Z = $10x_1 + 75x_2 + 5x_3$= (10×0)+(75×0.6436)+(5×0.7198)=48.27+3.599=Rs.51.869 Max.Z=Rs.51.869.

Similarly for Caculation part for Set B:

Max Z = $12.4x_1 + 5.5x_2 + 3x_3$, subject to Constraint: $17.2x_1 + 4.7x_2 + 18x_3 \leq 65$, $25.8x_1 + 3x_2 + 2x_3 \leq 35$, $5x_1 + 3x_2 + 0x_3 \leq 35$ and $x_1, x_2, x_3 \geq 0$

(X_1:Peanut, X_2: Milk, X_3:Potato) Max Z =Rs.64.16685

Calculation part for Set C

Max Z = $6.5x_1 + 30x_2 + 24.5x_3$, subject to Constraint: $11x_1 + 31.31x_2 + 18x_3 \leq 65$, $2.5x_1 + 11.93x_2 + 6.3x_3 \leq 35$, $0x_1 + 0.5x_2 + 2.5x_3 \leq 35$ and $x_1, x_2, x_3 \geq 0$

(X_1:Rice, X_2: Moong dal, X_3:Oats)

Max Z = Rs.88.47195

Incorporating Multiple Criteria into Decision-Making

Beyond cost, factors such as taste, quality, and availability play a crucial role in making wellrounded dietary decisions. To ensure a comprehensive evaluation, we can integrate multiple criteria into our decision-making process using the following steps:

Identify Key Criteria:

Begin by listing all relevant factors for evaluating food sets. These may include:

- **Cost** (affordability)
- **Taste** (palatability)
- **Quality** (nutritional value)
- **Availability** (ease of access)
- Any other factors that influence the decision

Assign Weights:

Determine the relative importance of each criterion by assigning weights based on priorities. For example:

- Cost: **40%** Taste: **30%** Quality: **20%** Availability: **10%**

  These weights can be adjusted based on specific needs.

Normalize Data:

Since different criteria are measured on different scales (e.g., cost in currency, taste rated from 1 to 10), normalization ensures comparability. Standardizing the data helps in accurate evaluation.

Evaluate Alternatives:

Assess each food set against the identified criteria using scoring or ranking methods. For example:

- Taste could be rated out of **10**
- Quality out of **5**
- Availability as a percentage

Calculate Overall Score:

Compute a weighted score for each food set by multiplying individual scores by their respective weights and summing them up. This provides a single comprehensive measure for comparison.

Make the Decision:

The food set with the lowest overall score is identified as the best choice based on all selected criteria.

By incorporating this structured approach, we can make balanced, data-driven dietary decisions that optimize both nutritional benefits and practical considerations.

Food/Weight/ Criteria	**Price**	**Taste**	**Nutritional value to reduce cancer**	**Quality**
Weight	.25	0.11	0.35	0.29
Set A	52	4	8.5	5
Set B	64	4.5	9.0	4.4
Set C	88	4.2	7.5	4.6

Food/ Weight/ Criteria	**Price**			**Taste**			**Nutritional value to reduce cancer**			**Quality**			**Per-form ance**	**Rank**
Weight	.25			.11			0.35			0.29				
Set A	52	6.37	1	4	9.16	3	8.5	11.9	2	5	35.71	10.36	68.02	2
Set B	64	7.84	2	4.5	10.3	1	9	12.6	1	4.4	31.43	9.114	65.94	1
Set C	88	10.8	3	4.2	9.62	2	7.5	10.5	3	4.6	32.86	9.529	102.16	3

Using mcdm method we can conclude that Set B is the best among the three.

Conclusion:

This paper introduces a novel approach to analyzing the relationship between diet and cancer cell growth through a mathematical modeling framework. By incorporating nutritional data from credible sources such as the WHO and RDA, we aimed to optimize dietary combinations to maximize health benefits while minimizing costs. Using the Linear Programming Problem (LPP), we identified three optimal food combinations that demonstrate potential in reducing cancer cell proliferation. Additionally, by applying the Multiple Criteria Decision Making (MCDM) method, we evaluated these food sets across multiple factors, offering valuable insights into their effectiveness in cancer prevention. The findings of this study highlight the crucial role of dietary choices in both cancer prevention and management. By identifying cost-effective and nutritionally beneficial food strategies, this research contributes to ongoing efforts to enhance public health and improve cancer care outcomes.

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THE GROWING THREAT OF FUNGAL INFECTIONS: CHALLENGES AND INNOVATIONS IN ANTIFUNGAL RESEARCH

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Introduction:

Fungal infections are emerging as a significant global public health concern, causing increasing morbidity and mortality in both clinical and agricultural contexts. The burden Growing morbidity and mortality in clinical and agricultural settings are the results of fungal infections, which are becoming a major global public health concern. The growing number of immunocompromised persons, such as those receiving chemotherapy, organ transplant patients, and those living with HIV/AIDS, has increased the burden of fungal illnesses. These populations are more susceptible to opportunistic fungal infections, which can be mild to fatal, because their immune systems are frequently compromised (Fisher *et al.* 2022; Rayens and Norris 2022; Denning, 2024). Additionally, fungi represent a significant danger in the agricultural sector, as fungal pathogens cause a variety of crop diseases that have a detrimental effect on global agricultural output and food security (Fisher *et al.* 2022; Case *et al.* 2022).

Growing morbidity and mortality in clinical and agricultural settings are the results of fungal infections, which are becoming a major global public health concern. The growing number of immunocompromised persons, such as those receiving chemotherapy, organ transplant patients, and those living with HIV/AIDS, has increased the burden of fungal illnesses. These populations are more susceptible to opportunistic fungal infections, which can be mild to fatal, because their immune systems are frequently compromised (Fisher *et al.* 2022; Rayens and Norris 2022; Denning, 2024). Additionally, fungi represent a significant danger in the agricultural sector, as fungal pathogens cause a variety of crop diseases that have a detrimental effect on global agricultural output and food security (Fisher *et al.* 2022; Case *et al.* 2022).

The treatment of fungal infections is still difficult, even with the availability of numerous antifungal medications. The range and efficacy of the antifungal medications currently on the market are constrained. There is a gap in the ability to resist a wider

spectrum of fungal diseases because many current treatments exclusively target particular species of fungi (Rauseo *et al.* 2020). Concern over the development of antifungal resistance is also developing. Fungal pathogens, especially those that cause systemic infections, have become more resistant to current treatments, which has made treatment more challenging and led to worse patient outcomes (Fisher *et al.* 2022; Rabaan *et al.* 2023). The ability of fungi to adapt to various settings, genetic alterations in fungus, and extended and improper use of antifungals are the causes causing this resistance (Hokken *et al.* 2019).

The toxicity of several antifungal medications is another important concern. Many of the medications on the market, particularly those used to treat serious infections, have serious adverse effects, such as hepatotoxicity and nephrotoxicity, which restricts their usage in susceptible groups, such as people with underlying medical disorders (Girois *et al.* 2006). Consequently, there is an urgent need to create new antifungal medications that are safe, effective, and able to overcome resistance's obstacles.

The purpose of this chapter is to give a summary of the state of antifungal research today while looking at the difficulties in creating novel antifungal treatments. We'll talk about the processes that underlie antifungal resistance and look at possible directions for further study. (Corbu *et al.* 2006; Ross and Santiagon, 2024) resistance mechanisms. Researchers are also investigating a variety of promising methods, such as the discovery and synthesis of novel natural and synthetic antifungal agents, as well as cutting-edge tactics including immunotherapy and combination therapies (Kim *et al.* 2022; Hetta *et al.* 2025). There has never been a more pressing need for safer, more potent antifungal drugs because of the rising incidence of fungal infections and the worldwide risks of toxicity and resistance, which necessitate creative solutions for both agricultural and public health.

The Rising Burden of Fungal Infections

A substantial and expanding worldwide health burden is posed by fungal infections, which are brought on by a wide variety of fungi. Molds (like Aspergillus species), dermatophytes (like Trichophyton species), and yeasts (like *Candida* species) are the main causes of these diseases, and they can all result in a variety of clinical symptoms. Many fungal infections, such athlete's foot or nail infections, are minor and self-limiting, but some can be serious and even fatal, especially in people with weakened immune systems (Denning, 2024). Individuals who are immunosuppressed or immunocompromised are

more at risk, and the severity of these illnesses is primarily determined by their immunological condition.

There is a substantial correlation between the expanding usage of immunosuppressive medicines and the rising incidence of fungal infections. Antibiotics and chemotherapy, which are frequently used in clinical practice to treat cancer and bacterial infections, can unintentionally reduce the immune system's capacity to fight off fungal infections (Jain *et al.* 2010). The increasing prevalence of invasive fungal infections, which are frequently challenging to identify and treat, has been greatly exacerbated by this increased susceptibility in immunocompromised patients, including organ transplant recipients, cancer patients, and people living with HIV/AIDS (Low *et al.* 2011).

The World Health Organization (WHO) estimates that fungal infections affect over one billion people worldwide, and fungal-caused diseases claim millions of lives annually. Most of these deaths take place in low- and middle-income nations with limited access to antifungal medications (WHO, 2022).

Fungal diseases are a serious hazard to world agriculture in addition to its clinical implications. Millions of tons of food are destroyed annually due to fungal diseases in crops, which has a significant impact on global agricultural economy and food security. In low-income nations, where agricultural systems may be more susceptible to fungal diseases because of a lack of resources for disease management, the effects of fungal infections in crops are especially severe (Nizamani *et al.,* 2024). In addition to lowering crop yields, fungi like *Fusarium*, *Aspergillus*, and *Puccinia* species can also produce mycotoxins that contaminate food and feed, exacerbating the problems with the economy and public health (El-Sayed *et al.* 2022). Because these mycotoxins are dangerous to both humans and animals, fungal illnesses in agriculture are a

Because of these mycotoxins' detrimental effects on both humans and animals, fungal diseases in agriculture pose a serious threat to the world's food supplies.

The combined impact of fungal infections on agriculture and human health highlights the critical need for novel antifungal therapies. Although some antifungal medications are available, managing clinical and agricultural fungal illnesses has proven challenging due to antifungal resistance, poor pharmacological efficacy, and the severe toxicity of several treatments (Agbadamashi and Price, 2025). This combined burden emphasizes how crucial it is to keep researching novel antifungal drugs, treatment approaches, and prophylactic measures to deal with this expanding worldwide issue.

Current Antifungal Agents: Limitations and Challenges

Fungal infections, which can vary greatly in severity and the populations they impact, require the use of antifungal medicines. Based on their mode of action, antifungal drugs are currently divided into a number of groups, each with unique benefits and drawbacks.

1. **Polyene Antifungals (e.g., Amphotericin B)**: Ergosterol, an essential part of fungal cell membranes, is the target of powerful antifungals called polyenes. These medications damage the fungal membrane and cause fungal cell death by attaching to ergosterol and creating holes in the membrane (Kristanc *et al.* 2019). Amphotericin B is still one of the best therapies for systemic fungal infections, but its usage is restricted due to nephrotoxicity, which necessitates cautious dosage and close observation to prevent kidney damage (Noor and Preuss, 2024).
2. **Azoles (e.g., Fluconazole, Itraconazole)**: By specifically targeting lanosterol demethylase, a crucial enzyme in the ergosterol biosynthesis pathway, azoles prevent the formation of ergosterol. These medications are frequently used to treat systemic and superficial fungal infections, especially those caused by *Aspergillus* and *Candida* species (Hossain *et al.* 2022). However, because of their effects on cytochrome P450 enzymes, azoles are linked to liver damage and can result in serious medication interactions when used over an extended period of time (Rakhshan *et al.,* 2023). Furthermore, azole resistance has been increasing, particularly in *Aspergillus* and *Candida* species, which reduces their efficacy (Logan *et al.* 2022).
3. **Echinocandins (e.g., Caspofungin)**: A class of antifungals known as echinocandins prevents the production of glucan, a crucial part of the fungal cell wall. These medications work well against *Aspergillus* and *Candida* species, especially when invasive infections are present (Szymański *et al.* 2022). They are not effective against all fungi, including Cryptococcus species and dermatophytes, and their effectiveness is restricted to specific fungal infections (Geddes-McAlister and Shapiro, 2019).
4. **Allylamines (e.g., Terbinafine)**: Squalene epoxidase, a crucial enzyme in the ergosterol biosynthesis pathway, is inhibited by allylamines, which stops ergosterol from being produced and damages the fungal membrane. They are not appropriate for treating systemic fungal infections, although they are quite efficient against dermatophytes and some yeasts (Hammoudi, 2022).

Notwithstanding their efficacy, these antifungal drugs' main drawbacks include their limited range of action, related toxicity, and the escalating issue of antifungal resistance. The effectiveness of current treatments is decreased by fungal resistance mechanisms, which include changes to drug targets, upregulation of the efflux pump, and mutations in the target enzymes (Hossain *et al.* 2022). The need for novel antifungal drugs is greater than ever since resistance, particularly among species of *Aspergillus*, *Candida*, and *Cryptococcus*, poses a serious danger to effective therapy.

Antifungal Resistance: An Emerging Crisis

Fungal resistance to antifungal agents is an increasingly serious global issue. Several mechanisms contribute to the development of resistance:

1. **Target Site Modification**: Mutations in key fungal enzymes, such as lanosterol demethylase (targeted by azoles), can render antifungal drugs ineffective (Lee *et al.,* 2020). These mutations alter the drug's binding site, preventing the drug from exerting its antifungal effects.
2. **Efflux Pumps**: Many fungi overexpress efflux pumps, such as ATP-binding cassette (ABC) transporters, which actively pump antifungal agents out of fungal cells, reducing the concentration of the drug at the target site and lowering its efficacy (Holmes *et al.* 2016). This mechanism is a significant contributor to the emergence of resistance, particularly in *Candida* and *Aspergillus* species.
3. **Biofilm Formation**: Biofilms are communities of fungal cells embedded in an extracellular matrix that protect the fungi from antifungal treatment. Biofilm-associated infections, particularly those caused by *Candida* species, are much harder to treat and often require higher drug concentrations or longer therapy duration (Desai *et al.* 2014). Biofilm formation contributes to persistent infections and complicates treatment options. These resistance mechanisms present a formidable challenge in the treatment of fungal infections, limiting the effectiveness of existing therapies and leading to higher mortality rates. The absence of new antifungal drug classes on the market exacerbates the crisis, underscoring the need for urgent research and development in this field.
4. **Emerging Strategies for Developing New Antifungal Agents:** To address the limitations of current antifungal therapies, researchers are exploring several innovative strategies to discover new antifungal agents and overcome resistance.

5. **Natural Products and Traditional Medicine**: Bioactive substances having antifungal qualities have long been found in natural products derived from bacteria, fungus, and plants. Antifungal action against several infections has been proven by compounds such as berberine, resveratrol, and curcumin (Desai *et al.* 2014). Furthermore, the antifungal potential of essential oils derived from plants like eucalyptus, oregano, and thyme is being investigated; preclinical research has shown encouraging results for certain molecules (Stan *et al.* 2021). A wealth of possible therapeutic compounds from these natural sources may be able to aid in the fight against resistant fungal diseases.
6. **Molecular Target-Based Drug Design**: Proteomics and genomics developments have made it easier to find novel molecular targets in fungal cells. According to Robbins *et al.* (2016), enzymes implicated in stress response, ergosterol biosynthesis, and cell wall production are becoming important targets for medication development. The discovery of inhibitors that target fungal chitin synthase or fungal-specific proteases, for instance, has created new opportunities for antifungal treatment that may be more successful against strains that are resistant.
7. **Nanotechnology**: An intriguing new tactic is the application of nanoparticles and nanomaterials in antifungal treatment. According to Mondel *et al.* (2024), metal-based nanoparticles such as silver and gold have shown antifungal efficacy by rupturing fungal membranes and producing reactive oxygen species (ROS) that harm fungal cells. A promising new treatment option for challenging fungal infections may be provided by nanomedicine, which could increase the effectiveness of antifungal medications while lowering their toxicity.
8. **Combination Therapies**: Combining multiple antifungal agents to target different fungal pathways is another promising strategy to overcome resistance. By using a combination of drugs that act on distinct fungal targets, researchers hope to increase treatment efficacy and prevent the development of resistance. For example, combining antifungal agents with compounds that inhibit biofilm formation or efflux pump activity may improve the effectiveness of treatment (Spitzer *et al.* 2017).
9. **Host-Defense Modulation**: Strengthening the host's immune response is another area of focus in antifungal research. Enhancing the activity of immune cells, such as macrophages and T-cells, could provide a new approach to fighting fungal infections, particularly in immunocompromised patients. This approach could be particularly

beneficial for individuals with weakened immune systems who are more susceptible to opportunistic fungal infections (Toepfer *et al.* 2024).

The Future of Antifungal Research

The future of antifungal research will likely involve a multifaceted approach, combining the development of new antifungal agents with advances in diagnostic technologies, personalized medicine, and host immune modulation. The goal is to create antifungal therapies that are not only more effective but also safer, with fewer side effects and lower potential for resistance.

In addition to discovering new antifungal agents, the development of rapid diagnostic methods to identify fungal infections and their resistance profiles will be critical in improving treatment outcomes. These diagnostic tools could enable clinicians to tailor treatments to the specific fungal pathogens causing an infection, ensuring that patients receive the most appropriate therapy. Personalized antifungal therapy, based on genetic and phenotypic characteristics of both the host and the pathogen, will allow for more effective and individualized treatment regimens, reducing the likelihood of resistance and improving overall patient care.

Conclusion:

The increased prevalence of fungal infections, especially in immunocompromised individuals, and the growth of antifungal resistance highlight the urgent need for new antifungal drugs. The toxicity, limited range of action, and quick emergence of resistance of existing antifungal treatments have made it evident that new approaches to treatment are desperately needed. Current antifungal medications, including allylamines, polyenes, azoles, and echinocandins, have been essential in the treatment of fungal infections; however, their efficacy is being undermined by increased resistance, unfavorable side effects, and limited activity against a variety of fungal pathogens (Agbadamashi *et al.* 2025; de Oliveira *et al.* 2022).

Innovative strategies that combine developments in immunology, pharmaceutical chemistry, molecular biology, and biotechnology are needed to address these issues. Finding novel targets within fungal cells, such as enzymes involved in cell wall formation, stress response, and ergosterol biosynthesis, is the main goal of research into new antifungal medication classes (Fisher *et al.* 2022). Because these substances frequently have distinct modes of action and low host toxicity, research into natural products—including those produced from plants and microbial metabolites—remains crucial (Nasim

et al. 2022). Additionally, by using nanoparticles that break down fungal cell membranes or enable targeted drug administration, nanotechnology provides promising ways to improve the effectiveness of already available medications and get past resistance mechanisms.

A potent tactic for battling resistant strains and improving therapeutic results is combination therapy, which combines many antifungal medications or antifungal medications with substances that block resistance pathways (Spitzer *et al.* 2017). Additionally, in addition to conventional antifungal therapies, the body's capacity to combat infections can be strengthened by the manipulation of host immune responses, which makes it a promising supplementary therapy, especially for immunocompromised individuals (Johnson and Perfect, 2010).

The substantial impact of fungal pathogens in agriculture and the development of innovative therapeutics for human illnesses both depend on sustained funding in antifungal research. Worldwide, fungus diseases result in significant crop losses, endangering both global economic stability and food security. Therefore, advancements in antifungal treatments could enhance agricultural output as well as public health results.

In conclusion, a multifaceted strategy combining innovative medication development, cutting-edge technologies, and customized treatment is needed to overcome the difficulties presented by fungal infections and resistance. Addressing the growing threat of fungal illnesses worldwide will require a concentrated effort to emphasize antifungal research in addition to the creation of quick diagnostic technologies. By encouraging interdisciplinary cooperation and guaranteeing ongoing research funding, we can open the door to safer, more efficient antifungal therapies that satisfy the demands of both the agricultural sector and patients.

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RESTORING BALANCE: UNDERSTANDING HORMONAL IMBALANCE IN FEMALES AND NATURAL REMEDIES - A REVIEW

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Abstract:

Hormonal imbalance in females is a common condition influenced by various factors such as PCOS, menopause, stress, and thyroid disorders. It can lead to numerous physical, emotional, and psychological symptoms, affecting overall well-being. Conventional treatments are often complemented by herbal remedies, which offer a natural approach to hormonal regulation. Herbs like Ashwagandha, Shatavari, Black Cohosh, and Chasteberry have demonstrated therapeutic potential in managing hormonal imbalances. This review explores the causes, symptoms, and diagnosis of hormonal imbalance in females, along with the role of herbal remedies and lifestyle modifications. Integrating these approaches can provide effective management and enhance quality of life.

Keywords: Hormonal Imbalance, Female Health, Herbal Remedies, PCOS, Menopause, Ashwagandha, Shatavari, Black Cohosh, Chasteberry, Hormonal Regulation.

Introduction:

Hormonal imbalance in females occurs when there is an excess or deficiency of specific hormones, leading to disruptions in various physiological functions. Hormones play a crucial role in regulating metabolism, reproduction, mood, and overall well-being. Conditions such as Polycystic Ovary Syndrome (PCOS), menopause, stress, and thyroid disorders are common contributors to hormonal imbalances. While conventional treatments are available, herbal remedies have gained popularity for their natural and holistic approach to restoring hormonal equilibrium. This review explores the causes, symptoms, and management of hormonal imbalance in females, emphasizing the role of herbal interventions and lifestyle modifications in promoting hormonal health.

Hormonal imbalance in females occurs when there is too much or too little of certain hormones in the body. Hormones play a crucial role in regulating various bodily functions, including metabolism, reproduction, mood, and menstrual cycles. When hormone levels are disrupted, it can lead to a range of physical and emotional symptoms.

Common Causes of Hormonal Imbalance in Females

Hormonal imbalance in females can occur due to various factors that affect hormone production and regulation. Understanding these causes is essential for effective management and treatment. Here are the most common causes:

1. **Polycystic Ovary Syndrome (PCOS):** PCOS is one of the most prevalent hormonal disorders in females of reproductive age. It is characterized by elevated levels of androgens (male hormones) and insulin resistance. Symptoms include irregular menstrual cycles, excessive hair growth (hirsutism), acne, and weight gain. Hormonal imbalances in PCOS can lead to infertility and other metabolic issues. [1]
2. **Menopause:** Menopause is a natural biological process that marks the end of a woman's reproductive years, typically occurring between the ages of 45 to 55. During menopause, estrogen and progesterone levels decline significantly, leading to symptoms such as hot flashes, night sweats, mood swings, and vaginal dryness. Hormonal changes during this period can also increase the risk of osteoporosis and cardiovascular diseases. [2]
3. **Stress:** Chronic stress triggers the overproduction of cortisol, commonly known as the stress hormone. High cortisol levels can disrupt the balance of other hormones, including estrogen, progesterone, and thyroid hormones. Stress can contribute to irregular menstrual cycles, anxiety, depression, and weight gain. [3]
4. **Thyroid Disorders:** The thyroid gland produces hormones that regulate metabolism and energy levels. Hypothyroidism (underactive thyroid) and hyperthyroidism (overactive thyroid) can lead to hormonal imbalances. Symptoms of thyroid disorders include fatigue, weight changes, hair thinning, mood disturbances, and irregular periods. [4]
5. **Pregnancy and Postpartum:** Hormonal fluctuations are common during pregnancy and after childbirth. Estrogen and progesterone levels increase dramatically during pregnancy and drop significantly postpartum. Postpartum hormonal imbalances can lead to mood swings, fatigue, and postpartum depression. [5]
6. **Use of Birth Control Pills:** Oral contraceptives alter the natural hormonal cycle by regulating estrogen and progesterone levels. Some women may experience hormonal imbalances after discontinuing birth control pills, resulting in irregular periods and hormonal acne. [6]
7. **Obesity or Sudden Weight Loss:** Excess body fat can lead to increased estrogen production, which can disrupt hormonal balance. On the other hand, extreme weight

loss or malnutrition can reduce hormone production, causing menstrual irregularities and fertility issues. [7]

8. **Poor Diet and Lifestyle Habits [8]:** A diet lacking in essential nutrients and a sedentary lifestyle can negatively impact hormonal health. Excess consumption of sugar, processed foods, and unhealthy fats can lead to insulin resistance and hormonal imbalances. Lack of exercise, inadequate sleep, and substance abuse can further exacerbate hormonal issues.

By identifying and addressing the underlying causes of hormonal imbalances, females can improve their overall well-being. In addition to conventional treatments, herbal remedies can offer natural support in restoring hormonal balance, which will be discussed in the following sections.

Symptoms of Hormonal Imbalance in Females

Hormonal imbalances can manifest through various physical, emotional, and behavioral symptoms. The symptoms may vary depending on which hormones are affected, and their severity can differ from person to person. Recognizing these symptoms early can help in seeking appropriate medical care.

1. **Irregular or Painful Periods:** Hormonal imbalances often disrupt the menstrual cycle, leading to irregular, missed, or heavy periods. Painful cramps (dysmenorrhea) or severe premenstrual syndrome (PMS) may also occur. Conditions like Polycystic Ovary Syndrome (PCOS) and thyroid disorders are common culprits.
2. **Weight Gain or Unexplained Weight Loss:** Estrogen, progesterone, and thyroid hormones regulate metabolism and appetite. Imbalances may result in sudden weight gain or difficulty losing weight. On the other hand, hyperthyroidism can lead to unexplained weight loss.
3. **Mood Swings and Depression:** Fluctuations in estrogen and progesterone levels can affect neurotransmitters like serotonin, leading to mood changes. Women may experience anxiety, irritability, depression, or difficulty concentrating. Severe mood changes are often linked to premenstrual dysphoric disorder (PMDD) or menopause.
4. **Fatigue:** Hormonal imbalances, particularly involving the thyroid, adrenal glands, or insulin, can cause persistent fatigue. Low energy levels may be accompanied by muscle weakness and difficulty in performing daily activities.
5. **Hair Thinning or Excessive Hair Growth (Hirsutism):** Elevated androgen levels, often seen in PCOS, may cause excessive facial and body hair growth (hirsutism). Conversely, low estrogen levels can lead to hair thinning or hair loss, especially during menopause.

6. **Skin Issues like Acne:** Excess androgens can trigger overproduction of sebum, leading to acne, particularly around the jawline and chin. Hormonal imbalances may also cause skin dryness, pigmentation changes, or increased sensitivity.
7. **Hot Flashes or Night Sweats:** A decline in estrogen levels, commonly seen during perimenopause and menopause, often results in hot flashes and night sweats. These sudden temperature changes can disrupt sleep and impact daily life.
8. Reduced Libido: Low levels of estrogen and testosterone can lead to a decreased sex drive. Vaginal dryness and discomfort during intercourse may also occur, contributing to sexual dysfunction. [9,10.11]

Herbal Remedies for Hormonal Imbalance in Females

Herbal remedies have been used for centuries to support hormonal balance naturally. Many herbs possess adaptogenic, anti-inflammatory, and hormone-regulating properties. Here are some effective herbs:

1. Ashwagandha (*Withania somniferous*): Adaptogen that reduces stress and supports adrenal function. Helps balance cortisol levels. Supports thyroid health. Ashwagandha (Withania somnifera) has shown promising effects in managing subclinical hypothyroidism (SCH), a condition characterized by elevated TSH levels with normal T4 levels. In a double-blind, randomized, placebo-controlled study by Ashok Kumar Sharma *et al.,* 50 patients with SCH were administered either 300 mg of Ashwagandha root extract twice daily or a placebo for 8 weeks. The study group demonstrated significant improvements, with a notable reduction in TSH levels and increased serum T3 and T4 levels compared to the placebo group. By the 8th week, T3 levels increased by 41.5%, T4 levels by 19.6%, and TSH levels decreased by 17.4%. These results suggest that Ashwagandha supplementation may be beneficial for regulating thyroid hormones in individuals with SCH. However, further research is necessary to confirm its efficacy and safety in broader thyroid dysfunction cases. [12]

2. Shatavari (*Asparagus racemosus*): Known as a female reproductive tonic. Supports estrogen balance. Relieves symptoms of menopause and PCOS. Shatavari (Asparagus racemosus) has shown significant efficacy in managing menopausal symptoms, as demonstrated in a double-blind, randomized, placebo-controlled clinical trial by Vani S Gudise *et al.* [13] In this multicenter study, 70 menopausal women were divided into two groups, with one receiving Shatavari root extract and the other a placebo (microcrystalline cellulose). The results indicated that the Shatavari group experienced substantial relief from symptoms such as hot flashes, night sweats, insomnia, anxiety, nervousness, vaginal dryness, and loss of libido. Additionally, the Utian Quality of Life (QoL) score significantly

improved in the Shatavari group compared to the placebo group. Importantly, no major adverse effects were observed, supporting the safety of Shatavari as a natural alternative to hormone replacement therapy (HRT). While the findings endorse the traditional Ayurvedic use of Shatavari for menopausal symptom management, further studies with larger sample sizes and longer durations are needed to confirm its broader applicability.

3. Black Cohosh (*Actaea racemosa*): Helps manage hot flashes and night sweats. Supports hormonal balance during menopause. Eases menstrual cramps. Black cohosh (Actaea racemosa) is commonly used as a natural remedy to support women's hormonal health, particularly for menopausal symptoms. Beyond menopause, it has been explored for various other conditions, though the evidence supporting these uses is limited. Some older studies suggest that black cohosh, when combined with clomiphene citrate (Clomid), may enhance ovulation and pregnancy rates in individuals with unexplained infertility or polycystic ovarian syndrome (PCOS). However, more recent research has not confirmed these claims. Additionally, black cohosh may aid in menstrual cycle regulation for those undergoing fertility treatments, but further studies are necessary. In a 3-month study involving 244 postmenopausal women, a daily dose of 40 mg of black cohosh resulted in a significant reduction in uterine fibroid size by up to 30%. While some anecdotal claims suggest its effectiveness for premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD), there is insufficient scientific evidence to support these uses. [14]

4. Chasteberry (*Vitex agnus-castus*): Regulates menstrual cycles. Reduces symptoms of PMS and menopause, Supports progesterone production. Vitex agnus-castus L. (chaste tree) is widely used as an herbal treatment for female reproductive conditions. A systematic review analyzed 13 randomized controlled trials to evaluate its efficacy and safety. Eight trials focused on premenstrual syndrome (PMS), with most showing Vitex to be more effective than placebo, pyridoxine, or magnesium oxide. In two studies on premenstrual dysphoric disorder (PMDD), Vitex was comparable to fluoxetine in one trial, while fluoxetine was more effective in the other. For latent hyperprolactinaemia, Vitex reduced prolactin levels and improved symptoms, with results comparable to bromocriptine. Adverse events were mild and infrequent. While the quality of studies varied, the findings suggest that Vitex may benefit women with PMS, PMDD, and hyperprolactinaemia, though further research is recommended. [15]

Besides above many herbal plants shows benefit on women's health. Table 1 provides a detailed overview of various medicinal plants and their uses, specifically focusing on women's health.

Table 1: Medicinal Plants for Women's Health with Their Uses, Reported Mechanisms, and Proposed Phytochemicals

Latin Name	Common Name	Indian Common Name	Use	Reported Mechanism	Proposed Phytochemical
Vaccinium macrocarpon	Cranberry	क्रैनबेरी, करौंदा (Cranberry)	UTI	Bacterial adhesion	Proanthocyanidins
Actaea/Cimicifuga racemosa	Black Cohosh	कालमेघ (Kalmegh)	Menopause	Serotonin	N-methylserotonin
Linum usitatissimum	Flaxseed	अलसी (Alsi)	Menopausea	Estrogen	Enterodiol/lenterolactone
Valeriana officinalis	Valerian	जटामांसी (Jatamansi)	Menopause/ PMS	Serotonin	Valerenic acid
Zingiber officinale	Ginger	अदरक (Adrak)	Nausea/PMS	Prokinetic	Gingerols/Shogaols
Silybum marianum	Milk Thistle	दूध थीस्ल (Doodh Thistle)	Lactation	Prolactin/Estrogen	Silybin B
Epimedium species	Horny Goat Weed	हर्बल पत्तियां (Herbal Patteyan)	Menopause/ PMS	Estrogen	Icaritin -> Desmethylicaritin
Lepidium meyenii	Maca	माका (Maka)	Menopause	Estrogen	Phytosterols
Trigonella foenum-graecum	Fenugreek	मेथी (Methi)	Lactation	Estrogen	Diosgenin, Apigenin, Luteolin
Glycine max	Soy	सोयाबीन (Soyabean)	Menopause/ Bone Health	Estrogen	Genistein, Daidzein -> Equol
Trifolium pratense	Red Clover	लाल तिपतिया (Lal Tipatiya)	Menopause/ Bone Health	Estrogen	Biochanin A -> Genistein

Pueraria lobata	Kudzu	कुडज़ू (Kudzu)	Menopause	Estrogen	Puerarin -> Daidzein
Eriosema laurentii	Guinea-Bissau	गिनी बिसाउ (Guinea Bissau)	Menopause	Estrogen	Lupinalbin A
Oenothera biennis	Evening Primrose	पीतसेवती (Sandhya Primrose)	Menopause/ PMS	Estrogen	γ-Linolenic Acid
Angelica sinensis	Dong Quai	डोंग क्वाई (Dong Quai)	Menopause/ PMS	SERM/Unknown	Ligustilide
Arctostaphylos uva-ursi	Bearberry	बेयरबेरी (Bearberry)	UTI	Antibacterial	Arbutin
Dioscorea villosa	Wild Yam	वनयाम (Van Yam)	Menopause/ PMS	Estrogen	Diosgenin
Glycyrrhiza species	Licorice	मुलैठी (Mulethi)	Menopause	Estrogen	Liquiritigenin
Humulus lupulus	Hops	हॉप्स (Hops)	Menopause	Estrogen	Xanthohumol -> 8-PN
Medicago sativa	Alfalfa	अल्फाल्फा (Alfalfa)	Menopause	Estrogen	Coumestrol
Rheum rhaponticum	Rhubarb	रेवंदचीनी (Revand Chini)	Menopause	Estrogen	Piceatannol
Vitex agnus-castus	Chasteberry	निरबंध फल (Nirbandh Phal)	Menopause/ PMS	CNS/Estrogen	Apigenin/Penduletin
Viburnum opulus/prunifolium	Cramp Bark/Black Haw	क्रैम्प बार्क (Cramp Bark)	PMS	Antispasmodic	Scopoletin

Lifestyle Tips for Hormonal Balance

In addition to herbal remedies, adopting a healthy lifestyle can significantly improve hormonal balance. Consider the following tips:

- Maintain a balanced diet rich in whole foods, fruits, and vegetables.
- Engage in regular physical activity.
- Manage stress through yoga, meditation, or breathing exercises.
- Get adequate sleep.
- Stay hydrated.
- Avoid excessive caffeine, alcohol, and processed foods.

Conclusion:

Hormonal imbalance in females is a prevalent and often challenging condition that can significantly affect physical, emotional, and mental well-being. Understanding the underlying causes, including factors such as PCOS, menopause, stress, thyroid disorders, and lifestyle choices, is crucial for effective management. Recognizing symptoms early and seeking appropriate medical advice can prevent further complications and improve quality of life.

Herbal remedies have shown promise as natural alternatives to conventional treatments. Adaptogenic and hormone-regulating herbs like Ashwagandha, Shatavari, Black Cohosh, and Chasteberry offer relief from symptoms by restoring hormonal balance. Additionally, various medicinal plants with phytochemical properties contribute to hormonal regulation and support women's health through different life stages.

Incorporating healthy lifestyle practices, such as maintaining a balanced diet, engaging in regular physical activity, managing stress, and ensuring adequate sleep, further enhances hormonal equilibrium. While herbal remedies provide a complementary approach, it is essential to consult with a healthcare provider before initiating any treatment, especially for individuals with pre-existing conditions or those taking medications.

Ultimately, a holistic approach that combines medical guidance, herbal interventions, and lifestyle modifications can effectively manage hormonal imbalances in females, promoting overall well-being and long-term health.

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ENSURING QUALITY IN THE PHARMACEUTICAL AREA: A COMPREHENSIVE REVIEW

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Abstract:

The study's objectives are to: Emphasise the most crucial quality standards and procedures in the pharmaceutical sector. To make it easier for future academics who want to go further into these standards and methods, arrange them into a handbook. Design: A survey of 102 papers was carried out; 56 of these publications explicitly addressed pharmaceutical quality, while 46 addressed general quality procedures. After those sources' material was examined, the following themes emerged: a. Research theme 1: Pharmaceutical quality guidelines. The second research subject is general procedures that have been used recently in the pharmaceutical sector. Primary outcome measures: In the study theme I, the WHO, FDA, EU, and ICH recommendations were identified and examined. Results: Upon examining the previously highlighted guidelines and the widely used practices in the pharmaceutical industry, it was observed that while there are many papers and articles explaining general guidelines and practices, there aren't many that describe their application, including case studies of pharmaceutical factories using them and their significance. Conclusions: More attention should be paid to the applicability and importance of guidelines and practices in the literature. To demonstrate the viability of such procedures, new case studies have to be conducted.

Keywords: Quality, QMS, Pharmaceutical industry

Introduction:

A QMS is a collection of methods and techniques that enhance the product quality.

The industry and company-specific regulatory requirements must be included in the QMS. ICH Q10 and ISO 9001:2015 are two significant quality standards and recommendations in the pharmaceutical business.[1]

The pharmaceutical industry's definition of quality, the Pharmaceutical QMS, A some of its components and specifications, and the function of QMS will all be covered in this chapter.

What Qualities Mean in the Pharmaceutical Sector

In the pharmaceutical area, Product quality is the extent to which a medicinal excipient or product fulfils its including the drug's identification, potency, and purity are included in this description.[2-3]

A drug's quality is essential to both patient safety and successful therapy. Patients may suffer if a medication is tainted or not pure.

In a similar vein, a medication may not work to treat the ailment for which it was prescribed if it lacks sufficient potency.

Pharmaceutical products must fulfil regulatory requirements before being approved for human use. As a result, a PQS comprises of every operation in a system that contributes in ensuring quality throughout the lifecycle of a pharmaceutical product.[4-5]

What is Pharmaceutical QMS?[6-9]

A pharmaceutical QMS, is a comprehensive collection of rules, standards, and procedures designed to ensure and maintain consistent, superior quality in the manufacture of pharmaceutical products.

The pharmaceutical sectors unique requirements Including any relevant regulatory requirements included the QMS.

Pharmaceutical firms may reduce risks, enhance customer happiness, and expedite quality procedures with the support of a robust PQS that conforms with applicable standards. The pharmaceutical QMS consists of numerous methods, including as: In addition to others, they include audit management, deviation management, document management, change control, training management, CAPA management.

The QMS system prioritises QMS to document all issues and their resolutions and use monitoring methods to prevent quality variations, such as quality assurance. For additional information, see our guide to the Quality Management System (QMS). Simpler QMS helps businesses consolidate all quality procedures in a single solution by offering QMS software for the pharmaceutical sector. Documents, modifications, CAPAs, suppliers, equipment, training, audits, deviations, and a lot more are all simple to handle.

Relevant Standards and Regulations for Pharmaceutical QMS[10-14]

The establishment and observance of the QMS are mandated by the pharmaceutical industry. To ensure consistent and high-quality products, businesses must implement a QMS that aligns with the applicable requirements.

The business must abide by all applicable rules and regulations that change based on a number of variables, such as the target market, and geographic area. Below is a description of some of the most prevalent guidelines and standards that apply to pharmaceutical QMS.

International Organization for Standardization (ISO)[15]

A worldwide organisation called the worldwide Organisation for Standardisation (ISO) creates standards for a number of sectors, including the pharmaceutical industry. ISO 9001:2005 was the former standard for Quality Management Systems (QMS), while ISO 9001:2015 is the current one.

This standard is used by some pharmaceutical businesses to enhance performance and guarantee that their QMS meets quality standards.[16]

Scheme for Pharmaceutical Inspection Cooperation

The Pharmaceutical Inspection Co-operation Scheme (PIC/S) is a non-binding, informal cooperative agreement amongst international regulatory bodies in the field of GMP of medicines intended for human or veterinary use.

A pharmaceutical quality management system is one of the criteria for pharmaceutical enterprises that are outlined in the publications. Regarding good manufacturing practices, the PIC/S GMP's criteria are the same as those of the EudraLex Volume 4 GMP.[18-19]

PIC/S GMP rules give pharmaceutical firms a framework for manufacturing procedures, control systems, and quality management systems to guarantee that their products are high-quality, safe, and consistent.

The guidelines address a number of GMP adherence topics, including:

- Documentation
- Self-inspection
- Personnel
- Quality control
- Premises and equipment
- Complaints and product recall

Current Good Manufacturing Practice (cGMP)[19-22]

The FDA, The United States federal agency that oversees the safe manufacture of pharmaceuticals, enforces the cGMP standards. Quantity, quality, and purpose must all be taken into account in order for the product to be safe for human consumption. In order to avoid product confusion, the output needs to be free of contaminants. The FDA conducts cGMP compliance inspections of pharmaceutical producers. Product recalls may result from noncompliance with cGMP regulations if an investigation determines that they are warranted. Seizures, penalties, and jail time may follow noncompliance with the FDA's following instructions.

FDA 21 CFR Part 210

A guarantee purity, quality, and safety of the product, the 21 CFR Part 210 regulation lays out the lowest standards for GMP for medication production, methods, packaging, and finish goods. Pharmaceutical businesses who advertise and market their products in the United States are expected to follow this guideline.[23]

FDA 21 CFR Part 211[24-25]

The GMP regulations for finished medications are described in 21 CFR Part 211.

The following topics are covered by this regulation:

- Buildings and facilities;
- Ventilation and air filtration system;
- Product labelling;
- Quality control;
- Personnel qualifications and skills;
- Warehouse needs.

21 CFR Part 11

The creation, upkeep, and storage of electronic documents are governed by 21 CFR Part 11. It also explains how electronic signatures are used by the appropriate supervisors to approve these papers. Go through our page on 21 CFR Part 11 requirements to find out more about this rule.

EU GMP Annex 11[26-28]

For computerised systems, acceptable manufacturing practices are outlined in EU GMP Annex 11. It is crucial to make sure that process control, quality assurance, and product quality are not jeopardised when a computerised system replaces a human process. Furthermore, the process's total risk shouldn't rise.

Guidelines on the following subjects are also included:

- Data Storage
- Security
- Electronic Signature
- Batch release
- Personnel
- Risk Management

ISPE GAMP5

The ISPE created the GAMP5 as a standard for computerised systems. In order to guarantee that computerised systems are efficient, of superior quality, and in compliance with relevant legislation, as well as appropriate for their intended purpose, GAMP aims to offer an affordable framework of best practices. An eQMS system designed specifically for the pharmaceutical sector is offered by Simpler-QMS. The system facilitates adherence to PIC/S GMP, EU, ICH, ISO, and cGMP regulations. You may save time and concentrate on activities that provide value because Additionally, it is verified in compliance is re-validated with ISPE GAMP5 whenever new versions or standards are released upgrades. Our software ensures adherence to electronic signatures, electronic recordkeeping, and computerised manufacture of systems rules by adhering to EU GMP Annex 11 and FDA 21 CFR Part 11.

Pharmaceutical QMS Components[29-31]

There are several QMS and components procedures that make up a pharmaceutical QMS. No "fixed" exists. Depending based on the product's requirements and the intended market, the pharmaceutical producer can incorporate various procedures. Additionally, this chapter will give instances of how QMS software may streamline and improve procedures.

A few elements of the product lifecycle in ICH Q10 are as follows:

- Product quality and process performance monitoring system;
- Corrective action and preventative action (CAPA) system;
- Change management system;
- Management evaluation of product quality and process performance.

System for Monitoring PP and PQ[32-33]

One essential component of a business's endeavours to provide a consistent and superior product is the system for monitoring product performance and processes. It

illustrates the business's dedication to maintaining control and resources. Four phases of the product lifecycle are subject to process performance and product quality monitoring: Pharmaceutical development: The data acquired about the product and process throughout development and monitoring may be used to create a production control plan.

- Technology transfer: Monitoring during scale-up operations demonstrates process performance and successful integration into production.
- Commercial manufacturing: A robust system for monitoring process performance and product quality must be implemented in order to provide continuous control and identify opportunities for improvement.
- Product discontinuation: Stability testing and monitoring should continue until the studies are completed, even if production stops.

Techniques for risk assessment can be applied to identify process stage flaws. Analysing specified parameters may also be done using specialised tools and feedback. To find errors or malfunctions, the Quality Department and production staff randomly inspect the inspection system. Fortunately, Simpler-QMS's Deviation Management Software automates data gathering, directing, and past-due activity notifications. This makes it much easier to keep an eye on the safety and performance of your processes and products.

CAPA System[34]

CAPA is a technique for identifying the underlying causes of issues and preventing them from occurring again. A CAPA triggered in response to deviations, complaints, audit results, and other problems. After deciding to escalate to a CAPA, the CAPA form is filled out. Although every company may have a different CAPA form and structure, in general, it contains the following information:

The division where the process flaw is found; the issue detail and its consequences; the effect of the error on the process or product; the corrective action to fix the problem; the preventive action to stop the issue from happening again; the deadline for putting the corrective and preventive actions into place; and the next review date to evaluate the efficacy of the corrective action.

The CAPA is resubmitted to the appropriate parties for consent after the implementation of the required corrective and preventative measures. After approval, The CAPA has been closed and documented. Pharmaceutical research, knowledge transfer, commercial manufacturing, and product development are just a few of the product stages

where the CAPA method is utilised. It places a strong focus on feedback, feedforward, continuous improvement, and regular evaluations of its effectiveness discontinuance.

CAPA Management Software makes it simple to automate the procedure shown in the aforementioned example. You may better manage corrective and preventative actions by automating routing, data collection, follow-ups, alerts, escalation of past-due operations. You may read our post on what CAPA is in the pharmaceutical sector to have a better understanding of how this procedure operates.

Change Management System[35]

A regulate and oversee any modifications procedures, made to documents and pharmaceutical businesses need to possess a system for change control and management.. The change management system may be used at many phases of the product lifecycle.:

- **Pharmaceutical Research and Development:** Changes made during the process should be documented, and the formality of the change management approach should match the stage of pharmaceutical development.
- **Technology Transfer:** It's critical to monitor and document process changes made during technology transfer activities..
- **Commercial Manufacturing:** The supervision of the quality unit ought to provide adequate scientific research and risk-based appraisal for a change.
- **Product Discontinuation:** Any modifications made after the product has been discontinued should still adhere to a good change management process.

Thankfully, the change management process is considerably simplified with Simpler-QMS's Change Management Software. In addition to creating and assigning particular tasks that will be electronically signed upon approval, it enables you to automatically document the change process.

Assessment of Process Efficiency and Product Quality by Management[36]

A comprehensive evaluation of the whole quality management system's efficacy is called a management review. During this process, the product, documentation, processes, and procedures are all assessed. Determining if the QMS is performing as the business expected and identifying areas that need improvement are the goals of the management review.

The following might be included in the management review:

- Quality commitment;
- Customer complaints;

- Nonconformances;
- CAPA review;
- Audit results;
- Process performance;
- Any outstanding issues or follow-up from an earlier management review
  A management review is necessary at every step of the product lifecycle.

During pharmaceutical development, management reviews should evaluate the product's and process design's appropriateness. A Management reviews should be conducted throughout technology transfer to make sure the process and product designs are appropriate for large-scale production. To support continual improvement in commercial production, a systematic management review system must be used. Management reviews after product discontinuance should also include a number of topics, such as quality complaints and product stability.

All things considered, management review plays a critical role in guaranteeing the consistency and quality of pharmaceutical goods during their development and termination. Simpler-QMS facilitates management reviews by offering a methodical way to assess how well a pharmaceutical company's operations and goods are performing.

Management of staff training; calibration and maintenance of equipment; management of suppliers; and management of audits

Training Management

Every employee whose actions might affect the quality of the product should get training from the pharmaceutical company. In addition to specialised training catered to their work responsibilities, personnel should get training on the theory and application of the Pharmaceutical QMS Practice. It is necessary to provide ongoing training and conduct regular reviews. You may identify skill shortages by managing staff training, lead learning exercises, and keep thorough training records that satisfy legal requirements. Businesses may benefit from a number of features that the Simpler-QMS training management module offers to support the training process, such as automated email alerts, tracking of training progress, assessments of training effectiveness, and more.

Equipment Calibration and Maintenance

Equipment calibration and maintenance are crucial to ensuring the safety and quality of the products produced in the pharmaceutical industry. The objective is to ensure that the equipment used in the production process is functioning properly and delivering

accurate and dependable results. Pharmaceutical manufacturing equipment needs to be maintained, cleaned, and calibrated in accordance with established procedures. To prevent contamination or malfunctions that might jeopardise the drug product's identity, safety, strength, quality, or purity, procedures must be followed.

Supplier Management[36]

A dependable supply chain, reduced risk of product quality problems, and regulatory compliance for pharmaceutical businesses in controlling materials used in manufacturing are all made possible by effective supplier management. Companies must have a documented procedure in place for selecting, screening, and monitoring raw material, packaging, and other suppliers that are crucial to the quality of their products. The supplier management process should include a risk-based approach that considers the potential impacts on the quality and safety of the finished product. To help speed up all supplier-related operations, Simpler-QMS offers comprehensive supplier management tools, including the ability to certify suppliers, maintain Approved Supplier Lists (ASL), and track their performance over time.

Audit Management

One crucial element of the GMP criteria is self-inspection. Internal audits are a good way for businesses to keep an eye on how GMP applied and followed, as well to suggest any required remedial actions. The company's designated competent individuals should carry out internal audits in a thorough manner. Furthermore, independent audits conducted by outside specialists might be helpful in confirming adherence to GMP regulations. All facets of manufacturing and quality control activities, including buildings, machinery, staff, supplies, production, testing, and documentation, should be included in the audit plan. Any pertinent supplier-related procedures should also be included. Additionally, Simpler-QMS offers resources for efficiently handling internal audits through the early detection and resolution of any quality problems.

Role of Pharmaceutical Quality Management Software

If businesses have the necessary resources to manage the manual paperwork, they can use manual solutions to manage their QMS. However, because of the numerous interconnected procedures and extensive paperwork needed, pharmaceutical quality systems can be complicated. More output at lower costs and in less time is now possible thanks to the digital revolution in the medication manufacturing sector. Regular tasks may be handled by digital technologies without sacrificing the quality of the final result, freeing

up business owners to concentrate more on innovation and new opportunities. Digital technologies like warehouse management systems (WMS) and computerised maintenance management systems (CMMS) are already used in the pharmaceutical sector. These tools have a track record of successfully streamlining procedures. A growing number of businesses have chosen to use eQMS in recent years. Improved processes, lower expenses and time, cloud-based document storage, automatic alerts, and more are all advantages of a complete e-QMS. More output at lower costs and in less time is now possible thanks to the digital revolution in the medication manufacturing sector. Regular tasks may be handled by digital technologies without sacrificing the quality of the final result, freeing up business owners to concentrate more on innovation and new opportunities. Digital technologies like warehouse management systems (WMS) and computerised maintenance management systems (CMMS) are already used in the pharmaceutical sector. These tools have a track record of successfully streamlining procedures. A growing number of businesses have chosen to use eQMS in recent years. Improved processes, lower expenses and time, cloud-based document storage, automatic alerts, and more are all advantages of a complete e-QMS.

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HUMAN MICROBIOME AS A HEALTH TOOL: SCOPES FOR RESEARCH

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Abstract:

The human microbiome is seen as a rather complicated system of microorganisms living inside and outside of the human body, which plays a pivotal role in controlling health and homeostasis. This comprises bacteria, viruses, fungi, and archaea in a well-organized, symbiotic relationship with cells of eukaryotic origin, which help to modulate such key biological processes as digestion, immune response, and synthesis of important nutrients. A well-balanced microbiome acts to promote a healthy condition in a very different way: imbalances in it have been reported to be connected with several diseases, including inflammatory bowel disease, diabetes, obesity, cardiovascular conditions, and neurological disorders. The composition of the microbiome is shaped by certain environmental factors, which include diet, antibiotics, and lifestyle, thus possibly determining the diseases from which they are most susceptible. Microbiome research now raises the possibility of the development of personalized medicine through manipulation of the microbiome to find new treatments, like the use of probiotics, prebiotics, and fecal microbiota transplantation. The knowledge that the microbiome interacts with human health has transformed the approach to the prevention and treatment of diseases, stressing the essential role that microbial balance should have for total well-being.

Keywords: Microbiome, Human Health, Probiotics, Prebiotics

Introduction:

The human stomach, skin, mouth, and respiratory system are all colonized by billions of bacteria, viruses, fungus, and other microorganisms that make up the complex and ever-changing human microbiome [1]. By aiding in food digestion, vitamin synthesis, immune system regulation, and defense against harmful bacteria, microorganisms are essential to maintaining an individual's health. Because it is in charge of the digestion of complex food molecules, the manufacture of vital nutrients like short-chain fatty acids, and even the control of metabolism, the gut microbiome in particular is one of the most studied

topics. The immune system and the microbiome are closely related; the former helps to train and control immune responses, protecting against infection while preventing overreactions that may lead to autoimmune disease [2]. Furthermore, recent research suggests that the microbiome may have a significant role in mental health, with changes in gut flora linked to anxiety, depression, and possibly autism spectrum disorders through the gut-brain axis. A person's diet, genetics, environment, and use of antibiotics can all affect the microbiome's diversity and composition. Numerous health issues, including obesity, heart disease, diabetes, and inflammatory bowel disease, have also been linked to disruptions in this microbial balance, also known as dysbiosis [3]. Probiotics, prebiotics, and microbial-driven treatments like FMT, which show great promise as a treatment for specific imbalances and related diseases of microbes, are among the new opportunities brought about by our growing understanding of the microbiome. In the end, the human microbiota is a significant and complex component of human health that is constantly being revealed for its role in maintaining general health as well as in the prevention and management of disease [4].

Human Microbiome and Health:

The human microbiome has a critical role in preserving well-being through enabling diverse physiological functions and immunity from diseases. It controls critical functions such as digestion, the function of the immune system, and even psychological status. Within the gut, for example, favorable bacteria enable nutrient breakdown from consumed food, provide essential nutrients, and help sustain the lining integrity of the intestinal wall so that pathogenic substances are kept away from entering into the circulatory system [5]. The microbiome also educates the immune system to have an optimal immune response that protects against infection without causing inflammation and autoimmune responses. Dysbiosis, which occurs due to imbalances in the microbiome, is responsible for contributing to various health disorders, such as gastrointestinal disorders like IBS, metabolic disorders like obesity and diabetes, and even neurological disorders like depression and anxiety via the gut-brain axis [6]. New research is investigating means of restoring a healthy microbiome via diet, probiotics, and other treatments, providing new hope for the prevention of disease and tailored treatments. Ultimately, a balanced microbiome is essential for overall health, affecting both physical and mental well-being.

Personalized Medicine and Microbiome:

Personalized medicine, which is also customizing the treatments for disease with a person's individualized genetic, environmental, and lifestyle characteristics, is increasingly crossing into microbiome study [7]. The characteristic makeup of everyone's microbiome can impact what they are going to do against diseases, on drugs, or with treatments. For instance, differences in intestinal bacteria can vary how effectively one person processes medicine, perhaps how effective or detrimental it is for them. By examining the microbiome of an individual, physicians are able to more accurately forecast disease susceptibility, tailor diet advice, and even choose better treatments [8]. In addition, treatment with microbiome products, such as probiotics, prebiotics, and fecal microbiota transplantation (FMT), is being developed as a promising personalized therapeutic tool for diseases including inflammatory bowel disease, obesity, and even neuropsychiatric illnesses [9]. With the progression of our knowledge of the microbiome, personalized medicine will provide more effective, targeted, and individualized care, maximizing health benefits while avoiding side effects.

Probiotics and Prebiotics:

Probiotics and prebiotics are both necessary to sustain a healthy and well-balanced microbiome. Probiotics are live, non-pathogenic microorganisms, usually bacteria or yeast, that, when ingested in proper quantities, may provide health benefits, with a focus on the gut. Probiotics restore the balance of the microbiome by repopulating helpful microbes, most especially after disturbance such as the use of antibiotics. Popular sources of probiotics are fermented foods such as yogurt, kefir, sauerkraut, and kimchi [10]. Prebiotics, however, are indigestible food substances, typically fibers, which promote the growth and activity of good bacteria in the gut. Garlic, onions, bananas, and whole grains are some foods that contain prebiotics. Probiotics and prebiotics act synergistically together, with prebiotics acting as a source of food for the good probiotics, allowing them to grow and sustain a healthy microbiome [11]. Their incorporation into the diet can enhance the health of the digestive system, boost immune system function, and possibly lower the risk of disease states such as irritable bowel syndrome, obesity, and even some mental disorders, highlighting the significance of balanced and diverse gut microbiota.

Microbiome Research: Current Status

Microbiome research has sparked excitement and seen quick progress broadening our grasp of human health. Scientists now delve into the complex links between the

microbiome and various bodily functions, from digestion to immunity and even mental well-being. Recent studies have shed light on how microbes play key roles in keeping the immune system in check, helping break down food making vitamins, and fending off harmful bugs [12]. Yet, we still have much to learn about how the microbiome interacts with genes, surroundings, and lifestyle choices to shape health outcomes. Cutting-edge tools like metagenomics now allow researchers to explore the vast world of microbes by looking at genetic material from whole microbial communities, without having to grow each microbe on its own. More and more, studies focus on figuring out how an unbalanced microbiome, or dysbiosis, might lead to health issues like obesity, diabetes, gut inflammation, and brain disorders [13]. While there's still a lot to uncover ongoing research is opening doors to new microbiome-based treatments. These include probiotics, prebiotics, and even fecal microbiota transplants (FMT), which show promise in treating various conditions. As this field grows, it offers thrilling possibilities for tailored medicine and fresh more effective ways to boost health and stop diseases before they start [14].

Microbiome as Health Tool: Challenges and Solutions:

The application of the microbiome as a therapeutic tool is full of promise, but it also has a number of challenges that must be overcome before it can be fully adopted in clinical practice. One of the biggest challenges is the variability and complexity of the microbiome itself; every person's microbiome is different, depending on genetics, diet, environment, and use of medications. This heterogeneity makes it challenging to develop universal treatments or diagnostic tests based on microbiome profiles alone [15]. Moreover, the science of the microbiome is continually evolving, and numerous causal associations between microbial communities and particular diseases remain poorly understood. Another challenge is the absence of standardized testing and interpretation methods for microbiomes, which makes it challenging for clinicians to integrate microbiome information into decision-making [16]. In spite of these challenges, scientists are finding solutions, ranging from establishing more accurate and individualized microbiome-based treatments, like custom probiotics or diets that are designed to meet a person's unique microbial requirements, to furthering metagenomics and bioinformatics to better understand and interpret microbiome information, and continuing clinical trials to define the success of microbiome treatments. With these issues overcome, the microbiome has the potential to be a useful tool in disease treatment, preventative healthcare, and personalized medicine.

Conclusion and Future Perspectives:

In summary, the human microbiome is an integral and active part of our overall wellness that affects digestion and immune function through to mental wellness and disease protection. As our understanding of the microbiome grows, it's becoming increasingly obvious that keeping microbial balance is a key to being well, but upsetting this harmony can contribute to a wide range of ailments. Personalized medicine, probiotics, prebiotics, and microbiome-based treatments hold tremendous potential to enhance health outcomes and provide more specific treatments [17-18]. Issues persist in deciphering the intricacies of the microbiome and bringing the insights into accessible applications. In spite of these challenges, the microbiome is an arena of medical science that holds the key to transforming the delivery of healthcare with personalized, effective prevention and treatment of disease. The future of microbiome research is promising with the potential to transform healthcare and medicine. The more we understand the microbiome, the better we may get at preventing, diagnosing, and treating all sorts of disease. A possible area is personalized microbiome-based treatments, where a patient's treatments such as probiotics, prebiotics, and dietary regimen are personalized to their own distinctive microbial composition to enhance their efficacy and reduce their side effects. Also, microbiome-based diagnostics would become mainstream, enabling quicker diagnosis of diseases, such as metabolic disorders, gastrointestinal diseases, and even some cancers, by detecting microbial signatures that are linked to these illnesses.The gut-brain axis, or the intersection of the gut microbiome with mental health, may bring to bear new mental health treatments through the manipulation of the microbiome by diet or microbiota-therapy interventions, for disorders including anxiety, depression, and autism spectrum disorder. In addition, the growth in metagenomics and artificial intelligence will enhance the capacities to explore the intricate dynamics among the microbiome, to arrive at more efficacious and focused therapeutic strategies [19-20].Yet, hurdles exist, such as overcoming the high individual variability of the microbiome, the development of standard testing and treatment protocols, and the regulatory roadblocks for therapies based on the microbiome. As science moves forward and these hurdles are breached, the microbiome will emerge as a keystone of personalized medicine, providing innovative solutions that maximize health, forestall disease, and enhance general well-being.

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FERMENTED BIOPLASTIC USING SUGARCANE WASTE

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Abstract:

The environmental degradation caused by conventional plastics necessitates the exploration of sustainable alternatives. Fermented bioplastics, particularly those derived from sugarcane waste like bagasse, offer an eco-friendly solution. This chapter delves into the complete lifecycle of bioplastic production, from the treatment of raw sugarcane waste to its conversion into useful polymeric materials. By addressing key challenges and showcasing various applications, this study highlights the potential of bioplastics to replace traditional plastics across multiple industries, including packaging, agriculture, and healthcare. Future advancements and innovations are also discussed, emphasizing the significance of this field in promoting a circular economy. This chapter investigates the potential of sugarcane-based bioplastics as a sustainable solution to mitigate environmental issues caused by conventional plastics. By leveraging sugarcane juice as a renewable raw material, advanced fermentation technologies enable the production of eco-friendly biopolymers such as polylactic acid (PLA). These bioplastics exhibit remarkable properties, including biodegradability, reduced greenhouse gas emissions, and suitability for diverse applications in packaging, automotive, medical, and agricultural industries. Despite the significant advantages, challenges like high production

Keywords: Bioplastics, Sustainable Development, Sugarcane Bagasse, Fermentation, Polyhydroxyalkanoates (Phas), Environmental Sustainability, Lignocellulosic Biomass, Renewable Resources.

Introduction:

Plastic waste has become a global crisis, with its impact evident in polluted oceans, disrupted ecosystems, and overflowing landfills. The reliance on petroleum-based plastics exacerbates this issue due to their non-biodegradable nature. Bioplastics, derived from renewable resources, emerge as a promising alternative. Among these, sugarcane bagasse—a byproduct of sugar extraction—stands out for its abundance, low cost, and rich composition of lignocellulosic materials. This chapter explores the scientific and industrial

aspects of converting sugarcane bagasse into biodegradable plastics, focusing on microbial fermentation processes, innovative technologies, and real-world applications. Bioplastics are derived from renewable resources such as plant starch, vegetable oils, or microorganisms. Among these, sugarcane—a widely cultivated agricultural crop—has garnered significant attention due to its high yield and rich sucrose content. Sugarcane not only serves as a sustainable feedstock for bioplastic production but also aligns with the global push towards a circular economy, where waste and by-products are repurposed into valuable materials. The primary bioplastics derived from sugarcane are Polylactic Acid (PLA) and Polyhydroxyalkanoates (PHAs). These polymers are biodegradable and offer physical and mechanical properties comparable to conventional plastics, making them suitable for a wide range of applications.

Fig. 1: Sugarcane

Fig. 2: Sugarcane Baggase

The production process of sugarcane-based bioplastics typically involves fermentation, wherein sugarcane juice or molasses is utilized as a substrate for microbial activity. The fermentation process converts the sugars into lactic acid or other precursors, which are then polymerized into bioplastics. Additionally, the use of sugarcane in bioplastic production offers several economic and environmental benefits. Sugarcane is a fast-growing crop with the ability to sequester significant amounts of carbon dioxide during its growth. Moreover, the by-products of sugarcane processing, such as bagasse and molasses, can be effectively utilized in energy generation and fermentation processes, ensuring minimal waste. This chapter explores the production of bioplastics using sugarcane as a primary feedstock. It delves into the upstream (fermentation) and downstream (purification) processes, highlights the advantages of sugarcane-derived bioplastics over petrochemical counterparts, and discusses the applications and future potential of this

innovative material. By integrating sustainability into material science, sugarcane-based bioplastics pave the way for a greener, more sustainable future.

Table 1: Global Plastic Pollution Statistics

Category	Statistics
Annual Plastic Production	Over 300 million tons globally
Plastic Waste Mismanagement	Approximately 32% of all plastic produced
Decomposition Time	500-1,000 years for conventional plastics
Marine Impact	8 million tons of plastic enter oceans annually

What are Bioplastics?

Bioplastics are materials derived from renewable resources such as plants, algae, or microorganisms. Unlike conventional plastics, bioplastics are biodegradable or compostable, breaking down into natural elements under specific conditions. Their production also results in a lower carbon footprint, aligning with global sustainability goals.

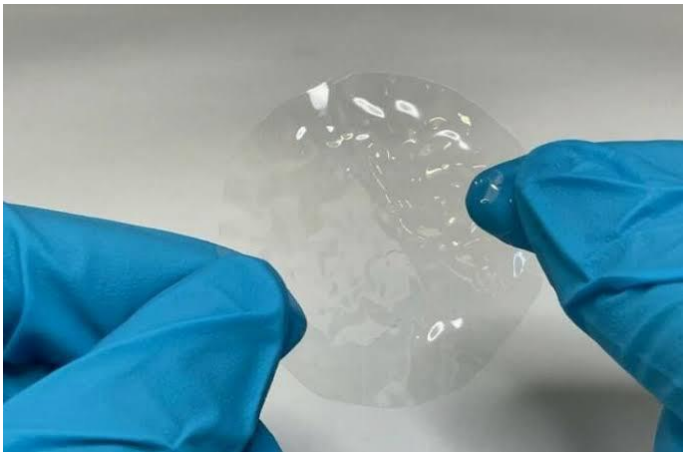


Fig. 3: Bioplastic made from sugarcane Baggase

Significance of Sugarcane in Bioplastic Production

Sugarcane has emerged as one of the most promising feedstocks for bioplastic production. It is widely cultivated in tropical and subtropical regions and boasts several advantages:

- High yield: Sugarcane provides a rich source of sucrose, which serves as a fermentable sugar for bioplastic production.
- Fast growth cycle: Unlike fossil fuels, sugarcane is a renewable resource that can be harvested multiple times annually.

- By-product utilization: Sugarcane processing generates molasses and bagasse, which can be repurposed for energy production or as substrates in fermentation.

Key Bioplastics Derived from Sugarcane

- Polylactic Acid (PLA): Produced through the microbial fermentation of sugarcanejuice into lactic acid, PLA is widely used in packaging, textiles, and disposable items.
- Polyhydroxyalkanoates (PHAs): These bioplastics are synthesized directly by microorganisms using sugarcane as a carbon source. PHAs are known for their biodegradability and compatibility with various industrial applications.

Advantages of Sugarcane-Based Bioplastics

Using sugarcane as a raw material offers several benefits:

- Sustainability: Sugarcane absorbs CO_2 during its growth, contributing to carbon sequestration.
- Economic viability: Many sugar-producing countries can integrate bioplastic production into their existing agricultural systems.
- Minimal waste: Residual biomass from sugarcane processing can be converted into bioenergy or organic fertilizers.

•Challenges in Scaling Up Production

- Despite their advantages, sugarcane-derived bioplastics face challenges, including:
- High initial investment costs for setting up fermentation and purification facilities.
- Competition with food production for agricultural resources.
- Ensuring consistent quality and scalability for commercial applications.

Scope of the Chapter

This chapter provides an in-depth analysis of the processes involved in sugarcane-based bioplastic production, focusing on upstream (fermentation) and downstream (purification) stages. It also highlights the economic and environmental benefits, discusses potential applications across industries, and explores future trends and technological advancements to enhance scalability and cost-effectiveness.

Background

1. The Plastic Problem

Plastics have become ubiquitous due to their versatility, durability, and cost-effectiveness. However, their non-biodegradable nature poses significant environmental challenges:

- Long decomposition times, often exceeding hundreds of years.
- Accumulation in oceans, causing harm to marine ecosystems.
- Release of microplastics into the environment, affecting both human and animal health.

2. **Bioplastics as a Sustainable Alternative**

Bioplastics, derived from renewable resources, biodegradable, and environmentally friendly. Common types include:

- Polylactic Acid (PLA): Derived from starch-based materials.
- Polyhydroxyalkanoates (PHAs): Produced by microorganisms during fermentation.

Sugarcane Waste: A Valuable Resource

Sugarcane is one of the most widely cultivated crops globally. After juice extraction, sugarcane bagasse—a lignocellulosic material—is left behind. This waste is rich in cellulose, hemicellulose, and lignin, making it a suitable feedstock for bioplastic production.

Materials Required

The production of bioplastics from sugarcane waste involves several key steps, from raw material preparation to polymer synthesis and final product formation.

1. **Sugarcane Bagasse**: A renewable and abundant source of lignocellulose.
2. **Microorganisms**: Strains like Clostridium or Ralstonia eutropha for PHA production.
3. **Enzymes**: Cellulase and amylase for hydrolysis of cellulose into fermentable sugars.
4. **Chemical Reagents**: For pre-treatment (e.g., dilute acid or alkali).
5. **Lab Equipment**: Autoclave, fermenter, centrifuge, and bioplastic molding apparatus.

Production of Bioplastic from Sugarcane Waste

The production of bioplastic from sugarcane bagasse involves intricate steps that ensure the efficient transformation of agricultural waste into valuable polymeric materials. This process can be categorized into upstream processing (USP) and downstream processing (DSP), each playing a pivotal role in ensuring product quality and sustainability.

1. Upstream Processing (USP) -Pre-treatment of Bagasse:

The initial step involves the breakdown of lignocellulosic biomass to release fermentable sugars. Examples of methods include -

-Chemical Pre-treatment:

Using acids or alkalis to disrupt the complex lignin-cellulose bonds.

- Mechanical Pre-treatment:

Grinding and milling to reduce particle size and enhance accessibility.

- Enzymatic Hydrolysis:

Employing enzymes like cellulases to convert cellulose into glucose.

2. Microbial Fermentation

During fermentation, microbes metabolize the sugars derived from pre-treatment into biopolymers. Notable aspects include:

- Microorganisms:

Bacteria such as *Cupriavidus necator* and *Ralstonia eutropha* are widely utilized.

- Conditions:

Optimizing factors like temperature (30–37°C) and pH (6.5–7.0) enhances efficiency. And duration of (48-72) hours .

- Yield Optimization:

Genetic modifications have been introduced to improve polymer production by over 50% in recent studies.

3. Downstream Processing (DSP)

This phase focuses on recovering and purifying the bioplastic from the fermentation medium. Steps include:

- Cell Harvesting:

Using centrifugation or filtration to separate microbial cells.

- Polymer Extraction:

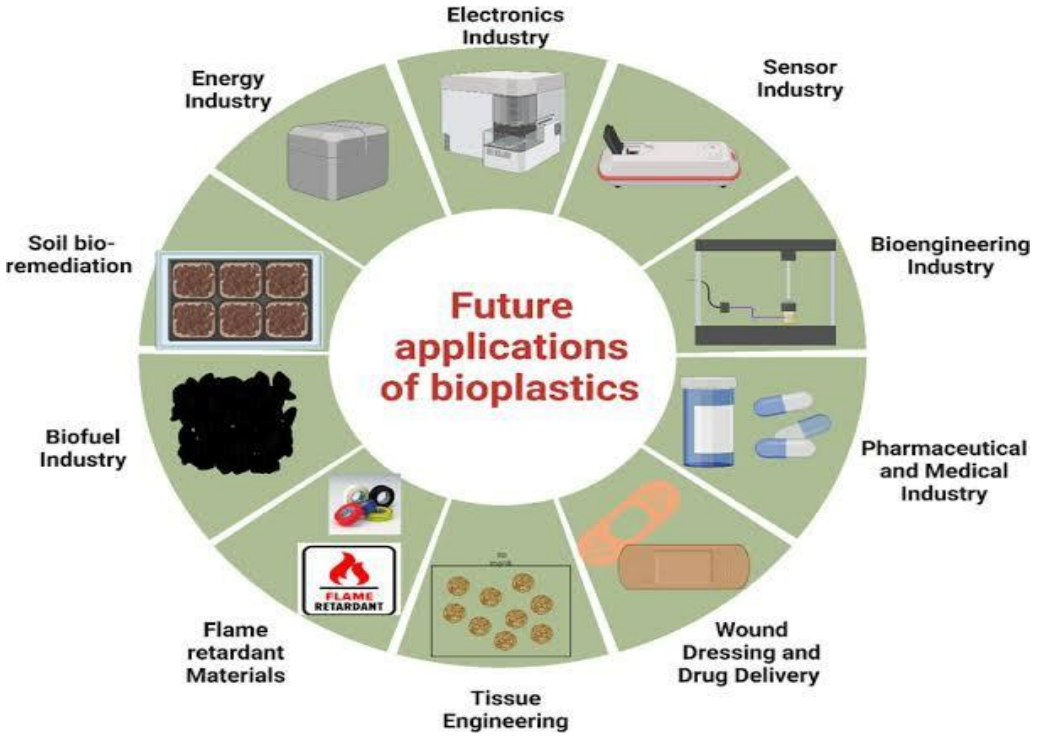
Solvent-based methods, such as chloroform extraction, are commonly employed.

- Purification and Drying:

The biopolymer is precipitated using alcohol and dried for further processing.

Applications of Bioplastics

Bioplastics derived from sugarcane bagasse have gained prominence across diverse sectors due to their biodegradable nature and comparable properties to conventional plastics. Some examples include:



- Packaging:

Used for producing biodegradable bags, wrappers, and food containers.

- Agriculture:

Compostable mulch films and seed trays improve soil health while reducing waste.

- Healthcare:

Applications include biodegradable sutures, implants, and drug delivery systems.

- Consumer Goods:

Production of disposable cutlery, plates, and drinking straws.

Table 2: Comparison Between Conventional Plastics and Bioplastics

Aspect	Conventional Plastics	Bioplastics
Raw Material	Petroleum-based	Renewable resources (e.g., bagasse)
Decomposition Time	500–1,000 years	1–5 years
Cost	Lower	Moderate
Environmental Impact	High carbon footprint	Low carbon footprint

Future Perspectives

The field of bioplastics continues to evolve, with significant advancements expected in the coming years. Key trends include:

- Innovation in Feedstock Utilization:

Exploring alternative agricultural residues as raw materials.

- Enhanced Production Techniques:

Incorporating artificial intelligence and automation in fermentation processes.

- Policy Interventions:

Governments worldwide are implementing policies to promote bioplastic adoption

- Public Awareness:

Educational campaigns are vital in driving consumer preference for sustainable products.

The potential for expanding the use of sugarcane waste-derived bioplastics lies in:

1. Technological Advancements
   -Development of cost-effective and eco-friendly pre-treatment methods.
   -Genetic engineering of microbes for higher polymer yields.
2. Policy and Regulation
   -Government incentives for bio-based products.
   -Implementation of bans on single-use plastics to increase demand for bioplastics.
3. Industrial Scalability
   -Optimization of fermentation processes for large-scale production.
   -Reduction in costs through integrated sugarcane processing facilities.
4. Market Expansion
   -Collaborations with industries to incorporate bioplastics in mainstream production.
   -Consumer education on the benefits of biodegradable plastics.

Results and Discussions :

The results of this study emphasize the viability of using sugarcane waste, specifically bagasse, as a raw material for bioplastic production. The key findings are as follows:

1. Yield and Efficiency

- The efficiency of bioplastic production depends on factors like:
- The pre-treatment method used.

Microbial strain employed.

- Fermentation conditions.

2. Properties of Bioplastic

The bioplastics produced from sugarcane bagasse exhibit the following characteristics:

- Mechanical Properties: High tensile strength and flexibility, comparable to conventional plastics.
- Biodegradability: Complete decomposition within weeks to months in soil or compost.
- Thermal Stability: Suitable for low to moderate-temperature applications.

3. Environmental Benefits

- Reduces dependency on fossil fuels.
- Decreases agricultural waste and associated environmental issues.
- Mitigates plastic pollution through biodegradability.

4. Challenges and Limitations

- High Production Costs: Due to the pre-treatment and fermentation processes.
- Scaling Up: Difficulty in transitioning from laboratory-scale to industrial-scale production.
- Competition with Petrochemical Plastics: Conventional plastics are cheaper and more widely available.

Results:

The results of this study emphasize the viability of using sugarcane waste, specifically bagasse, as a raw material for bioplastic production. The key findings are as follows:

Yield of Bioplastics

- The fermentation of pre-treated sugarcane bagasse resulted in the production of polyhydroxyalkanoates (PHAs), a type of bioplastic.
- The yield ranged from 30% to 40% of the total biomass depending on the pre-treatment method and microbial strain used.
- Enzymatic hydrolysis proved to be the most effective, with a 40% increase in sugar release compared to chemical methods.

Material Properties

- The bioplastics produced were analyzed for mechanical and thermal properties.

- Tensile strength was comparable to that of polyethylene, with an average of 25–30 MPa.
- Thermal degradation occurred at higher temperatures, making it suitable for industrial applications like packaging and consumer goods.

Biodegradability

- The bioplastics degraded completely within 6 months in controlled composting conditions.
- In natural environments like soil and water, degradation time was slightly longer but remained significantly faster than conventional plastics.

Economic Feasibility

The cost of production was analyzed and compared to traditional plastics. The results indicate a 20% higher cost for bioplastics; however, advancements in technology and economies of scale are expected to reduce this difference.

Discussion:

Effectiveness of Sugarcane Bagasse

Sugarcane bagasse emerged as a cost-effective and renewable resource. Its high lignocellulosic content ensures a steady supply of fermentable sugars after pre-treatment. Compared to other agricultural residues like corn stalks or rice husks, sugarcane bagasse demonstrated superior yields due to its lower lignin content.

Microbial Efficiency

- The use of genetically engineered strains of Ralstonia eutropha enhanced bioplastic production.
- By optimizing fermentation conditions such as pH, temperature, and nutrient supply, microbial productivity increased by 25%.

Environmental Impacts

- Life-cycle assessment (LCA) showed that bioplastics from sugarcane bagasse reduced greenhouse gas emissions by 50% compared to petroleum-based plastics.
- The carbon footprint of the production process is largely offset by the renewable nature of the feedstock.

Challenges Identified

- The variability in sugarcane bagasse composition due to seasonal and regional factors affects consistency in bioplastic quality.

- High costs associated with enzymatic hydrolysis and downstream processing remain significant barriers.

5. Economic Impact of Sugarcane-Based Bioplastics

- Job Creation: Boosts employment opportunities in agriculture, biotechnological research, and manufacturing.
- Revenue Generation: Adds value to sugarcane by-products, increasing profitability for farmers and industries.
- Global Market Growth: The bioplastics market is projected to grow at a CAGR of 15% by 2030, with sugarcane-based products being a key driver.

Challenges and Limitations

- Cost Competitiveness: High production costs compared to traditional plastics hinder large-scale adoption.
- Land Use: Allocating agricultural land for bioplastics may compete with food production. -Infrastructure Requirements: Specialized facilities for fermentation and downstream processing are needed

Policy and Regulation Support

- Governments and international organizations are implementing policies to promote bioplastics:
- Subsidies for bioplastic manufacturers.
- Bans on single-use plastics in several countries.
- Certifications like ASTM D6400 and EN 13432 to standardize biodegradability.

Integration with Renewable Energy

- Bioenergy Production: Sugarcane bagasse can be used as a biofuel for energy generation, powering fermentation plants.
- Zero-Waste Production: Combines energy production with bioplastic manufacturing to achieve sustainability.

Real-World Case Studies

Some of successful projects or companies producing sugarcane-based bioplastics:

- Braskem (Brazil): A leader in sugarcane-derived bioplastics, producing "I'm green" polyethylene.
- NatureWorks: Utilizes sugarcane as a sustainable feedstock for PLA production.

Conclusion:

The production of fermented bioplastic using sugarcane waste represents a sustainable approach to addressing plastic pollution and agricultural waste management. Although challenges exist, ongoing advancements in biotechnology and material science hold the potential to make this process economically viable and widely adopted. By harnessing waste materials and biological processes, this innovation paves the way for a greener and more sustainable future. The findings demonstrate the potential to address key environmental challenges while promoting the use of renewable resources.

Environmental Benefits

- The complete biodegradability of bioplastics reduces the burden on landfills and oceans.
- Using sugarcane bagasse, an agricultural waste product, minimizes resource wastage and supports circular economy principles.

Industrial Feasibility

- The comparable mechanical properties of bioplastics make them suitable for diverse applications, including packaging, agriculture, and healthcare.
- With further advancements in microbial engineering and pre-treatment technologies, the cost of production can be significantly reduced, making bioplastics competitive with traditional plastics.

Future Prospects

- Policy interventions, such as subsidies and tax incentives, can encourage the adoption of bioplastics.
- Continued research into alternative pre-treatment methods, such as bio-enzymes and green solvents, can enhance efficiency and reduce environmental impacts.

This study emphasizes the importance of interdisciplinary approaches, combining biotechnology, material science, and environmental policy, to address the growing plastic waste crisis. Bioplastics from sugarcane bagasse represent a crucial step toward a more sustainable and eco-friendly future.

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BEYOND GUT HEALTH: REVIEW ON THE EXPANDING ROLE OF NEXT-GENERATION PROBIOTICS IN HUMAN HEALTH

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Abstract:

Next-generation probiotics (NGPs) are emerging as a promising solution to overcome the limitations of conventional probiotics. Derived from the human gut microbiota, these probiotics exhibit enhanced therapeutic potential, providing targeted benefits for various gastrointestinal, metabolic, and immune-related disorders. Recent advances in sequencing technologies and bioinformatics have enabled the identification of beneficial strains with specific health-promoting properties. This review highlights the key characteristics, mechanisms of action, and clinical applications of NGPs. Furthermore, it explores their role in gut microbiome modulation, disease prevention, and personalized medicine. Challenges such as safety concerns, regulatory frameworks, and large-scale production are also addressed. By bridging the gap between research and clinical application, NGPs hold significant potential in revolutionizing human health and well-being.

Keywords: Next-Generation Probiotics, Gut Microbiota, Microbiome Modulation, Therapeutic Applications, Personalized Medicine, Human Health, Microbial Strains, Clinical Applications, Biotechnology, Functional Foods.

Introduction:

The human body is home to trillions of microorganisms that play a fundamental role in maintaining health. While traditional probiotics — mainly species of *Lactobacillus* and *Bifidobacterium* — have long been used to support gut health, a new wave of beneficial bacteria known as next-generation probiotics (NGPs) is taking center stage.

Next-generation probiotics are strains of bacteria, often derived from the human microbiome, that offer targeted therapeutic benefits. From preventing chronic diseases to combating infections and enhancing immune response, these microbes are shaping the

future of personalized medicine. With advancements in microbiome research, NGPs are now emerging as potential treatments for conditions ranging from obesity and inflammatory bowel disease (IBD) to sexually transmitted diseases (STDs) and even cancer [1,2]. Next-Generation Probiotics (NGPs) refer to newly developed and enhanced strains of beneficial bacteria created through advanced technologies such as genomics and metagenomics. These Next-Generation Probiotics are designed to offer superior health benefits compared to traditional probiotics by targeting specific health conditions and exhibiting unique characteristics, such as increased potency, stability, and survivability in the gut. Additionally, Next-Generation Probiotics may be engineered to produce specific compounds or molecules with therapeutic properties, further enhancing their potential health benefits.

Chronic diseases, defined as health conditions lasting one year or more that require continuous medical attention, limit daily activities, or both, are a major concern globally. Next-Generation Probiotics are being developed to address the limitations of conventional probiotics and offer more effective treatments for chronic diseases. Unlike traditional probiotics, Next-Generation Probiotics are designed to provide targeted and specific therapeutic effects.

One innovative approach in the development of Next-Generation Probiotics involves engineering specific bacterial strains to express therapeutic molecules or proteins. For example, Lactobacillus strains can be engineered to produce anti-inflammatory compounds like interleukin (IL)-10 or transforming growth factor (TGF)-β, which can help reduce inflammation in the gut and alleviate symptoms of inflammatory bowel disease (IBD). Similarly, Bifidobacterium strains can be modified to produce antimicrobial peptides that can be used to treat infections.

In addition to targeted therapies, Next-Generation Probiotics can be personalized to meet individual health needs. By analyzing a person's gut microbiome, probiotics can be tailored to restore or modulate specific bacterial populations associated with particular diseases. For example, personalized probiotics can be designed to stimulate the growth of beneficial bacteria linked to improved metabolic health, providing potential treatments for obesity and type 2 diabetes.

Despite the promising potential of Next-Generation Probiotics in treating chronic diseases, further research is necessary to establish their safety and efficacy. Additionally, the development of efficient and cost-effective methods for producing and delivering these

Next-Generation Probiotics remains a crucial area of focus. As advancements in biotechnology continue, Next-Generation Probiotics represent a significant step forward in personalized medicine and the management of chronic health conditions. Probiotics represent a significant step forward in personalized medicine and the management of chronic health conditions, benefiting human health.

What Are Next-Generation Probiotics?

Next-generation probiotics are newly identified bacterial strains with specialized health benefits. Unlike conventional probiotics found in yogurt and supplements, NGPs are typically derived from the human gut microbiota and are known to establish a symbiotic relationship with their host

1. *Akkermansia muciniphila*: Promotes metabolic health and reduces inflammation [3]. The study by Khalili L, Park G, Nagpal R, and Salazar G. analyzed the effects of *Akkermansia muciniphila* (*A. muciniphila*) and its derivatives, including extracellular vesicles (EVs) and outer membrane proteins, on gut and metabolic health through a meta-analysis of 39 mouse model studies. Results showed that both live and heat-killed *A. muciniphila* reduced inflammation, improved liver enzyme levels, regulated glycemic responses, and enhanced lipid profiles. The bacteria also strengthened gut barrier integrity and influenced body weight, preventing weight loss in gastrointestinal (GI) disorders and reducing it in metabolic disorders. Live bacteria demonstrated greater efficacy, forming beneficial microbial clusters. These findings suggest that *A. muciniphila* may offer enhanced therapeutic benefits for cardiometabolic and age-related diseases, supporting further research and clinical applications.

2. *Faecalibacterium prausnitzii*: Possesses strong anti-inflammatory properties [4] Anderson R, *et al.* Shows that the disruption of gut homeostasis in metabolic diseases is closely linked to intestinal immune function. Acting as a physiological barrier, the intestine prevents harmful substances from infiltrating the body. The intestinal barrier comprises biological, physical, chemical, and immune components' [5]. Table 1 summarizes the key benefits of *Akkermansia muciniphila*, its associations with metabolic diseases such as type 2 diabetes, obesity, and NAFLD, and the dietary factors that can promote its growth, including prebiotic fibers and polyphenol-rich foods.

Table 1: Overview of *Akkermansia muciniphila* Role in Metabolism and Disease

Benefits of *Akkermansia muciniphila*	
Weight management	Benefits in weight loss and maintenance by regulating fat storage and metabolism.
Improved glucose metabolism	Enhances insulin sensitivity and glucose uptake in the gut.
Reduced inflammation	Exhibits anti-inflammatory properties, helping alleviate metabolic disorders.
Improved lipid metabolism	Regulates cholesterol and triglyceride levels.
Association with Metabolic Diseases	
Type 2 Diabetes	Decreased levels of *A. muciniphila* are observed in individuals with type 2 diabetes.
Obesity	Lower levels of *A. muciniphila* are commonly found in obese individuals.
Non-Alcoholic Fatty Liver Disease (NAFLD)	May have a protective role against the development of NAFLD.
Dietary Influences	
Prebiotic Fibers	Prebiotic-rich foods like fruits, vegetables, and whole grains promote *A. muciniphila* growth.
Polyphenol-Rich Foods	Berries, green tea, and dark chocolate, which are high in polyphenols, support *A. muciniphila*.

Bacteroides fragilis: Regulates immune responses and strengthens gut barrier function. *Bacteroides fragilis* is a gram-negative, anaerobic, non-spore-forming bacterium that is a key member of the human gut microbiota. It plays a crucial role in maintaining gut homeostasis by contributing to digestion, modulating the immune system, and preventing colonization by pathogenic microbes. However, under certain conditions, it can become an opportunistic pathogen, leading to infections. [6]

Table 2: Overview of *Bacteroides fragilis* as a Probiotic

Category	Description
Potential Benefits	
Immune System Modulation	*B. fragilis* produces polysaccharide A (PSA), enhancing immune tolerance and reducing inflammation.
Gut Barrier Integrity	Supports intestinal barrier function by increasing mucin and tight-junction protein production.
Anti-Inflammatory Effects	Reduces inflammatory responses, which may benefit individuals with autoimmune and inflammatory diseases.
Pathogen Defense	Competes with harmful microbes, reducing the risk of gut infections.
Metabolic Regulation	Produces short-chain fatty acids (SCFAs) like butyrate, promoting gut health and regulating metabolism.
Therapeutic Applications	
Inflammatory Bowel Disease (IBD)	May alleviate symptoms of ulcerative colitis and Crohn's disease by reducing intestinal inflammation.
Colorectal Cancer (CRC) Prevention	Some non-toxigenic strains may help reduce the risk of CRC by maintaining gut health.
Immune-Related Disorders	Supports immune homeostasis, potentially reducing autoimmune disease progression.
Safety Considerations	
Strain Selection	Non-toxigenic strains of *B. fragilis* are preferred for therapeutic use to minimize adverse effects.
Immunocompromised Individuals	Use with caution in immunocompromised patients, as it can become opportunistic in certain cases.
Dietary Influences	
High-Fiber Diets	Promotes the growth of beneficial strains through the fermentation of dietary fibers.
Probiotics and Prebiotics	Supplementing with prebiotics like inulin can enhance *B. fragilis* activity in the gut.

4. *Lactobacillus crispatus*: Supports vaginal health and protects against sexually transmitted infections [7]. Overview of *Lactobacillus crispatus* as a Probiotic is shown in table 3

Table 3: Overview of *Lactobacillus crispatus* as a Probiotic

Category	**Description**
Potential Benefits	
Vaginal Health Support	*L. crispatus* helps maintain a healthy vaginal microbiome by producing lactic acid, lowering pH levels, and preventing infections.
Protection Against STIs	Demonstrates protective effects against sexually transmitted infections (STIs) by inhibiting pathogen growth.
Antimicrobial Properties	Produces bacteriocins and hydrogen peroxide (H_2O_2), which help eliminate harmful bacteria.
Urinary Tract Health	May prevent urinary tract infections (UTIs) by maintaining a balanced microbial environment.
Immune Modulation	Supports immune system function by reducing inflammation and enhancing barrier protection.
Therapeutic Applications	
Bacterial Vaginosis (BV)	*L. crispatus* supplementation can help restore vaginal microbiota balance, reducing BV recurrence.
Urinary Tract Infections (UTIs)	May lower UTI risk by preventing colonization of uropathogens in the urinary tract.
STI Prevention	Reduces susceptibility to infections like chlamydia, gonorrhea, and HIV.
Safety Considerations	
Probiotic Use	Generally recognized as safe (GRAS) and well-tolerated for vaginal and oral probiotic applications.
Strain Selection	Select specific strains of *L. crispatus* for optimal efficacy and safety.
Dietary Influences	
Probiotic Supplements	Available in capsule, tablet, or vaginal suppository forms to support vaginal and urinary health.
Fermented Foods	Consuming fermented dairy products like yogurt and kefir may indirectly support a healthy microbiome.

These microbes are particularly effective because they are naturally adapted to the human body, offering enhanced therapeutic effects compared to conventional probiotics.

Next-Generation Probiotics vs. Traditional Probiotics:

The table 4 "Next-Generation Probiotics vs. Traditional Probiotics" provides a comparative overview of the key differences between traditional probiotics and next-generation probiotics (NGPs).

Table 4: Next-Generation Probiotics vs. Traditional Probiotics

Feature	**Traditional Probiotics**	**Next-Generation Probiotics**
Common Strains	*Lactobacillus*, *Bifidobacterium*	*Akkermansia*, *Faecalibacterium*, *Bacteroides*, *Lactobacillus crispatus*
Source	Fermented foods, supplements	Human gut and vaginal microbiota
Targeted Benefits	General gut health, immunity	Specific diseases like IBD, obesity, cancer, STDs
Mechanism of Action	Restores microbiome balance	Modulates immune response and metabolism
Clinical Applications	Limited in complex diseases	Expanding into chronic disease and infection treatment

Health Risk Assessment of Next-Generation Probiotics (NGPs)

Assessing the health risks of next-generation probiotics (NGPs) is crucial to ensure their safety and efficacy before clinical applications. This involves a comprehensive evaluation of multiple factors, including strain-specific characteristics, host factors, long-term effects, and immune responses. The following are key components of the health risk assessment process:

1. Strain-Specific Analysis

Each strain of NGPs must undergo rigorous analysis to evaluate its safety. Key considerations include:

1) **Pathogenicity:** Evaluating whether the strain has any traits that could cause harm, such as virulence factors or the ability to invade host tissues.
2) **Toxin Production:** Screening for the production of harmful toxins that may pose risks to human health.

3) **Antibiotic Resistance:** Assessing the presence of antibiotic resistance genes to prevent the transfer of resistance to pathogenic bacteria. Whole-genome sequencing (WGS) is commonly used for this purpose.
4) **Genetic Stability:** Ensuring the strain's genetic stability to avoid unexpected mutations leading to pathogenicity.

2. Host-Specific Factors

The effects of NGPs can vary depending on the characteristics of the host. Important host-specific factors include:

1) **Health Status:** Individuals with compromised immune systems, underlying diseases, or gastrointestinal disorders may experience adverse effects.
2) **Age and Physiology:** Infants, pregnant women, and the elderly may respond differently to probiotics.
3) **Microbiome Composition:** The host's baseline gut microbiota influences the colonization and efficacy of NGPs.
4) **Genetics:** Genetic predispositions may affect immune responses and probiotic interactions.

3. Long-Term Safety Studies

Evaluating the long-term effects of NGP consumption is essential to identify potential risks associated with chronic exposure. Considerations for long-term safety studies include:

1) **Duration and Dosage:** Determining safe dosage levels for both short-term and prolonged use.
2) **Adverse Events Monitoring:** Tracking adverse effects like gastrointestinal symptoms, infections, or systemic inflammation.
3) **Carcinogenicity and Mutagenicity:** Assessing the risk of cancer development or genetic mutations through comprehensive toxicology studies.
4) **Reversibility:** Evaluating whether any adverse effects resolve after discontinuation of NGP consumption.

4. Immune Response Evaluation

NGPs often modulate the immune system, making immune response evaluation a critical aspect of health risk assessment:

1) **Inflammatory Response:** Monitoring for signs of excessive inflammation or autoimmune reactions.

2) **Cytokine Profile Analysis:** Assessing the production of pro-inflammatory and anti-inflammatory cytokines.
3) **Immune Tolerance:** Ensuring that NGPs do not trigger immune hypersensitivity or tolerance breakdown.
4) **Allergenicity:** Screening for allergenic components that may provoke allergic reactions in sensitive individuals.

Challenges and Future Directions:

Next-generation probiotics (NGPs) offer significant therapeutic potential, but their development faces several challenges. Regulatory approval remains complex, as NGPs are often classified as live biotherapeutics, requiring extensive clinical trials and stringent regulatory pathways. Additionally, ensuring the stability and viability of these strains during production, storage, and delivery poses a major hurdle. The effectiveness of NGPs can also vary based on an individual's microbiome composition, highlighting the need for personalized medicine approaches. Despite these challenges, advancements in microbiome sequencing, synthetic biology, and targeted delivery systems are expected to drive the successful clinical application of NGPs, opening new avenues in disease prevention and treatment.

Conclusion:

Next-generation probiotics represent a revolutionary advancement in the field of microbiome therapeutics. By harnessing the power of beneficial bacteria naturally found in the human body, these strains offer targeted, personalized healthcare solutions. From managing metabolic syndrome and inflammatory diseases to preventing sexually transmitted infections and enhancing cancer treatment, the applications are vast and transformative. As the scientific community continues to unravel the complex relationship between the microbiome and human health, next-generation probiotics are poised to become a cornerstone of modern medicine. In the years to come, these innovative therapies will not only improve health outcomes but also pave the way for a more personalized and preventive approach to healthcare.

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SAUSSUREA OBVALLATA (BRAHMA KAMAL): AN ANCIENT MEDICINAL PLANT

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Abstract:

Saussurea obvallata also known as Brahma Kamal an endemic herb of the Himalayan region was an ancient plant that was not much known for its rareness. Generally found in the Indian Himalayan region, Kedarnath, northern Burma, the Valley of Flowers, Tungnath Hemkund Sahib, and southwest China. Many ancient landmarks which give spiritual knowledge about the Brahma Kamal in Indian mythology like Mahabharat and Ramayana. The Asteraceae genus Saussurea has roughly 490 species. Herbs of this genus are utilized as traditional remedies in a variety of nations. Brahma Kamal (*Saussurea obvallata* (DC.) Edgew.) is a critically endangered species of this genus that is utilized for traditional, decorative, and religious uses. It is reported that the plant contains phenolic, proteins, saponins, and corticosteroids. It is used to treat minor burns and bruises. It has a significant influence on wound healing. The current review effort aims to investigate earlier work done on the indicated facility. The goal of this study is to evaluate and comprehend previous scientific work on *S. obvallata*, including ethnomedicinal usage, bioactivity characterization, phytochemistry, pharmacology, micro-propagation, and critical conservation aspects.

Keywords: *Saussurea obvallata*, Brahma Kamal, Anti-Microbial, Antioxidant

Introduction:

The people of India have a long and rich history of using medicinal plants, likely stemming from their abundance of botanical riches located at higher altitudes in the Western Himalayan ranges. There are also a variety of important and endemic medicinal plants found in this region, making it an important biodiversity hotspot. Medicinal plants are a wealthy source of drugs that play a pivotal role in traditional systems of medicine, modern medicines, nutraceuticals, food supplements, Vedic medicines, folk medicines, and pharmaceutical intermediates and chemical entities for synthetic drugs. And from the research, it was reviled that *Saussurea obvallata* also known as Brahma Kamal was used as an ancient herb for curing many diseases from ancient times.

On thinking about Asteraceae's own family, *Saussurea obvallata* is one of its biggest genera. This species may be encountered across the entire Himalayan province, and it grows at an altitude of 3000-4800 m. *S. obvallata* became discovered among other Asian nations like China, Nepal, and Pakistan. *Saussurea obvallata* grows as much as 5-10 cm on the top, its plant life blooms in July-august and is easily identified via its crimson(purple) colour, which is barely hidden from mild inexperienced bracts which are light-green tends to be papery which can be vital for his or her survival throughout the coldest days in the mountain regions. The vegetation blooms at the height of the monsoons and is abundant in excessive-altitude places like the valley of flowers.

Mythological Tales

Hindu mythology says that Brahma Kamal was created by Lord Brahma to assist Lord Shiva in placing the head of an elephant on Lord Ganesha. The flower shed "Amruta"—the elixir of life—on the body from its petals. Additionally, it's thought that the Sanjeevani was used to revive Lakshmana, and in jubilation, the Gods showered Brahma Kamal with divine blessings. So, Brahma Kamal dropped to the ground and established himself in the Valley of Flowers. In the area, the plant has great religious significance. It is presented to the Lord as a spiritual blossom. Lord Shiva at the Kedarnath temple and Vishnu at the Badrinath shrine. Brahma Kamal is offered in temples during the festival of Nanda Ashtami in September or October and is also given out as "prasad."

Botanical Characters

- A little perennial plant that can reach a height of 60 cm.
- Usually purple to reddish brown, the stems are upright, ribbed, and hollow.
- Leaves are basal and cauline; basal leaves are rosulate, petiolate, elliptic-spathulate or lanceolate, 10–25 ×1–5.5 cm, noticeably expanded and sheathing at base, denticulate cuspidate and scarious at edges, acute to obtuse or cuspidate at the apex.
- Inflorescences with two to many discoid capitula that are terminal and surrounded by involucriform bracts that are creamy white or pale yellow.
- Florets have two sexes(bisexual).
- Corolla is tubular with bluish-purple or violet
  linear-lanceolate lobes. Oblong or obovoid are cypselae,
  with a white pappus, pale creamy, brown, or greyish.
- Blossoms typically appear in July and August, and the flowers can be seen until mid-October when the
  plant dies and becomes apparent again in April. Flowers appear to be.
- They're lovely but stink, which may explain why people don't carry them home.

Scientific classification	
Kingdom	Plantae
Order	Asterales
Family	Asteraceae
Genus	Saussurea
Species	*S. obvallata*

Microscopic Observation

A single layer of the epidermis, a thick cuticle, stomata, spongy parenchyma, and vascular bundles are all visible under a microscope in the leaves. Phloem fibers, ground tissue, highly developed palisade tissue, and rather big intercellular gaps amid sponge tissue, whereas the leaf powder contained cork cells, pitted vessels, endocarp fragments, leaf fragments, and xylem fragments. A transverse section of the stem revealed many prominent ridges on the outer side, as well as epidermis, parenchyma, collenchyma cells, cortex, endodermis, pericycle, and vascular bundles, whereas the powdered stem revealed cork cells, pitted vessels, annular vessels, calcium oxalate crystals, iodine, and a group of lignified fibers. A transverse incision of the roots revealed the existence of the epidermis, cortex, endodermis, single-layered pericycle, and vascular tissue. bundles, as well as a tiny pith area Cork cells, tracheids, starch, tracheid reticulate channels, and fibers, were found in the powdered rhizome. In *S. obvallata*, the powered flower reveals the presence of tracheid, pitted vessels, parenchyma cells, prismatic crystals, fibers, and oil globules.

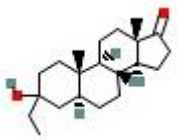
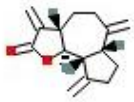
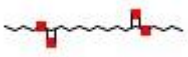
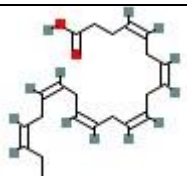
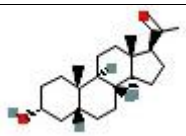
These anatomical components showed a link between leaf architecture and adaption in the alpine environment. (Assessment of non-timber Brahma Kamal (*Saussurea obvallata* (DC.) Edgew.), an important Himalayan medicinal plant: Ethnomedicinal, phytochemical and pharmacological overview)

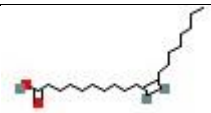
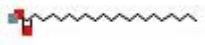
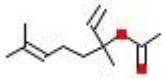
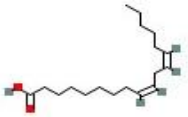
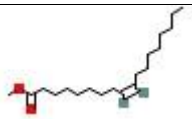
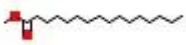
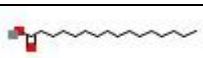
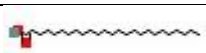
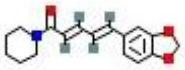
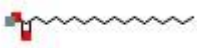
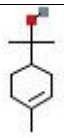
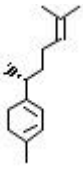
Phytochemistry

In general, medicinal herbs generate significant secondary compounds; however, several Himalayan medicative plant species produce more responses to cold stress produced by critical weather (Alonso-Amelot *et al.,* 2004, Zlati & Stankovi, 2017). These plants are getting more popular because of their distinct medicinal benefits (Mangal *et al.,* 2018, Tewari, 2014). Earlier publications on phytochemical analyses found saponins, phenol, tannins, terpenoids, flavonoids, glycosides, proteins, and alkaloids in *S. obvallata*

flowers and leaf extracts (Semwal *et al.,* 2014). The GC-MS tests revealed the presence of squalene and -linolenic acid methyl ester in a petroleum ether extract of *S. obvallata* (Mishra *et al.,* 2018). Another phytochemical experiment described both qualitative and quantitative examination of chemical contents contained in *S. obvallata* leaves and flower extracts (Semwal *et al.,* 2014, Semwal & Painuli, 2019). The presence of 78 phytocompounds in methanolic leaves and flower extracts of *S. obvallata* was discovered in this research. There are just a few important chemicals presented.

Inorganic compounds report on physicochemical examinations of *S. obvallata*, including protein, crude fiber, ash value, phosphorus, calcium, magnesium, potassium, iron, silica, reducing sugars, and amino acid content (Tiwari *et al.,* 1986). The largest percentages of protein (26.25%), iron (0.042%), and crude fibers (20.00%) were found in the flowers, leaves, and stems, correspondingly. The amino acid content of the stem was greater than the values reported for the leaves and flowers. Aspartic acid, alpha-alanine, beta-alanine, glycine, histidine, leucine, isoleucine, lysine, methionine, phenylalanine, serine, threonine, and tryptophan were recognized as amino acids.

Sl.no	**PubChem CID**	**Compounds**	**Chemical Structure (2D)**	**Molecular Formula**
1	12620	1-Docosanol		C22H46O
2	14681481	Androstan-17-one, 3-ethyl-3-hydroxy-, (5alpha)-		C21H34O2
3	46881232	Bupleuronol		C17H20O2
4	73174	Dehydrocostus lactone		C15H18O2
5	7986	Dibutylsebacate		C18H34O4
6	445580	Doconexent		C22H32O2
7	31402	Eltanolone		C21H34O2

8	5282768	Gondoic acid		C20H38O2
9	16898	Henicosanoic acid		C21H42O2
10	8294	Linalyl acetate		C12H20O2
11	5280450	Linoleic acid		C18H32O2
12	12311315	Litsomentol		C30H52O2
13	5249326	Methyl asterrate		C18H18O8
14	5364509	Methyl oleate		C19H36O2
15	8181	Methyl palmitate		C17H34O2
16	985	Palmitic acid		C16H32O2
17	10468	Pentacosanoic Acid		C25H50O2
18	638024	Piperine		C17H19NO3
19	5281	Stearic acid		C18H36O2
20	17100	α –Terpineol		C10H18O
21	12304273	γ-Curcumene		C15H24

Ethnomedicinal Significance

The species is widely utilized in traditional medicine and continues to play an important role in the treatment of a variety of old and new diseases.

Plant parts	Ethnomedicinal use	Application form	References
Leaves & roots	It is used in the curation antiseptic and also used for healing cuts and bruises.	Paste formulated from the plants and applied to the affected parts of the body	Kirtikar & Basu 1984, Negi *et al.,* 2015
Roots	Cure boils, cuts and Bruises, fractures	Paste formulated from the plants and applied to the affected parts of the body	Bano *et al.,* 2014
Whole Plant & Roots	Used in the medication for paralysis of limbs and cerebral ischemia cure fever and cough, medication for headaches and other body pain	Paste formulated from the plants and applied to the affected parts of the body	
Whole inflorescence	Used to protect woolen clothes from the damages caused by insects		Chauhan 1999
Flower Buds	Used to treat boils, hydrocele and Reproductive disorders	Paste formulated from the plant's flowers and applied to the affected parts of the body	Kala *et al.,* 2006
Flower head	Cure hydrocele	Inflorescence heads are cooked with ghee and one to two teaspoons (full) are given to patients in the morning for medicinal purposes. between three and six days	Kala *et al.,* 2006
Flower buds	Treat urinary infections in Cattle	Raw form	Saklani & Rao 1996
Roots	Cure leukoderma, skin disease		
Bracts	Used to cure cough and Respiratory problems		Gupta *et al.,* 2013
Seeds	Used to cure mental disorders	Seed powder soaked in water for 24 hrs and purified (1 cupful)	Phondani *et al.,* 2010

New illnesses have emerged. Several Saussurea species are employed in traditional/folk medicine systems in India, China, Tibet, Nepal, Pakistan, Bangladesh, Uyghur, Mongolia, Kazakhstan, and other Asian countries (Butola & Samant 2010, von Raab-Straube 2017).

S. obvallata has traditionally been used by Himalayan communities in Tibet, China, Nepal, and India for the cure/treatment of various diseases and disorders such as paralysis, cerebral ischemia, wounds, and cardiac and mental disorders; some people also use it as an antiseptic and to heal cuts (Kirtikar & Basu 1984, Pant & Semwal 2013, Negi *et al.,* 1999, Phondani *et al.,* 2010, Tsarong 1986). Table 2 has further information on *S. obvallata* in traditional uses.

Propagation

For the most part, propagation (conventional and in vitro) and culture techniques are absent. Saussurea species omitting S. costus, *S. obvallata*, and S. medusa. Farming of S. costus in the Lahaul Valley's Cold Desert began in the 1920s, and the plant is now being produced commercially. Several indigenous populations have reportedly reported small-scale cultivation of the plant in Uttarakhand's Nanda Devi Biosphere Reserve (2000-3500 m). Due to the great medicinal and culinary potential of S. laniceps, as well as its scarcity, efforts are being undertaken in Tibet to conserve and cultivate it. The Rock Garden Plant Database website has information on the propagation and cultivation of various Saussurea species.

Medicinal Applications

Saussurea obvallata has traditionally been used to treat paralysis, cerebral ischemia, wounds, and cuts. bruising, liver diseases, bone-ache, cough, intestinal and urinary issues. Ground roots are used to treat wounds, pain, inflammation, boils, and skin problems. Animal medicine is also employed. *Saussurea obvallata* is used to lower body temperature while simultaneously increasing appetite. Eating of Soup prepared from this plant can help to reduce liver inflammation. Used to treat STDs, arthritis, paralysis, and other conditions.

Wound Healing Activity

Wound healing is often divided into three stages. These are Inflammation, Proliferation, and Andre modelling. It is made up of complicated processes and interactions between cells and mediators. Wounds are physical injuries that cause the skin to break. *Saussurea obvallata* plant extract is used for wound healing. Inflammation suppression and Fibroblast stimulation are two mechanisms involved in *Saussurea obvallata* wound healing. The in vitro testing of the processes is essential in determining the plant's wound-healing ability. In vitro scratch tests, Electric Cell-substrate Impedance Sensing, microfluidic

chambers, and Boyden chamber-based transmembrane assays are the most often used in vitro wound healing assays.

Antimicrobial activity

Four bacterial strains and three fungus strains were tested for antimicrobial activity. Pseudomonas aeruginosa, Klebsiella pneumoniae, and Staphylococcus aureus were all inhibited by *S. obvallata* extracts, while Escherichia coli was resistant (lower zone) compared to the other three bacteria. In terms of antifungal activity, the extract inhibited Candida glabrata the most, followed by Candida albicans and Candida tropicalis. Based on retention time (Rt) and area percent, GC-MS analysis of methanolic extracts of *S. obvallata* leaves and flowers revealed the presence of 36 and 48 components, respectively.

Pharmacology

- **Anti-hypoxic activity**

In hypoxia mouse models, the anti-hypoxic action of *S. obvallata* was investigated. Moreover, adenosine triphosphate (ATP) and adenosine nucleotide (ADN) These models were also tested for triphosphatase (ATPase) activity in the brain and cardiac muscle, lactic acid (LAC) and lactate dehydrogenase (LDH) activity in the blood and cardiac muscles, and blood sugar and glycogen levels in the liver and skeletal muscles (Ma H-P *et al.,* 2011). *Saussurea obvallata* showed remarkable outcomes in terms of survival time (36.34 min) and prolonging rate (20.52%) in this investigation, whereas Involcucrata Saussurea (Kar. et Kir.) At a dosage of 1000 mg/kg, Sch.-Bip displayed the greatest anti-hypoxic action (survival time=40.78 min, prolongation rate=33.13%). Also, the LAC content of mice plasma was 2.84 mmol/L for *S. obvallata* and 1.93 mmol/L for S. involucrate at a dosage of 1000 mg/kg, which may be useful in the treatment of acute mountain sickness. Hai-li LI *et al.,* (2016) investigated *S. obvallata* (crude extract) anti-hypoxic efficacy in EA. hy926 cells. Sodium dithionite was used to create the hypoxia injury experimental model. When compared to the control, the plant extract enhanced the EA. hy926 cell survival rate in the model of hypoxia damage (from a dose of 1.25 mg/mL).

- **Anticancer activity**

The anticancer efficacy of *S. obvallata* leaves and flower extracts against MCF-7 breast cancer cell lines was investigated, and the extracts showed significant action. When extracts were compared to the positive control, the results were recorded (unpublished data). The antimicrobial property of *S. obvallata* petroleum ether extract (1- 3 mg/disk) against strains of bacteria Staphylococcus aureus, Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli, Bacillus cereus, and Bacillus subtilis was evaluated (Mishra *et al.,* 2018). The disc diffusion technique was used to perform the antibacterial experiment. In this investigation, the leaf extract inhibited S. aureus (15.2 mm) at 3.0 mg/disk, but P.

aeruginosa was the less susceptible bacterial strain. The MIC value of *S. obvallata* extract against several bacterial strains ranged from 87.2 to > 100 g/mL.

Semwal and Painuli (2019) have demonstrated the antibacterial efficacy of *S. obvallata* extracts (20 l of 5mg/mL) against four microorganisms (Pseudomonas aeruginosa, Pseudomonas aeruginosa, Pseudomonas aeruginosa aeruginosa, Escherichia coli, Staphylococcus aureus, and Klebsiella pneumoniae) and three fungal strains (Candida albicans, Candida glabrata, and Candida tropicalis). The antimicrobial test was carried out utilizing the good diffusion technique. In this investigation, methanolic and aqueous extracts showed effective antibacterial and antifungal activity against all strains with zones of inhibition ranging from 8.87 to 20.50 mm and 8.30 to 15.90 mm, respectively. Two in-vitro experiments were used to determine the antioxidant activity of *S. obvallata* extracts (20 l of 1mg/mL). H2O2 techniques were used, and significant antioxidant activity was found in both extracts, ranging from 29.25 to 82.88% and 39.75 to 41.05%, respectively (Semwal & Painuli 2019).

Conclusion:

The ethnobotanical literature study revealed many mysteries about the ancient medicinal herb brahma kamal or *Saussurea obvallata*. This study gives us many data that how wonderful this plant was its microscopic study revealed its anatomical structure, and botanical character telling us the importance of the plant. it was a very rare and special species of the northern Himalayan region. Many studies were done on this plant and the extracted data was impressive. the environmental study gives the significance of this plant and its important ecological importance for nature. It's It has many medicinal qualities like healings wounds, fracture cuts, it also cures many reproductive disorders, and viral fever, and body pains. These ethnomedicinal activities came from the phytocompounds theatre extracted from the *Saussurea obvallata*. The phytochemicals study revealed that GC-MS analysis of methanolic extracts of *S. obvallata* leaves and flowers revealed the presence of 36 and 48 components. By all these properties they can be Anti-tumour, anti-bacterial, anti-inflammatory, immunomodulation, antiulcer, and other biological properties. Anti-microbial, anti-cancer, anti-hypoxia, anti-fatigue, antioxidative, and anti-aging effects of *Saussurea obvallata*.

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Dr. (Ms) Sree R. Nair is an academic and researcher, currently serving as Assistant Professor and Head of Life Sciences at Sophia College for Women, Mumbai. With over a decade of teaching experience, her research spans microbial ecology, neuroprotective drug studies using Dictyostelium, and hyperglycemia's effects on Caenorhabditis elegans. She has received research grants from UGC and RUSA and is a member of the Indian Academy of Neurosciences. Dr. Nair has significantly contributed to scientific research, publishing extensively in national and international journals. Her work focuses on marine microbial interactions, phytoremediation, autophagy in neurodegeneration, and environmental sustainability. She has presented at various conferences, fostering discussions in biological and environmental sciences. A dedicated mentor, she plays a crucial role in academic research initiatives, shaping young scientists. Through her commitment to education and interdisciplinary research, Dr. Nair continues to drive advancements in life sciences.

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