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Recent Research in Biosciences

RECENT RESEARCH IN BIOSCIENCES

First Edition

Dr. R. B. Tripathi
Dr. P. Subbulakshmi
D.E. Nirman Kanna

THANUJ INTERNATIONAL PUBLISHERS, TAMIL NADU, INDIA

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Preface

Recent advances in biosciences have brought about remarkable progress in various fields, including insect ecology, myocardial ischemia, cardiovascular interventions, avian species toxicity, and sustainable resource management in the context of fish, fisheries, and food. This book aims to provide an overview of the latest research and developments in these areas, shedding light on the intricate workings of nature and the implications for human health and ecological balance. This book presents a collection of recent research findings and updates across diverse fields in biosciences. By bringing together experts and their cutting-edge work, we hope to provide readers with a comprehensive overview of the latest discoveries, challenges, and future directions in insect ecology, myocardial ischemia, cardiovascular interventions, avian species toxicity, and sustainable resource management in fish and fisheries. It is our sincere hope that this compilation will inspire further research and foster collaborations to address the pressing issues facing our environment and human well-being

The compilation of chapters offers a glimpse into diverse areas of research within the field of medical science correspondingly. By exploring topics such as organoprotection, nanotechnology, non-anesthetic benefits of lignocaine, earthworm gut microbes, oral dysbiosis, mosquito control, pharmacological activities of Pergulariadaemia, pesticide use, and honey bees, we aim to provide readers with a comprehensive overview of the latest advancements, challenges, and future directions in these fields. It is our hope that this book will inspire further research, foster interdisciplinary collaborations, and ultimately contribute to improving human health and the well-being of our environment

The book presents a comprehensive collection of chapters covering diverse topics in the medical and biological sciences. By highlighting the latest research findings, advancements, and future directions in cerebellar ataxia, diabetes mellitus, infectious diseases, pediatric ECMO, antidiabetic potential of Indian medicinal plants, mycoremediation, stem cell research, endophytic fungi, cardiac transplantation, 3D printing technology in pharmaceutical drug delivery, and synthetic seed technology.

We aim to foster scientific curiosity, inspire further research, and contribute to the advancement of knowledge in these fields.

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CONTNETS

Insect ecology: Unveiling the vitality of nature's tiny architects in ecosystem dynamics

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Abstract

With millions of insect species worldwide, they occupy diverse niches and perform a wide range of ecological functions. From pollination to decomposition, from herbivory to predation, insects contribute to various ecological processes that shape the structure and functioning of ecosystems. Furthermore, insects exhibit remarkable adaptations and behaviors that enable them to thrive in different environments. Their ability to exploit diverse resources and occupy distinct habitats enhances their impact on ecosystem dynamics. Insect populations can respond rapidly to environmental changes, making them valuable indicators of ecosystem health and stability. Understanding the role of insects in ecosystem ecology is vital for managing and conserving natural systems. Their conservation is crucial not only for preserving biodiversity but also for sustaining essential ecosystem services, such as pollination and decomposition. Moreover, the study of insect ecology provides insights into the potential effects of climate change, habitat loss, and other anthropogenic disturbances on ecosystem functioning.In conclusion, this abstract highlights the captivating world of insect ecology and its significance in ecosystem dynamics. Insects, with their diversity, abundance, and multifaceted interactions, contribute significantly to the flow of energy and nutrients within ecological systems. Their conservation and the understanding of their ecological roles are of utmost importance for the maintenance and preservation of healthy and resilient ecosystems.

Keywords: Biodiversity**,** Abundance**.** Diversity**,** Ecosystem services**,** Pollination**,** Decomposition**,** Adaptations, Environmental changes, Anthropogenic disturbances, Resilience

Introduction

Ecosystem ecology is the study of the interactions between organisms and their environment, focusing on the flow of energy and nutrients through ecosystems. Insects, being one of the most diverse and abundant groups of organisms on Earth, play a crucial role in ecosystem ecology.Insects play a crucial role in food webs as an integral component of the trophic structure within ecosystems (Basset, Y., *et al.* 2012). They serve as a vital food source for numerous organisms, including birds, mammals, reptiles, and other insects. Ecosystem ecology is a branch of ecology that investigates the intricate interactions between organisms and their environment within ecosystems. It aims to understand the flow of energy and nutrients through ecological systems and how these interactions shape the structure and functioning of ecosystems (Basset, *et al.*2021). Within the realm of ecosystem ecology, insects emerge as a fascinating and indispensable group of organisms. With their remarkable diversity and abundance, insects contribute significantly to the dynamics and processes of ecosystems.

Insects, comprising millions of known species, inhabit virtually every corner of the planet, occupying a wide range of habitats and niches (Didham, *et al.* 2005). Their ecological importance stems from their interactions with other organisms and the environment, making them key players in ecosystem functioning. As primary producers, herbivores, predators, decomposers, and pollinators, insects occupy various trophic levels within ecosystems, influencing energy flow, nutrient cycling, and the distribution of resources (Hunter, *et al.*2013). In this context, the study of insects in ecosystem ecology encompasses a broad range of topics. It involves investigating how insects interact with primary producers, such as plants, and the subsequent effects on community dynamics and species diversity. Understanding the feeding behaviors of herbivorous insects and their impact on plant populations provides insights into plant community structure and the development of defense mechanisms (Haddad, *et al.* 2015). Predatory insects, on the other hand, help regulate populations of herbivores and other prey species, exerting top-down control on trophic interactions and contributing to ecosystem stability. The activities of decomposer insects, such as dung beetles and certain fly larvae, contribute to nutrient recycling and organic matter decomposition, influencing soil fertility and nutrient availability.

Moreover, insects' crucial role as pollinators shape the reproductive success and diversity of flowering plants, impacting ecosystem productivity and the availability of fruits, seeds, and nuts. Their interactions with other

organisms, including birds, mammals, reptiles, and even other insects, create complex food webs and energy transfer pathways that sustain the overall balance and stability of ecosystems.

The study of insects in ecosystem ecology not only provides fundamental insights into their ecological roles but also highlights the interconnectedness and interdependencies within ecological systems. By unraveling the mechanisms and consequences of insect-environment interactions, scientists gain a deeper understanding of ecosystem processes, resilience, and responses to environmental changes. In conclusion, insects play a crucial role in ecosystem ecology, contributing to energy flow, nutrient cycling, and ecological interactions within ecosystems. Their diverse and abundant presence across habitats makes them essential components of ecological systems (Hurlbert, *et al.*2021).

Trophic interactions

Insects occupy various trophic levels within ecosystems, serving as primary producers (e.g., leaf-mining insects), herbivores (e.g., caterpillars), predators (e.g., ladybugs), and decomposers (e.g., dung beetles). These trophic interactions help regulate population dynamics and nutrient cycling within ecosystems (Tscharntke, & Hawkins, 2002).Trophic interactions refer to the feeding relationships between different organisms in an ecosystem, where energy and nutrients are transferred from one trophic level to another (Inouye, 2008). Insects play diverse roles across trophic levels, contributing to the regulation of population dynamics and nutrient cycling within ecosystems. Here's an overview of the various trophic roles insects fulfill:

Primary producers

Insects that engage in photosynthesis, such as certain species of leaf-mining insects, act as primary producers. They extract energy from sunlight and convert it into organic matter through photosynthesis. These insects play a vital role in ecosystem productivity by synthesizing carbohydrates, which subsequently support higher trophic levels.Insects that engage in photosynthesis represent a fascinating group within the insect world. While most insects are heterotrophic, relying on external food sources, some species have evolved the ability to harness sunlight and perform photosynthesis, making them unique primary producers within ecosystems. Leaf-mining insects are a notable example of such insects.Leaf-mining insects are a diverse group that includes various species of beetles, flies, and moths. What sets them apart is their ability to live and feed within the tissues of plant leaves. These

insects possess specialized adaptations that allow them to extract energy from sunlight and convert it into organic matter through the process of photosynthesis.The leaf-mining process begins when the female insect lays her eggs on the surface of a leaf. After hatching, the larvae burrow into the leaf and create characteristic tunnels or mines as they feed on the leaf tissue. Within these mines, specialized cells called chloroplasts are present. Chloroplasts contain chlorophyll, a pigment responsible for capturing sunlight and facilitating photosynthesis.Through photosynthesis, leaf-mining insects are able to convert carbon dioxide and water into glucose, a simple sugar. Glucose serves as the main energy source for the insect, providing the necessary fuel for growth, development, and reproduction. Additionally, excess glucose is stored as starch or other carbohydrates (Jones, *et al.* 2018).

The photosynthetic abilities of leaf-mining insects have important implications for ecosystem productivity. As primary producers, they contribute to the synthesis of organic matter within the ecosystem. The carbohydrates they produce, such as glucose, provide a valuable energy source that supports higher trophic levels.The organic matter generated by leaf-mining insects becomes available to other organisms within the ecosystem through various pathways. For instance, when leaf-mining insects complete their life cycle or are consumed by predators, the energy and nutrients stored within their bodies are transferred to higher trophic levels. Decomposers also play a role by breaking down the remains of leaf-mining insects, releasing the stored energy and nutrients back into the ecosystem (Leather, *et al.* 2019).Furthermore, the feeding activities of leaf-mining insects can impact the health and structure of plant communities. By selectively consuming leaf tissue, they can influence plant growth patterns, alter photosynthetic rates, and trigger plant defense responses. These interactions can have cascading effects on other organisms, influencing herbivores, predators, and even the composition of plant communities. Leaf-mining insects that engage in photosynthesis represent a unique group of primary producers within ecosystems. Their ability to convert sunlight into organic matter through photosynthesis contributes to ecosystem productivity by synthesizing carbohydrates. These insects play a vital role in the flow of energy and nutrients, supporting higher trophic levels and influencing plant communities. Understanding the ecological significance of leaf-mining insects helps us appreciate the diverse strategies organisms have evolved to thrive within ecosystems

Herbivores

Many insects are herbivores, feeding on plant material. For instance, caterpillars are well-known herbivorous insects that consume leaves, flowers, and other plant parts. Herbivorous insects can exert a significant influence on plant populations, affecting their growth, reproduction, and survival(Perfecto, *et al* 2010). They contribute to shaping plant communities and can trigger various ecological responses in plants, such as the production of defensive compounds.Herbivory, the consumption of plant material by insects, is a widespread feeding strategy among many insect species. Caterpillars, in particular, are well-known herbivores that feed on various plant parts, including leaves, flowers, and stems. The impact of herbivorous insects on plant populations goes beyond mere feeding and can have profound ecological implications. Here's an overview of the role and influence of herbivorous insects on plant communities:

Feeding Habits:

Herbivorous insects have evolved specialized mouthparts and digestive systems that enable them to efficiently consume plant material. Caterpillars, for instance, possess strong mandibles that allow them to chew and consume plant leaves. By feeding on plants, herbivorous insects acquire energy, nutrients, and other essential resources necessary for their growth, development, and reproduction.

Impact on Plant Populations:

Herbivorous insects can significantly influence plant populations by exerting pressure on individual plants and affecting their growth, reproduction, and survival. Heavy herbivory can lead to reduced plant biomass, lower reproductive output, and even plant mortality. The intensity and duration of herbivory can determine the magnitude of these effects.

Plant Responses:

Plants have evolved various defense mechanisms to protect themselves against herbivores. When attacked by herbivorous insects, plants can trigger a range of ecological responses. These responses can include the production of defensive compounds, such as toxic chemicals or secondary metabolites, which deter or inhibit herbivore feeding. Some plants may also induce structural changes, such as the thickening of leaf tissue or the production of tough fibers, to make it harder for insects to feed on them.

Coevolutionary Dynamics:

Herbivorous insects and plants have engaged in a coevolutionary arms race over millions of years. As herbivores adapt to exploit specific plant defenses, plants, in turn, evolve new defense mechanisms to counteract herbivory. This ongoing interaction drives the diversification of plant defenses and herbivore feeding strategies, shaping the coevolutionary dynamics between plants and herbivorous insects.

Plant Community Structure:

Herbivorous insects play a key role in shaping plant communities. Their feeding preferences and selectivity can influence the abundance, distribution, and composition of plant species within an ecosystem. By selectively feeding on certain plant species or parts, herbivorous insects can impact the competitive interactions among plants, altering community dynamics and species diversity.

Indirect Effects:

The impact of herbivorous insects extends beyond plants themselves. The presence and activity of herbivores can indirectly affect other organisms within the ecosystem. For example, predatory insects may be attracted to areas with high herbivore densities, leading to changes in predator-prey dynamics. In some cases, the absence or suppression of herbivores can have negative consequences, disrupting ecological balance and ecosystem functioning.Understanding the ecological role of herbivorous insects in plant communities is crucial for unraveling the complexities of ecosystem dynamics (Pimm, *et al.* 2014). s. It highlights the interconnectedness of organisms within ecosystems and the intricate web of interactions that shape community structure and function. Conservation efforts aimed at preserving plant diversity and managing herbivore populations can help maintain the integrity and stability of ecosystems

Predators

Insects also act as predators, preying on other organisms. Ladybugs, for example, are predatory insects that feed on aphids, mites, and other pests. Predatory insects help regulate populations of herbivorous insects and other prey species, exerting top-down control on their abundance and preventing outbreaks. These interactions contribute to maintaining a balance in the ecosystem and preventing the overconsumption of plant resources.Insects exhibit a remarkable diversity of feeding strategies, and many species act as predators, feeding on other organisms within their ecosystems. Predatory

insects play a crucial role in regulating populations of herbivorous insects and other prey species, exerting top-down control on their abundance. One example of such predatory insects is ladybugs, which are known for their voracious appetite for aphids, mites, and other pests. Here's an overview of the importance of predatory insects in maintaining ecosystem balance:

Pest Control:

Predatory insects, including ladybugs, lacewings, and assassin bugs, provide natural pest control services. They prey on herbivorous insects, such as aphids, caterpillars, and mites, which are known to cause damage to crops, gardens, and ornamental plants. By feeding on these pests, predatory insects help regulate their populations, reducing the risk of outbreaks and minimizing the need for chemical pesticides.

Top-Down Regulation:

Predatory insects exert top-down control on prey populations, meaning they limit the abundance of herbivorous insects and other prey species in the ecosystem. By consuming large numbers of pests, predatory insects can prevent their populations from reaching levels that would lead to excessive damage to plants. This regulation helps maintain a balance between herbivores and their food resources, preventing overconsumption and promoting overall ecosystem health.

Trophic Cascades:

The presence of predatory insects can trigger trophic cascades, which are indirect effects that propagate through multiple trophic levels. When predatory insects reduce the population sizes of herbivorous insects, it can have cascading effects on the entire ecosystem. For instance, lower herbivore densities can alleviate the pressure on plants, allowing them to grow and reproduce more effectively. This, in turn, can influence the abundance and diversity of other organisms dependent on those plants.

Biological Control Services:

Predatory insects are valuable allies in biological control programs, which aim to manage pest populations using natural enemies. Many agricultural and horticultural practices now incorporate the use of predatory insects as a sustainable and environmentally friendly alternative to chemical pesticides. By releasing or conserving predatory insects, farmers, and gardeners can reduce pest populations and promote ecosystem-based pest management strategies.

Conservation of Biodiversity: Predatory insects contribute to the maintenance of biodiversity within ecosystems. They interact with a wide range of prey species and can adapt their feeding behavior to changing conditions. The diversity of predatory insects reflects the complexity of trophic interactions and the evolutionary adaptations within ecosystems. Conserving these predator populations is crucial for preserving biodiversity and promoting ecological resilience.

In summary, predatory insects, such as ladybugs, play an important role in maintaining ecosystem balance by preying on herbivorous insects and other pests. Their feeding activities help regulate prey populations, prevent outbreaks, and minimize damage to plants. By providing natural pest control services and promoting sustainable agricultural practices, predatory insects contribute to the health and sustainability of ecosystems. Recognizing and protecting the vital role of predatory insects is essential for maintaining biodiversity, promoting ecosystem services, and reducing reliance on chemical pesticides

Decomposers

Insects, including dung beetles and certain fly larvae, fulfill the role of decomposers. They consume dead organic matter, such as plant material, animal carcasses, and feces, breaking them down into simpler compounds. Decomposer insects facilitate the decomposition process, releasing nutrients back into the ecosystem and recycling them for use by other organisms. They contribute to nutrient cycling and the overall health of ecosystems.These trophic interactions involving insects are essential for the functioning and stability of ecosystems. They regulate population sizes, control pest species, shape plant communities, and facilitate the flow of energy and nutrients through different trophic levels. Disruptions to these interactions, such as the loss of predator populations or the introduction of invasive herbivorous insects, can have significant ecological consequences, leading to imbalances, reduced biodiversity, and altered ecosystem dynamics.Understanding and studying the trophic interactions of insects within ecosystems are crucial for ecosystem management, conservation efforts, and sustainable agriculture. It allows for the development of strategies that promote beneficial interactions, minimize the negative impacts of pests, and preserve the integrity and resilience of ecosystems.Insects play a crucial role in the decomposition process within ecosystems, with certain species acting as important decomposers. Dung beetles and certain fly larvae are notable examples of insects that fulfill this vital ecological role. As decomposers, they contribute to nutrient cycling,

organic matter breakdown, and the overall health of ecosystems. Here's an overview of their role and significance:

Decomposition and Nutrient Cycling: When animals produce waste, such as dung or carcasses, it represents a rich source of organic matter. Decomposer insects, including dung beetles and fly larvae, utilize these resources by breaking down the organic material. They feed on and digest the waste, converting it into simpler compounds and facilitating the release of nutrients back into the ecosystem. By decomposing organic matter, these insects play a key role in nutrient cycling, ensuring the recycling of essential elements like carbon, nitrogen, and phosphorus.

Organic Matter Breakdown:

Decomposer insects possess specialized adaptations for breaking down organic material efficiently. Dung beetles, for example, are well-known for their ability to process and bury dung. They roll dung into balls and transport it to underground chambers, where it serves as a food source and a site for egg-laying. Fly larvae, commonly known as maggots, thrive in decaying organic matter, including carcasses. They consume the organic material, breaking it down into smaller pieces and accelerating the decomposition process.

Accelerating Decomposition:

Decomposer insects play a crucial role in accelerating the decomposition of organic matter. By feeding on and fragmenting waste material, they increase the surface area available for microbial activity. This, in turn, enhances the activity of bacteria, fungi, and other microorganisms that break down complex organic compounds into simpler forms. The combined action of decomposer insects and microorganisms speeds up the decomposition process, making nutrients more accessible to other organisms in the ecosystem.

Habitat Modification:

The activities of decomposer insects, particularly dung beetles, can modify habitats and influence nutrient distribution within ecosystems. Dung beetles help disperse and bury dung, which not only aids in decomposition but also contributes to soil fertility. By burying dung balls, they create underground chambers that provide shelter and nutrition for their offspring. These actions can enhance soil structure, nutrient availability, and water infiltration, benefiting both plant growth and the wider ecosystem.

Ecological Services:

Decomposer insects provide essential ecological services. Their activities contribute to waste management, preventing the accumulation of organic material that could become a breeding ground for pathogens and disease vectors. By breaking down animal waste and carcasses, decomposer insects help reduce potential health risks to humans and other animals. Additionally, their actions contribute to the overall cleanliness and ecological balance of ecosystems.Understanding the role of decomposer insects in ecosystem functioning is critical for appreciating the intricate web of interactions within ecosystems. Their contribution to nutrient cycling, organic matter breakdown, and habitat modification is fundamental to the health and sustainability of ecosystems. Protecting and conserving these decomposer populations is essential for maintaining balanced nutrient dynamics, healthy soil ecosystems, and overall ecosystem resilience.

Pollination:

Insects, particularly bees, butterflies, moths, and flies, are major pollinators. They transfer pollen between flowers, facilitating the fertilization and reproduction of flowering plants. Pollination by insects is essential for the production of fruits, seeds, and nuts, contributing to the diversity and abundance of plant species within ecosystems.Insects play a vital role as pollinators in ecosystems, with bees, butterflies, moths, and flies being among the major contributors to the process of pollination. Their activities facilitate the transfer of pollen between flowers, enabling the fertilization and subsequent reproduction of flowering plants. Here's an overview of the significance of insect pollinators and their impact on plant diversity and abundance:

Pollination Process:

Pollination is a crucial step in the reproductive cycle of flowering plants. Insects, attracted by the flowers' colors, shapes, scents, and nectar, visit them in search of food. As they move from flower to flower, they inadvertently carry pollen grains on their bodies, which they transfer to the stigma of other flowers. This transfer of pollen allows for the fertilization of the ovules, leading to the production of seeds and fruits.

Key Insect Pollinators:

Bees, including honeybees and native solitary bees, are perhaps the most well-known and important pollinators. They have coevolved with flowering plants, forming mutually beneficial relationships. Butterflies, moths,

and certain species of flies also play significant roles in pollination. These insects have specialized mouthparts or proboscises that allow them to access nectar deep within flowers, increasing the chances of pollen transfer.

Plant Reproduction and Diversity:

Pollination by insects is essential for the reproduction and diversity of flowering plants. The transfer of pollen enables cross-fertilization, leading to genetic diversity within plant populations. This genetic diversity enhances the resilience and adaptability of plant species, enabling them to respond to environmental changes, such as climate variations or the emergence of new pests and diseases.Fruits, Seeds, and Nuts: Pollination by insects directly contributes to the production of fruits, seeds, and nuts. Fruits are the mature ovaries of flowering plants and are important food sources for many animals, including birds and mammals. Seeds and nuts, on the other hand, enable the dispersal and propagation of plant species. Insects play a crucial role in the formation of these reproductive structures by facilitating pollination.

Ecosystem Functioning and Food Webs:

The pollination activities of insects have broader implications for ecosystem functioning and food webs. Many animals rely on the fruits, seeds, and nuts produced through insect pollination as a source of food. These include birds, mammals, and even other insects. Thus, the reproductive success of flowering plants, driven by insect pollination, supports the overall stability and functioning of ecosystems.

Agricultural importance:

Insect pollinators are of tremendous economic and agricultural importance. They contribute to the pollination of many crops, including fruits, vegetables, nuts, and oilseeds. Honeybees, in particular, are extensively managed and transported by beekeepers to provide pollination services to agricultural fields. The pollination services of insects are estimated to significantly enhance crop yields and quality, contributing to global food security and agricultural economies.Protecting and conserving insect pollinators is crucial for maintaining the health and diversity of ecosystems. Habitat preservation, reducing pesticide use, and creating pollinator-friendly landscapes are important strategies to support insect pollinators. Recognizing the value of these insects as vital contributors to plant reproduction and ecosystem functioning is essential for promoting sustainable agriculture, biodiversity conservation, and the overall well-being of ecosystems

Decomposition:

Insects, along with other detritivores, play a crucial role in the decomposition process. They break down organic matter, such as dead plants and animals, into simpler compounds, releasing nutrients back into the ecosystem. Insects like beetles, ants, and termites are efficient decomposers, contributing to nutrient recycling and soil formation.Insects, along with other detritivores, are key players in the decomposition process within ecosystems. They contribute to the breakdown of organic matter, such as dead plants and animals, and play a crucial role in nutrient cycling and soil formation. Insects like beetles, ants, and termites are particularly efficient decomposers, facilitating the release of nutrients back into the ecosystem. Here's an overview of their role and significance in the decomposition process:

Decomposition Process:

Decomposition is the process by which organic matter is broken down into simpler compounds. Insects, along with bacteria, fungi, and other detritivores, actively participate in this process. They feed on organic material, such as dead leaves, plant litter, and animal carcasses, initiating the breakdown and fragmentation of the organic matter.

Nutrient Recycling:

The decomposition activities of insects contribute to nutrient recycling within ecosystems. As they consume organic matter, insects break it down into smaller pieces, exposing a larger surface area for microbial activity. This enhances the activity of bacteria and fungi, which further decompose the material, releasing nutrients like nitrogen, phosphorus, and carbon back into the soil.

Efficient Decomposers:

Insects such as beetles, ants, and termites are highly efficient decomposers. For example, beetles (e.g., burying beetles) specialize in decomposing animal carcasses, while ants and termites play crucial roles in breaking down plant material. These insects possess specialized adaptations, such as strong mandibles or symbiotic gut microorganisms, which allow them to efficiently process and digest organic matter.

Soil Formation:

The decomposition activities of insects contribute to the formation and enrichment of the soil. As organic matter breaks down, it mixes with mineral particles and contributes to the development of humus, a dark, nutrient-rich

component of soil. Insects, through their decomposition activities, help incorporate organic matter into the soil, improving its structure, fertility, and water-holding capacity.

Ecosystem Productivity:

The decomposition process facilitated by insects contributes to ecosystem productivity. By breaking down organic matter, insects release nutrients that can be taken up by plants, supporting their growth and vitality. These nutrients are essential for plant photosynthesis, reproductive processes, and overall ecosystem functioning.

Detritus Food Chain:

Insects form a vital component of the detritus food chain. They serve as a food source for other organisms, such as birds, mammals, and other insects. Insects that feed on decomposing organic matter, like beetles and fly larvae, become prey for predators higher up the food chain, thereby transferring energy and nutrients through the ecosystem.Understanding the role of insects in the decomposition process highlights their importance in nutrient cycling, soil formation, and ecosystem functioning. Protecting and conserving these decomposer populations is essential for maintaining healthy soils, sustaining productivity, and promoting the overall resilience of ecosystems. Additionally, managing organic waste and promoting sustainable agricultural practices can further support the crucial ecosystem services provided by insects in the decomposition process.

Forensic science

Forensic Science is a multidisciplinary field that utilizes scientific methods and techniques to investigate and solve crimes. Insects, specifically forensic entomology, play a crucial role in this field by providing valuable information about the time, location, and circumstances surrounding a crime. Here's an overview of how insects are used in forensic science:Estimation of Postmortem Interval (PMI): One of the primary applications of forensic entomology is the estimation of the postmortem interval, which is the time elapsed since death. Insects colonize a body shortly after death, attracted by the decomposition process. By studying the insect species, their life cycle stages, and the temperature-dependent development rates, forensic entomologists can determine the approximate time of death or the period when the body was exposed.

Succession Patterns:

Insects follow a predictable pattern of colonization and succession on a decomposing body. Different species of insects arrive and depart at different stages of decomposition. By studying the insect succession pattern, forensic entomologists can gain insights into the timeline of events, such as whether a body has been moved or disturbed after death.

Identification of Human Remains:

Insects associated with human remains can provide important evidence for identification purposes. For example, certain species of blowflies are attracted to decomposing flesh and can help indicate the presence of human remains. The presence of specific insects or their life stages on a body can provide valuable information to forensic investigators.

Determination of Manner and Cause of Death:

Insects can also provide clues about the manner and cause of death. For instance, the presence of certain species of insects, such as those associated with decomposing bodies found in water, may suggest drowning as the cause of death. Insects can also help detect the presence of toxins or drugs in the body through their feeding activities.

Location of Crime Scenes:

Insects collected from a crime scene can provide insights into the location of the event. By analyzing the insect fauna present, forensic entomologists can determine whether the crime scene is indoors or outdoors, rural or urban, or associated with specific environmental conditions. This information can assist investigators in narrowing down their search and focusing their efforts.

Case Reconstruction and Legal Proceedings:

Insect evidence can be crucial in reconstructing the events surrounding a crime. The data collected from insect specimens, along with other forensic evidence, can help create a timeline, corroborate or challenge witness statements, and support the prosecution or defense during legal proceedings.Forensic entomology has proven to be a valuable tool in solving crimes and providing critical information to investigators. The use of insects in forensic science helps determine the postmortem interval, establish the sequence of events, identify human remains, and contribute to the overall understanding of crime scenes. Continued research and advancements in this field further enhance its applicability and reliability in forensic investigations.

Food web dynamics:

Insects are integral components of food webs, serving as prey for numerous organisms, including birds, mammals, reptiles, and other insects. They provide a vital food source for higher trophic levels, influencing population dynamics and energy transfer within ecosystems.Insects play a crucial role in food webs as an integral component of the trophic structure within ecosystems. They serve as a vital food source for numerous organisms, including birds, mammals, reptiles, and other insects. Here's an overview of their significance in food webs and their influence on population dynamics and energy transfer:

Prey Base:

Insects form a significant portion of the prey base for many organisms. Birds, such as swallows and flycatchers, rely heavily on insects as a primary food source, especially during the breeding season when they need to feed their young. Mammals, such as bats and shrews, also consume large quantities of insects. Additionally, reptiles, amphibians, and other insects themselves rely on insects as a crucial part of their diet.

Energy Transfer:

Insects serve as a conduit for energy transfer within ecosystems. They efficiently convert energy from primary producers, such as plants, into a form that is accessible to higher trophic levels. Through their feeding activities, insects transfer energy from plants to predators, thereby facilitating the flow of energy through the food web. This energy transfer is essential for sustaining populations at higher trophic levels and maintaining ecosystem stability.

Population Dynamics: Insects can influence the population dynamics of both predators and prey. Fluctuations in insect populations can have cascading effects on other trophic levels. For example, if there is a decline in insect populations due to factors such as climate change, habitat loss, or pesticide use, it can directly impact the abundance and reproductive success of insectivorous birds, mammals, and other predators. Conversely, when insect populations experience outbreaks, it can lead to an increase in predator populations (Woodcock, *et al*.2016).

Trophic Interactions: Insects participate in complex trophic interactions within food webs. They can be both herbivores, consuming plant material, and predators, feeding on other organisms. This dual role allows insects to directly influence the abundance and distribution of plant populations, shaping plant communities and affecting the overall structure of ecosystems. Additionally,

certain insects also act as parasites or parasitoids, influencing the survival and behavior of their host organisms.

Biodiversity and Stability: Insects contribute to the biodiversity and stability of ecosystems. Their presence and diversity support a wide range of other organisms in the food web. Insect diversity ensures the availability of a variety of prey items for predators, helping to maintain a balance in population sizes and reducing the risk of prey depletion. The loss of insect species can have far-reaching consequences for the stability and functioning of ecosystems.Understanding the role of insects in food webs emphasizes their importance in sustaining ecological balance and the interconnectedness of species within ecosystems(Wagner, *et al.* (2011). The conservation and protection of insect populations are crucial for maintaining biodiversity, promoting ecosystem health, and ensuring the availability of food resources for higher trophic levels.

Habitat Engineers: Certain insect species act as habitat engineers by modifying their environment. For example, ants construct intricate underground tunnels, termites build mounds, and leafcutter bees create nests from leaves. These activities can influence soil structure, plant growth, and microhabitat availability, affecting the overall ecosystem structure and function.

Pest Control and Regulation: While some insects are considered pests due to their impact on crops or human activities, many insects also provide natural pest control services. Predatory insects, such as ladybugs and lacewings, feed on agricultural pests, helping to regulate their populations and reduce the need for chemical pesticides.

Indicator Species: Insects can serve as indicators of ecosystem health and environmental change. Sensitivity to environmental conditions makes them responsive to habitat degradation, pollution, and climate change. Monitoring changes in insect populations and diversity can provide valuable insights into the overall health and stability of ecosystems.

Biodiversity and Ecological Balance: Insects represent a significant portion of global biodiversity, with estimates of millions of species yet to be discovered. Their diversity and abundance contribute to the overall ecological balance of ecosystems (Winder, & Alexander, 2019). The loss of insect populations can have cascading effects on other organisms and disrupt ecosystem functioning.Understanding the ecological roles of insects and their interactions within ecosystems is vital for conserving biodiversity, maintaining ecosystem services, and ensuring the sustainability of natural systems.

Conservation efforts aimed at protecting insect populations, preserving their habitats, and promoting sustainable land management practices are crucial for maintaining healthy and resilient ecosystems (Yang, *et al.*2021).

Conclusion

Insect ecology is a fascinating field that unravels the vital role of nature's tiny architects in shaping ecosystem dynamics. The interactions between insects and their environment, including energy flow and nutrient cycling, have a profound impact on the functioning of ecological systems. Insects, with their abundance and diversity, serve as integral components of trophic structures and food webs, providing essential food sources for various organisms. The vitality of insects lies in their multifaceted contributions to ecosystem processes. They perform crucial functions such as pollination, decomposition, herbivory, and predation, which influence the structure and functioning of ecosystems. Their remarkable adaptations and behaviors enable them to occupy diverse habitats and respond rapidly to environmental changes, making them important indicators of ecosystem health and stability.

Understanding insect ecology is paramount for effective ecosystem management and conservation. Conserving insect biodiversity not only preserves nature's intricate tapestry but also ensures the continuity of vital ecosystem services, including pollination and decomposition. Moreover, studying insect ecology provides insights into the potential impacts of climate change, habitat loss, and other human-induced disturbances on ecosystem functioning. In conclusion, unveiling the vitality of nature's tiny architects in ecosystem dynamics highlights the invaluable role that insects play in maintaining ecological balance. By appreciating their diversity, abundance, and intricate interactions, we can foster sustainable practices and safeguard the health and resilience of our ecosystems for future generations.

Insects, as vital components of ecosystems, play an indispensable role in maintaining ecological balance and functioning. Through their diverse interactions with the environment and other organisms, insects contribute to energy flow, nutrient cycling, pollination, decomposition, and predation, among other ecological processes. Their remarkable adaptations and behaviors enable them to occupy various niches and respond to environmental changes, making them important indicators of ecosystem health.The significance of insects in ecosystem dynamics extends beyond their ecological functions. They serve as essential food sources for numerous organisms, shaping the trophic structure and food webs within ecosystems. Insects also contribute to the

biodiversity of ecosystems, with their abundance and diversity enriching the overall species richness and ecological resilience.

However, insects face numerous challenges, including habitat loss, climate change, pollution, and pesticide use, which threaten their populations and the ecosystems they inhabit. The decline of insect populations can have cascading effects on other species and ecosystem processes, leading to imbalances and disruptions. Recognizing the crucial role of insects in ecosystems is crucial for effective conservation and sustainable management practices. Conservation efforts should focus on preserving and restoring insect habitats, promoting biodiversity-friendly agricultural practices, reducing the use of harmful pesticides, and raising awareness about the importance of insects in maintaining ecosystem health.

In conclusion, insects are key players in the intricate web of life, contributing to the stability, productivity, and diversity of ecosystems. Understanding and valuing their ecological roles is essential for the conservation and sustainable management of our natural environments. By protecting and promoting the well-being of insects, we safeguard the integrity and resilience of ecosystems for current and future generations

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Role of BCL2 and ERK 1 / 2 in Myocardial Ischemia

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Abstract

Myocardial ischemia is one of the important cardiovascular diseases. In modern era of molecular medicine, deep understanding the crucial role of various conserved signaling molecules helps to gain knowledge about pathophysiology and the molecular mechanisms. The aim of this paper to emphasize the role of BCL2 and ERK 1 / 2 signaling transduction pathway in myocardial ischemia. Deep understanding the role is need of the hour to further explore the therapeutic approaches and lead to the discovery of novel remedial strategies.

Keywords: Myocardial ischemia, Myocardial Ischemic-reperfusion injury (IRI), BCL2 /Bax regulatory genes, ERK 1 / 2 signaling transduction pathway, molecular mechanism.

Introduction

As per WHO, it is estimated that 17.9 million people died from CVDs in 2019, representing 32% of all global deaths. Of these deaths, 85% were due

to heart attack and stroke[1].Ischemic heart disease (IHD) is one of the life-threatening and most prevalent cardiovascular (CVD) diseases. Myocardial ischemia (MI) is an ischemic disease which occurs when there is an imbalance between the coronary blood supply and demand, causes deficient of oxygen in myocardium[2]. It may due to impairment in various factors such as myocontractility, heartrate and the diastolic ventricular pressure[3].Although, clinical interventions and innovations are wide, public awareness has improved, myocardial ischemia remains the dominant cause of death throughout the world[4].

Pathophysiology of myocardial ischemia:

The process of MI initiates with the ultrastructural changes, followed by mitochondrial alterations. The prolonged ischemia results in liquefactive necrosis of myocardial tissue, which spreads from sub-endocardium to sub-epicardium[5].Clinical manifestations are due to narrowing of epicardial coronaryarteries, atherosclerotic plaque, and micro vascular dysfunctionwhich may seriously damage the myocardium and result in severeischemia. Once ischemia is triggered, hypoxic condition prevails in the myocytes. Anaerobic glycolysis begins, followed by tissueacidosis from the lactate production, coronary sinus oxygendesaturation, ion pump disturbances causing an increase in Na+and Ca2+, decrease in pH, and reduction of adenosine triphosphate (ATP) availability are some of the important validates of myocardialischemia[6].

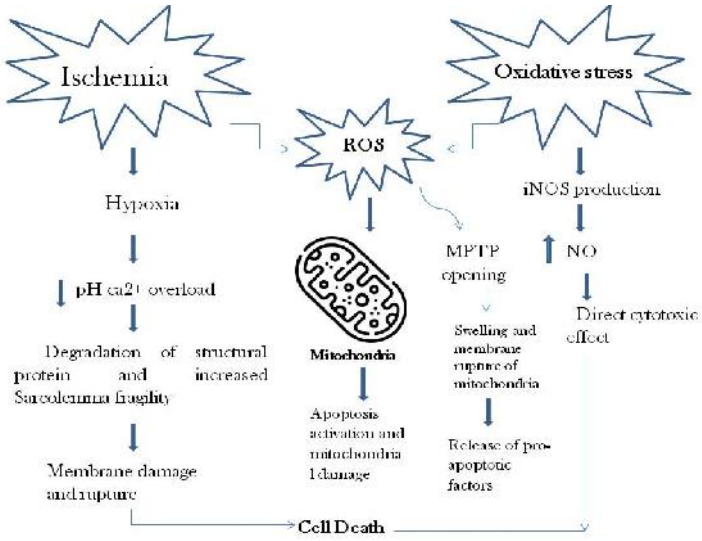

Fig 1: Schematic representation of Myocardial ischemia contributing to tissue injury and cell death

Multiple plays of BCL2

BCL2 (B-cell lymphoma 2), a mitochondrial membrane protein, called as anti-apoptotic gene.it is one of the important gene which prevents cells undergoing apoptosis[7].BCL-2 family proteins, are localized in inner mitochondrial membrane, many ofthese also seen at the Endoplasmic Reticulum (ER) and nuclear envelope[8].The BCL2 gene family possesses eight additional homologs such as BCL-x_L, MCL-1, BCL-w, BFL-1/A1, BCL-B, BAX, BAK, and BOK. The size ranging from 20 to 37 kDa .Also, five amino acid sequenceBCL2L12, BCL-Rambo (BCL2L13), BCL-G (BCL2L14), BFK (BCL2L15), and BID are some of the less related proteins sharing significant similarity have been identified in the human genome[9].

BAX & BAK are pro-apoptotic effectorproteins involve in mediating mitochondrial outer membrane permeabilization (MOMP).BCL-x_L, MCL-1, BCL-w, BFL-1/A1, prevents the action of mitochondrial outer membrane permeabilization (MOMP).Whereas, BH3 pro-apoptotic proteins,the only protein which promote apoptosis either directly by binding and oligomerizing BAX and BAK indirectly by neutralizing anti-apoptotic family members[10,11,12,13].

Intrinsic mitochondrial pathway gets activated, as soon as Cytochrome C from mitochondria leaked in the cytoplasm. Caspase9 facilitates the caspasecascades[14,15,16]. As a result, initiation of biochemical alterations, which is regulated by the BCl2 and its family members[17,18,19].BCL2 works against apoptosis, while BAX stimulates it[20].When BAX expression is high, homodimer BAX/BCL is formed to stimulate apoptosis, and when BCL-2 expression is high, heterodimer BCL-2/BAX is formed to inhibit the occurrence of apoptosis[21,22].

BCL2 over expression increasethe lifespan of B cells and maintains memory B cells, plasma cells and neurons by prolonging life span without cell division. It may participate in ion channel formation and alteration of membrane permeability, necessary for initiation of apoptosis. Non-phosphorylated BCL2 inhibits apoptosis, and BAX homodimers normally cause apoptosis, canbind, and inhibit non-phosphorylated BCL2, promoting apoptosis.

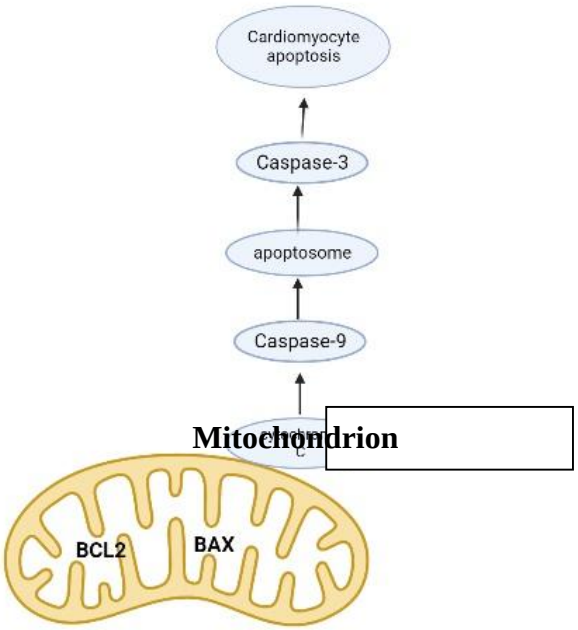

Fig 2: Schematic representation of BCL2/BAX regulated apoptotic process

BCL2 Expression in myocardial ischemia

Considerable evidence supports that necrosis and apoptosis are involved in various cardiovascular diseases such as congestive heart failure, myocardial ischemia, and reperfusion injury. Although, necrosis and apoptosis, ends in the cell death, their mechanism, cellular and morphological aspects are different[23-26]. Necrosis is a type of cell death due to tissue injury, trauma, toxins and infection with certain viruses, results in the loss of membrane integrity, swelling and depletion of ATP[27].Whereas, apoptosis is a programmed cell death, highly regulated and energy requiring process.Various regulatory proteins are involved[23].in balancing the play between the pro-and anti-apoptotic proteins. One such important regulatory proteinis BCL-2 family. These protein members consolidate the survival and death signals to decide the fate of the cells.

During MI, cell prevails to hypoxic conditions and the reactive oxygen species (ROS) are formed causes, oxidative stress to the myocardium.This impairs the antioxidant system, results in the elevations of antioxidant enzymes

like superoxide dismutase (SOD), Catalase (CAT)[28]. Intracellularly, mitochondrial apoptotic signaling cascades activated because of the imbalance in the oxidants and anti-oxidants.BCL2, an anti-apoptotic and anti-oxidant proteininvolve in inhibiting the apoptosis whereas Bax, a pro-apoptotic member of BCL2 family[29-31]·induces the apoptosis when it is over expressed. The expression of these regulatory proteins, BCL-2 and Bax, has been studied in the hearts of patients who died of AMI[32].

In a normal myocardium, majority of Bax is found in the cytosol, but apoptotic signaling activated. On rapid activation, Bax translocate to the mitochondria to form protein-permeable pores on its membranes. Cytochrome C and pro-apoptotic factors are released into cytosol, stimulates Apaf-1 and Caspase-9 to form apoptosomes, and then activates Caspase-3, leading to cell death[30,31,33]. In myocardial ischemia, increased expression of Bax and decreased expression of BCL2 indicates the role of these regulatory proteins in the experimental study on the ischemia induced apoptosis in rats[23].

ERK 1 / 2 Signalling pathway

Extracellular signal-regulated kinase 1/2 (ERK), is one of the important cell signaling pathways, belongs to the mitogen-activated protein kinase (MAPK) family. It is a kind of serine/threonine protein kinase that transmits the mitogen signals. It involves in regulating a wide variety of stimulated cellular processes, such as proliferation, differentiation, and survival, apoptosis, and the stress response[34,35].

ERK signaling molecules are the highly regulated cascades which transfers extracellular signals to intracellular targets. It transmits the signal by regulating the activity and expression of multiple nuclear transcription factors and cytosolic proteins. Viruses, cytokines, growth factors, G-protein coupled receptor ligands and some oncogenes are some of the stimulators involved in the activation of ERK pathway.

Around 200 distinct substrates of ERK1/2 accounts for the induction and regulation of various ERK1/2-dependent processes[36,37.] TheERK signaling molecules activated through the external stimulus and reach the nucleus with the double phosphorylated molecules. It has three subsystems involves in the formation of the SOS complex, ShC-Grb2-SOS, from the extracellular growth factors. The SOS complex, mediates the activation of Ras is the second subsystem. Third subsystem constitutes Ras which activates the double phosphorylated ERK, the MAPK subsystem (or the Raf-MEK-ERK

pathway)[38].Among the five subgroups ERK1 –ERK5, ERK_1 and ERK_2 are the most widely studied subgroups, both express 90% homology[39].

ERK1 / 2involves in regulating the transcription factors of pro-apoptotic and anti-apoptotic activity. ERK cascades enhances the activity of anti-apoptotic proteins, promotes cell-survival by upregulation of transcription factors.Insame way,down regulating the transcription factors to decrease the activity of pro-apoptotic molecules.

ERK 1/2 Expression in myocardial ischemia

Abnormal activation of ERK 1/2 signaling pathway plays a crucial role in the development of worsening the pathophysiological role ofmyocardial ischemia and reperfusion injury.The occurrence of ischemia-reperfusion injury (IRI), terribly serious in the aging heartand other vital organs such as brain, kidney, and various other organs. Elevation of ERK1 / 2 signaling pathway is closely related to the development and the metabolic mechanisms of IRI[40].During ischemia, numerous endogenous protective signals are activated to protects heart, which is compromised in the aging heart of the population around the world.

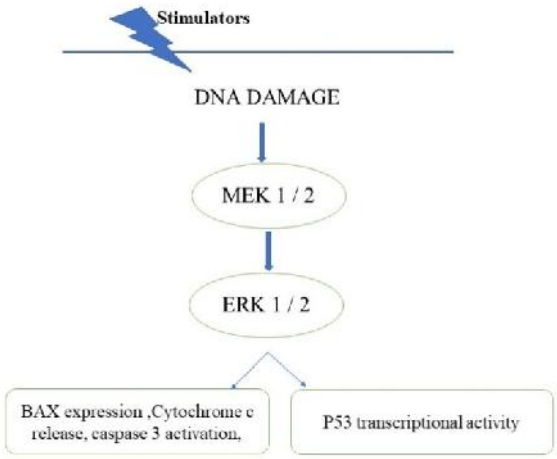

Fig 3: Schematic representation of ERK 1 / 2 in response to some DNA damage stimuli

Promotes cell apoptosis by enhancing activity of some pro-apoptotic signaling molecules. p38 signaling indirectly regulates the anti-apoptotic effect of ERK1/2[41-43].The mechanism by which ERK1/2 activation inhibits apoptosis is complicated and varies, depending on the cell and tissue type involved and the cellular regulatory influences that the cell receives.

Conclusion

In Recent days, variousinvestigations are carried out to improve the prognosis of MI treatment involving both pre and post therapy. It is reported in many research interventions that signaling cascades are the important therapeutic target of cardiovascular diseases.The BCL2 and ERK1/2 are the important regulatory genes expressed by either upregulating and downregulating during the anti-apoptotic and sometimes pro-apoptotic activity.Increasing number of studies have reported that activating the signaling pathway plays a protective role in MI, myocardial ischemia and Ischemic - reperfusion injury.

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Current updates on intra aortic Ballon pump- A mechanical life saver

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Abstract

An intra-aortic balloon pump (IABP) is a invasive mechanical device that helps the heart to pump more amount blood and improves coronary perfusion, on the same hands it reduces the work load of heart. An intra-aortic balloon pump connects to a machine which controls it when to inflate and deflate. The balloon is filled with helium gas, which reduces the chance of air embolism during accidental situations such as balloon rupture. IABP works on the principle of counter pulsation, balloon deflates at systolic phase (when your heart pumps blood out), then inflates during diastolic phase (when your heart relaxes), This phenomenon is known as counter pulsation. Deflation helps in pumping the blood throughout the body and inflation helps in improving both the systemic circulation and coronary circulation of heart. In this review we focused on current updates on IABP, its mechanism,triggers, augmentation, indication and contraindications.

Keywords: Intra-aortic balloon pump (IABP), Augmentation, ECG Trigger, Pressure Trigger, Counter Pulsation.

Introduction

An intra-aortic balloon pump (IABP) is a invasive mechanical device that helps the heart to pump more amount blood and improves coronary perfusion, on the same hands it reduces the work load of heart.Intra-aortic balloon pump (IABP) is one of the widely used circulatory assist device in critically ill patients with cardiac disease, especially in bradycardia condition with ischemic myocardial damage.

IABP is most frequently used mechanical circulatorysupport devicein the world, which was introduced byMoulopoulos at el in 1962 and described clinically by kantrowitz at et al in 1968.It offers the least complicated means of circulatory assistance.IABP catheter has two channels one for the passage of helium gas used to inflate and deflate the balloon.Other for direct monitoring of the arterial pressure inside the aortic lumen.Helium gas line is connected to a console that regulates the inflation and deflation of the balloon with the passage of helium.Helium is used because it is easily dissolved in blood and prevents the risk of air emboli if the catheter ruptures.Operation of the balloon is triggered with the ECG or Aortic pressure wave form, which inflates during diastole and deflates just before systolic ejection.

The National Centre of Health Statistics estimated that IABP was used in 42 000 patients in the USA in 2002. Advances in technology, including percutaneous insertion, smaller diameter catheters, sheathless insertion techniques, and enhanced automation, have permitted the use of counter pulsation in a variety of settings, with greater efficacy and safety.The balloon is filled with helium gas, which reduces the chance of air embolism during accidental situations such as balloon rupture. IABP works on the principle of counter pulsation, balloon deflates at systolic phase (when your heart pumps blood out), then inflates during diastolic phase (when your heart relaxes), This phenomenon is known as counter pulsation. Deflation helps in pumping the blood throughout the body and inflation helps in improving both the systemic circulation and coronary circulation of heart.

The primary goal of Intra-aortic balloon pump (IABP) treatment is to increase myocardial oxygen supply and decrease myocardial oxygen demand and also reduces the workload of heart. Juxtarenal balloon positioningcan lead to decreased urine output after the insertion of IABP. Haemolysis from mechanical damage to red blood cells can reduce the haematocrit by up to 5%. Suboptimal timing of inflation and deflation of the balloon produces haemodynamic instability. An IABP is highly thrombogenic, so before initiating IABP, the patient should always be anticoagulatedby using heparin.

Principles of IABP

IABP exerts it's effect by volume displacement and pressurechanges caused by rapidly shuttling helium gas in and out of the balloon chamber.This principle is called counter pulsation.Counterpulsation stands for balloon inflation in diastole and deflation in systole.

99% of coronary artery perfusion take place during the diastolic phase of cardiac cycle.During systole of cardiac cycle balloon deflates and balloon entering into aorta, that will decrease the workload of heart.When diastolic phase of cardiac cycle balloon inflate that will create a pressure in aorta,blood will enter into coronary artery thereby myocardial oxygen delivery is improved.

Figure 1

Figure 1 represents the Intra-Aortic Balloon Pump (IABP)

Position

The balloon should be placed 2 cm below the subclavian artery of aorta, and above the renal artery which should not occlude either renal artery or subclavian artery.

Effects of IABP

IABP increases diastolic aortic pressure, cardiac output and coronaryblood flow of heart and also increases the cerebral blood flow and renal blood flow.It also increases ejection fraction, pulse rate and systemic blood pressure and systemic perfusion. At the same time, it decreases left ventricular wall tension, preload and afterload, which maintains central venous pressure and pulmonary congestion.

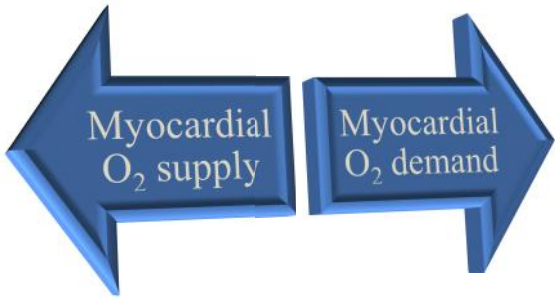

Figure 2

Figure 2 represents effect of IABP which maintains the myocardial oxygen supply and myocardial oxygen demand in equilibrium state.

Techniques of insertion

Percutaneous insertion and femoral artery cut down insertion are the most common techniques of IABP insertion, if these two techniques are not possible, intraoperatively inserting via ascending aorta, 2 cm below the subclavian artery, or else subclavian and trans-axillary insertion can be done.

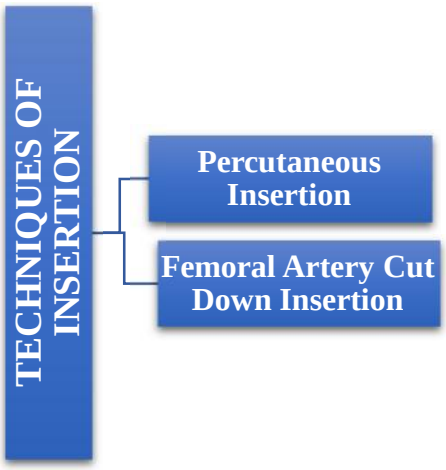

Figure 3

Percutaneous insertion

It is one of the minimal invasive procedures of IABP insertion, it is performed by wire guided technique, which provides a minimal blood loss compared to other methods of IABP insertion. This procedure can be followed out under local anesthesia.

Femoral artery cut down insertion

It is one of the invasive procedures of IABP insertion used commonly in obese or heavy weight patients and when percutaneous insertion is not possible. This procedure allows visualization of artery directly, the balloon can be inserted directly into the artery by using this procedure. This procedure can be followed either by using Dacron graft or using percutaneous sheet.

Timing of IABP

The precise timing of balloon inflationand deflation is essential to achievethe haemodynamic effect that increase coronary blood flow and decrease the workload of heart. Timing triggers are usually ECG, Mean Arterial Pressure (MAP), PACER A,PACER V/AV, Internal. When IABP is on ECG trigger, balloon deflates during R wave of ECG and inflates during mid T wave of ECG. Tachyarrhythmias, cardiac pacemakers, and poor ECG signals may cause difficulties in obtaining synchronization when the ECG mode is used. In such cases the arterial waveform may be useful for triggering.When IABP is on MAP trigger, balloon deflates during systolic BP and inflates during diastolic BP.

Figure 4

Figure 4 represents monitor of IABP

Normal timing of the IABP with inflation at the dicrotic notch (DN) and good diastolic augmentation, which increases coronary blood flow and increases mean blood pressure. Assisted systolic and end-diastolic pressures are lower than unassisted systolic and end-diastolic pressures.

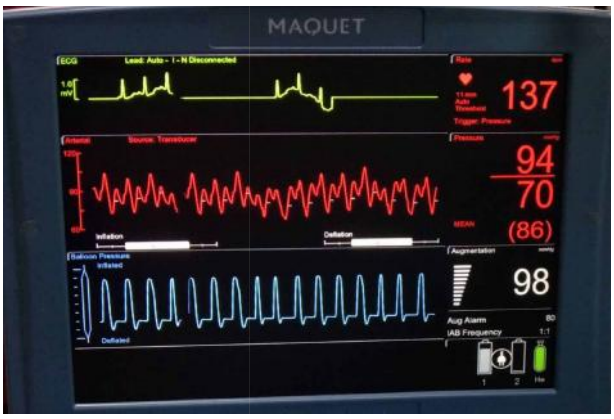

Figure 5

The most common cause of inadequate balloon counter pulsation is due to the inaccurate timing of inflation and deflation. Some errors associated with IABP timing will simply result in poor hemodynamic response to IABP, but

others are more dangerous for patients with already tenuous cardiovascular situations. The timing errors can be divided into two groups: systolic errors (early and late inflation) and diastolic errors (early and late deflation).

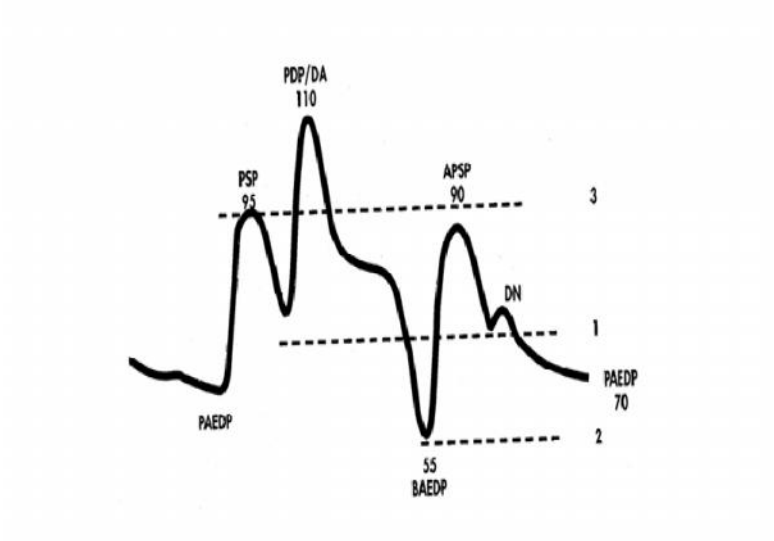

Figure 6

1.Inflation just prior to the dicrotic notch If > 40 ms before -> early inflation If dicrotic notch exposed -> late inflation 2. Deflation BAEDP < PAEDP BAEDP = Balloon Aortic End Diastolic Pressure PAEDP = Patient Aortic End Diastolic Pressure If violated -> late deflation 3. Deflation: Assisted Systole (APSP) < Peak PSP = Peak Systolic Pressure APSP = Assisted Peak Systolic Pressure If violated -> early deflation (Figure 5)

Indications of IABP

- Unstable angina
- Unstable Bradycardia
- Cardiogenic shock
- Acute myocardial infarction
- Mechanical complications of MI
- Adjunct to PTCA
- Adjunct to cardiac catheterization
- Bridge to cardiac transplant

Contraindications of IABP

- Abdominal aneurysm
- Thoracic aneurysm
- Aortic dissection
- Occluded aorta
- Aortic insufficiency
- Severe peripheral vascular diseases
- Chronic cardiomyopathy

Complications

- Aortic intimal layer rupture
- Aortic dissection
- Limb ischemia
- Thromboembolism
- Vascular injury
- Infection
- Severe bleeding
- Heparin induced thrombocytopenia
- Balloon rupture

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Wings of vulnerability: Understanding the impact of toxicants on avian species

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Abstract

Avian species, or birds, play essential roles in ecosystems, but they are increasingly facing threats from toxicants. Toxicants are harmful substances that can have severe physiological and ecological consequences when birds come into contact with them. This abstract provides an overview of the effect of toxicants on avian species, focusing on their exposure, mechanisms of toxicity, and implications for bird populations. Birds can be exposed to toxicants through ingestion, inhalation, or absorption through their feathers and skin. Common sources of toxicants include pesticides, heavy metals, petroleum spills, and air pollution. These substances can disrupt the nervous system, impair reproductive capabilities, suppress the immune system, and bioaccumulate in bird tissues. The presence of toxicants in avian populations has significant ecological implications. It can disrupt ecosystems by affecting pollination, seed dispersal, and nutrient cycling. Additionally, the decline of bird populations can have cascading effects on other organisms. Conservation efforts are being undertaken to mitigate the effects of toxicants on avian species. These efforts include regulatory measures, habitat protection, public awareness, and education. By understanding the sources and mechanisms of toxicity, and implementing responsible environmental practices, we can work towards creating a safer and healthier environment for avian species to thrive. In conclusion, toxicants pose a significant threat to avian species, affecting their health, reproduction, and ecological roles. By addressing these challenges through conservation and responsible practices, we can protect avian populations and preserve the vital contributions they make to our ecosystems.

Keywords: Avian species, Toxicants, Neurological effects, Reproductive impacts. Immunotoxicity Bioaccumulation, Ecological implications, Conservation

Introduction

Avian species, commonly known as birds, play vital roles in our ecosystems, from pollination and seed dispersal to controlling insect populations. However, these magnificent creatures are increasingly facing numerous threats in their habitats, including the presence of toxicants. Toxicants are substances that have harmful effects on living organisms, and when birds come into contact with these toxic substances, they can have severe physiological and ecological consequences. In this chapter, we will explore the impact of toxicants on avian species, focusing on their exposure, mechanisms of toxicity, and the implications for bird populations. we delve into the world of avian vulnerability and explore the profound impact of toxicants on these captivating creatures.

Toxicants, often originating from human activities, encompass a wide range of harmful substances. Pesticides, heavy metals, petroleum spills, and air pollution are among the common culprits that pose a significant threat to avian species. Birds can come into contact with toxicants through direct ingestion, inhalation of contaminated air, or absorption through their feathers and skin. The consequences of such exposure can be dire, leading to various physiological and ecological disturbances. Understanding the mechanisms of toxicity is key to comprehending the profound effect toxicants have on avian species. Neurological effects, such as impairment of motor function and coordination, can arise from the inhibition of crucial enzymes in the nervous system. Reproductive impacts, including reduced hatching success and altered hormone levels, jeopardize the continuation of avian populations. Additionally, the immune system of birds can be compromised, rendering them more susceptible to diseases and infections. Moreover, the bioaccumulation of certain toxicants in bird tissues over time poses long-term risks, particularly for higher trophic-level species.

The implications of toxicant exposure on avian species extend beyond individual health concerns. Ecosystems rely on intricate interactions between different organisms, and the decline of bird populations can disrupt vital ecological processes. Pollination, seed dispersal, and nutrient cycling are among the ecosystem services that birds provide, playing critical roles in maintaining biodiversity and ecosystem stability. The loss of certain bird species can have cascading effects, leading to imbalances in insect populations,

altered plant communities, and a ripple effect on other wildlife. Recognizing the urgency of this issue, conservation efforts are being undertaken to mitigate the effects of toxicants on avian species. Regulatory measures have been implemented to restrict the use of certain toxic substances, and habitat protection initiatives aim to preserve crucial avian habitats. Public awareness and education play a crucial role in fostering responsible environmental practices, emphasizing the importance of proper waste disposal, responsible pesticide use, and supporting conservation initiatives. In this exploration of "Wings of Vulnerability: Understanding the Impact of Toxicants on Avian Species," we embark on a journey to uncover the intricate relationship between toxicants and avian health. By gaining a deeper understanding of the sources, mechanisms, and ecological implications of toxicant exposure, we can work towards safeguarding these majestic creatures and the ecosystems they inhabit. Together, we can ensure a world where avian species can thrive, spreading their wings and inspiring us with their presence for generations to come.

Sources of toxicants

Toxicants can originate from various sources, both natural and human-made. Birds can be exposed to toxic substances through direct ingestion, inhalation of contaminated air, or absorption through their feathers and skin. Some of the primary sources of toxicants affecting avian species include:

Pesticides:

Birds are often exposed to pesticides, such as insecticides, herbicides, and rodenticides, which are commonly used in agricultural practices. Birds may directly consume treated seeds or prey on insects that have been exposed to these chemicals.Pesticides, which are chemical substances used to control pests and diseases in agriculture and other industries, have become a significant concern in relation to their impact on avian species. Birds can be exposed to pesticides through various pathways, including direct ingestion of treated seeds, consumption of contaminated prey or water, and exposure to pesticide drift or runoff. The presence of pesticides in avian habitats has been associated with a range of detrimental effects on bird populations, as outlined below.

Acute Toxicity:

Many pesticides, particularly insecticides, are designed to be highly toxic to target pests. Unfortunately, birds can also be affected by these chemicals, especially if they directly consume pesticide-treated seeds or insects. Acute pesticide poisoning can result in rapid and severe health effects, including impaired coordination, muscle tremors, convulsions, and even death.

Chronic Toxicity:

Prolonged exposure to low levels of pesticides can lead to chronic toxicity in avian species. Chronic exposure often occurs when birds consume prey or plants that have accumulated pesticides over time. This type of toxicity can result in a range of sublethal effects, including reproductive issues, immune system suppression, impaired growth and development, and hormonal disruptions. For example, some pesticides have been shown to cause eggshell thinning in birds, leading to reduced hatching success and population decline.

Disruption of Reproductive Success:

Pesticides can have significant impacts on avian reproductive success. Exposure to certain pesticides, such as organochlorine insecticides (e.g., DDT), can interfere with hormone regulation and lead to decreased fertility and hatching rates. Moreover, the exposure of parent birds to pesticides can result in impaired parental care, reduced nest attendance, and compromised nest-building behaviors, which can further impact the survival and well-being of offspring.

Altered Behavior and Foraging Patterns:

Pesticide exposure has been observed to alter avian behavior and foraging patterns. Some pesticides can impair cognitive function and motor skills, making birds more susceptible to predation or hindering their ability to find food and mates. Additionally, changes in the abundance and diversity of insect populations due to pesticide use can disrupt the food availability for insectivorous bird species.

Indirect Effects on Food Web Dynamics:

Pesticides not only directly affect birds but can also have indirect effects on the wider ecosystem. For instance, the decline of insect populations due to pesticide use can impact avian species that rely on insects as their primary food source. This disruption in food web dynamics can have cascading effects on other organisms and ecological processes within the ecosystem.

Efforts to mitigate the impact of pesticides on avian species include the development and promotion of integrated pest management (IPM) practices, which aim to minimize pesticide use by employing alternative pest control methods. Additionally, implementing buffer zones between treated areas and avian habitats, adopting targeted application techniques, and promoting the use of less toxic and more environmentally friendly pesticides can help reduce the negative impacts on avian populations. The effect of pesticides on avian

species is a significant concern due to their potential acute and chronic toxicity, disruption of reproductive success, altered behavior, and indirect impacts on food web dynamics. Recognizing the potential risks and implementing responsible pesticide use practices can help safeguard avian populations and maintain the balance of ecosystems in which they play crucial roles

Heavy Metals:

Industrial activities and pollution can lead to the release of heavy metals such as lead, mercury, and cadmium into the environment. Birds can be exposed to these metals by ingesting contaminated food, water, or soil.Heavy metals, such as lead, mercury, cadmium, and arsenic, are toxic substances that can have detrimental effects on avian species. These metals are often released into the environment through industrial activities, mining, combustion of fossil fuels, and improper waste disposal. Avian species can be exposed to heavy metals through various pathways, including ingestion of contaminated food, water, or soil. The presence of heavy metals in avian habitats has been associated with a range of adverse effects on bird populations, as outlined below.

Impaired Reproduction:

Heavy metals can significantly impact avian reproductive success. Exposure to metals like lead and mercury can lead to reduced fertility, decreased hatching success, and abnormal development of offspring. Some heavy metals, such as lead, can also cause eggshell thinning, resulting in weakened eggs and increased vulnerability to predation or breakage during incubation.

Neurological and Behavioral Effects:

Heavy metals can have neurotoxic effects on avian species. They can disrupt the normal functioning of the nervous system, leading to impaired motor function, altered behavior, and reduced cognitive abilities. Birds exposed to high levels of heavy metals may exhibit abnormal or erratic behaviors, including impaired flight, disorientation, and difficulty with feeding or reproduction.

Immunotoxicity:

Exposure to heavy metals can suppress the immune system of avian species, making them more susceptible to diseases and infections. Metals such as cadmium and mercury can disrupt immune function, compromising the

bird's ability to mount an effective immune response against pathogens. This can result in increased disease susceptibility and reduced overall fitness.

Bioaccumulation and Biomagnification:

Heavy metals have the potential to bioaccumulate in avian tissues over time. Birds that are exposed to heavy metals through their diet may accumulate these toxic substances in their bodies, particularly in organs such as the liver, kidneys, and feathers. This bioaccumulation can lead to high concentrations of heavy metals in higher trophic level birds, such as raptors, which can have severe health effects and can also biomagnify through the food chain, posing risks to other predators.

Physiological and Metabolic Disruptions:

Heavy metals can interfere with essential physiological processes and disrupt normal metabolic functions in avian species. For example, mercury can impair the function of enzymes involved in energy production and metabolism, leading to reduced energy levels and overall fitness. These disruptions can impact the growth, development, and overall health of affected birds.Efforts to mitigate the impact of heavy metals on avian species include the enforcement of regulations to control industrial emissions and promote responsible waste management practices. Additionally, habitat restoration and pollution remediation programs can help reduce heavy metal contamination in avian habitats.

Monitoring programs that assess heavy metal levels in avian populations can provide valuable data for conservation efforts and help identify areas of concern.Heavymetals pose a significant threat to avian species, affecting their reproductive success, neurological function, immune system, and overall health. Recognizing the sources of heavy metal pollution and implementing measures to reduce their release into the environment are crucial steps in protecting avian populations and preserving their important ecological roles.

Petroleum and Oil Spills:

Accidental oil spills pose a significant threat to avian species, especially those inhabiting coastal areas. Birds can become coated in oil, which affects their ability to fly, insulates them from the cold, and can lead to toxic effects when ingested during preening.Petroleum and oil spills pose a significant threat to avian species, as they can have profound and often devastating effects on birds and their habitats. These spills can occur from oil tanker accidents, offshore drilling mishaps, pipeline leaks, or improper handling and disposal of

petroleum products. Avian species can be directly affected by oil spills through exposure to oil-contaminated water, ingestion of oil-coated prey, or contact with oil-coated surfaces. The impact of petroleum and oil spills on avian species is multi-faceted and encompasses various aspects, as discussed below.

Physical Coating and Smothering:

When oil spills occur, birds can become coated in sticky and toxic substances. The oil coats their feathers, reducing their insulation properties, leading to loss of buoyancy, and impeding their ability to fly. This coating can also disrupt the natural waterproofing of feathers, leaving birds vulnerable to cold temperatures and waterlogged. As a result, affected birds may experience hypothermia, increased energy expenditure, and difficulty in feeding and escaping predators.

Respiratory Issues: The volatile organic compounds (VOCs) present in petroleum and oil spills can be inhaled by avian species, leading to respiratory problems. Birds exposed to these compounds may experience lung damage, irritation, and inflammation. Prolonged exposure to high levels of VOCs can even result in long-term respiratory complications and reduced respiratory function in affected individuals.

Toxicity: Petroleum and oil contain various toxic compounds, including polycyclic aromatic hydrocarbons (PAHs), which are particularly harmful to avian species. These compounds can be ingested by birds when they consume oil-contaminated prey or directly ingest oil droplets. The ingestion of PAHs can lead to a range of toxic effects, including organ damage, impaired immune function, and disruption of hormonal balance. Additionally, PAHs can be transferred from parent birds to their offspring, potentially impacting the development and survival of young birds.

Disruption of Feeding and Foraging: Oil spills can have significant impacts on the availability of food for avian species. Many bird species rely on coastal or marine habitats for foraging, and when these areas are contaminated by oil, their food sources become compromised. Oil can contaminate fish, invertebrates, and other prey species, making them either unavailable or toxic for birds. This disruption in the food web can lead to reduced feeding opportunities, malnutrition, and ultimately, population declines.

Habitat Destruction and Nesting Impacts: Oil spills can cause significant damage to avian habitats, particularly coastal and wetland areas. These habitats serve as critical breeding grounds, nesting sites, and foraging areas for numerous bird species. Oil can contaminate nesting materials, destroy vegetation, and render nesting sites uninhabitable. The loss of nesting habitats

can result in reduced reproductive success, decreased breeding populations, and long-term impacts on avian populations.Efforts to mitigate the impact of petroleum and oil spills on avian species include rapid response measures to contain and clean up the spills, wildlife rehabilitation programs to treat affected birds, and the establishment of protected areas and conservation initiatives to safeguard avian habitats. Implementing strict regulations and best practices in the oil industry, such as improved safety measures and spill prevention strategies, are crucial for minimizing the occurrence and severity of oil spills. Petroleum and oil spills have devastating consequences for avian species, affecting their physical well-being, respiratory health, reproductive success, and overall population dynamics. The protection and preservation of avian habitats, along with proactive measures to prevent oil spills and effectively respond to them, are essential for ensuring the survival and thriving of avian species in the face of this environmental threat.

Air Pollution:

Airborne toxicants, including sulfur dioxide, nitrogen oxides, and particulate matter, can have detrimental effects on avian respiratory systems. Birds living in urban areas or close to industrial sites are particularly vulnerable to these pollutants.Air pollution, caused by the release of harmful substances into the atmosphere from industrial activities, vehicle emissions, and other sources, poses a significant threat to avian species. Birds, as aerial creatures, are particularly vulnerable to the detrimental effects of air pollution. They can be exposed to pollutants through inhalation of contaminated air, consumption of polluted food and water, and direct contact with polluted surfaces. The impact of air pollution on avian species is diverse and can have wide-ranging consequences, as discussed below.

Respiratory Issues:

Avian respiratory systems are highly efficient but also sensitive to airborne pollutants. Birds inhale air more rapidly than mammals due to their unique respiratory anatomy, making them more susceptible to airborne toxins. Air pollution, including particulate matter, nitrogen oxides, sulfur dioxide, ozone, and volatile organic compounds, can irritate and damage the respiratory system of birds. Prolonged exposure to polluted air can result in respiratory diseases, reduced lung function, and increased susceptibility to respiratory infections.

Impaired Flight and Navigation:

Air pollution can affect the flight capabilities and navigation abilities of avian species. Fine particulate matter and smog can decrease visibility, making it challenging for birds to navigate their surroundings. Additionally, pollutants can accumulate on feathers, affecting their aerodynamic properties and reducing flight efficiency. Impaired flight and navigation abilities can have profound consequences on bird migration patterns, foraging behaviors, and overall survival.

Disruption of Breeding and Reproduction:

Air pollution can impact avian breeding and reproductive success. Pollutants, such as heavy metals and certain organic compounds, can accumulate in avian reproductive tissues, leading to reduced fertility, abnormal egg development, and decreased hatching success. Moreover, air pollution-induced changes in vegetation and food availability can negatively affect the breeding habitats and resources vital for successful reproduction.

Altered Behavior and Vocalization:

Air pollution has been shown to influence avian behavior and vocalization patterns. High levels of noise pollution from human activities, such as traffic or industrial noise, can interfere with bird communication, including mate attraction, territorial defense, and parent-offspring interactions. Changes in behavior and vocalization can disrupt social dynamics, breeding success, and overall population viability.

Ecological Impacts:

Avian species play essential roles in ecosystems as seed dispersers, pollinators, and insect controllers. Air pollution-induced declines in avian populations can have cascading effects on ecosystem functioning and biodiversity. Reductions in bird populations can disrupt seed dispersal, leading to changes in plant community composition and ecosystem dynamics. Additionally, declines in insectivorous bird populations can result in increased insect populations, potentially impacting agricultural systems and ecosystem balance.Efforts to mitigate the impact of air pollution on avian species involve reducing pollutant emissions and improving air quality. Implementing stricter regulations on industrial emissions, promoting the use of cleaner energy sources, and adopting sustainable transportation practices are vital steps in reducing air pollution levels. Preserving and restoring avian habitats, such as wetlands and forests, can also contribute to mitigating the effects of air pollution on avian species by providing cleaner air and suitable breeding

grounds. Airpollution poses a significant threat to avian species, affecting their respiratory health, flight capabilities, breeding success, behavior, and ecological interactions. Addressing the sources of air pollution and implementing measures to reduce emissions are crucial for the protection and preservation of avian populations and their vital ecological roles in maintaining healthy ecosystems

Mechanisms of toxicity

Toxicants affect birds through various mechanisms, depending on the specific substance and the route of exposure. Some common mechanisms include:

Neurological effects

Certain toxicants, such as organophosphate and carbamate pesticides, can inhibit the activity of acetylcholinesterase, an enzyme essential for proper nervous system function. This inhibition can lead to neurotoxic effects, including impaired motor function, coordination, and cognition.Toxicants, including pesticides, heavy metals, and other environmental pollutants, can have profound neurological effects on avian species. Birds, like other vertebrates, possess complex nervous systems that are vulnerable to the toxic effects of certain substances. Exposure to neurotoxicants can disrupt the normal functioning of the avian nervous system, leading to a range of neurological impairments and behavioral changes. The neurological effects of toxicants on avian species are diverse and can impact various aspects of their physiology and behavior, as discussed below.

Impaired Motor Function:

Exposure to neurotoxicants can lead to impaired motor function in avian species. Birds may exhibit difficulties in coordination, balance, and flight control. Toxicants can disrupt the transmission of nerve signals, affecting the avian brain's ability to coordinate movements. The impaired motor function can impact their ability to forage, escape predators, and engage in other vital behaviors.

Altered Behavior:

Neurotoxicants can induce changes in avian behavior. Birds may display abnormal or atypical behaviors, such as increased aggression, reduced or hyperactive activity levels, or disrupted social interactions. These behavioral changes can disrupt normal species interactions, breeding patterns, and overall ecological dynamics.

Cognitive Impairment:

Neurotoxicants can affect avian cognitive abilities. Birds exposed to certain toxicants may experience reduced learning capabilities, memory impairment, and decreased problem-solving skills. These cognitive impairments can impact foraging efficiency, predator avoidance, and overall survival in avian species.

Altered Vocalizations:

Toxicants can influence avian vocalizations. Birds may experience changes in their vocal repertoire, altered song structure, or decreased vocal performance. Vocalizations play crucial roles in mate attraction, territorial defense, and communication within avian communities. Disruption in vocalizations can impact breeding success, social interactions, and species recognition.

Neurodevelopmental Effects:

Avian species are particularly vulnerable to the neurodevelopmental effects of toxicants during embryonic and early post-hatch stages. Exposure to neurotoxicants during critical periods of brain development can lead to abnormal neural growth, impaired neuronal connectivity, and structural abnormalities in the avian brain. These developmental impairments can have long-lasting effects on cognitive function, behavior, and overall neurological health.

Disruption of Hormonal Regulation:

Some toxicants can interfere with hormonal regulation in avian species. Hormones play crucial roles in avian reproduction, molting, migration, and overall physiological homeostasis. Disruption of hormonal balance can lead to reproductive abnormalities, altered seasonal behaviors, and impaired overall health and fitness in affected birds.Efforts to mitigate the neurological effects of toxicants on avian species involve stricter regulation of toxicant use, implementing alternative pest control methods, and reducing environmental pollution. Environmental monitoring programs can help identify areas with high toxicant levels and guide conservation efforts. Additionally, preserving and restoring avian habitats can provide refuge and reduce exposure to toxicants. exposure to toxicants can have significant neurological effects on avian species, leading to impaired motor function, altered behavior, cognitive impairments, changes in vocalizations, neurodevelopmental abnormalities, and disruptions in hormonal regulation.

Reproductive Impacts

Many toxicants can disrupt the reproductive capabilities of avian species. Some pesticides and industrial chemicals, such as PCBs (polychlorinated biphenyls) and dioxins, have been linked to eggshell thinning, reduced hatching success, and altered hormone levels in birds.Toxicants, including pesticides, industrial pollutants, heavy metals, and other environmental contaminants, can have detrimental effects on the reproductive capabilities and success of avian species. Reproduction is a critical life process for maintaining healthy populations, and any disruptions in reproductive functions can have significant implications for the survival and viability of avian species. The effects of toxicants on avian reproduction are multifaceted and can manifest in several ways, as outlined below.

Reduced Fertility:

Exposure to toxicants can lead to reduced fertility in avian species. Toxicants such as pesticides and certain industrial chemicals can interfere with hormone production and regulation, disrupting the reproductive cycle. This disruption can result in decreased egg production, irregular ovulation, and impaired sperm quality, ultimately leading to reduced reproductive success.

Abnormal Egg Development:

Toxicants can also impact the development of avian eggs. Exposure to certain chemicals, such as organochlorine pesticides, can lead to thinning of eggshells, making them more susceptible to breakage during incubation or reducing their ability to provide a protective barrier for developing embryos. This can result in lower hatching success rates and decreased offspring survival.

Altered Embryonic Development:

Toxicants can negatively affect embryonic development in avian species. Exposure to certain pollutants during egg incubation can lead to developmental abnormalities, including malformations, growth retardation, and impaired organ development. These abnormalities can have long-term consequences for the survival, growth, and overall fitness of hatchlings.

Hormonal Disruption:

Many toxicants have endocrine-disrupting properties, which can interfere with the normal functioning of avian reproductive hormones. Disruptions in hormone levels and signaling pathways can affect courtship behavior, mating success, and overall reproductive behavior in avian species.

This can lead to reduced breeding activities, impaired pair bonding, and decreased reproductive output.

Nesting Habitat and Nesting Material Impairment:

Toxicants can impact avian nesting habitats and the availability of suitable nesting materials. Pollution and contamination of nesting sites can render them unsuitable for nesting or may expose birds to harmful substances during incubation. Additionally, certain toxicants can accumulate in nesting materials, affecting embryo development and hatchling health.

Parental Care and Offspring Survival:

Toxicant exposure can also impact parental care behaviors and offspring survival rates in avian species. Chemical pollutants can disrupt parental feeding patterns, decrease feeding efficiency, and impair parental vigilance, leading to reduced chick survival. This can result in reduced recruitment of new individuals into the population and population declines.Efforts to mitigate the toxicant effects on avian reproduction involve implementing stricter regulations on the use of toxic chemicals, promoting sustainable agricultural practices, and reducing pollution sources. Protecting and restoring avian habitats, particularly nesting sites, and foraging areas, can provide healthier environments for avian reproduction. Additionally, monitoring programs can help identify areas with high toxicant levels and guide conservation efforts to protect vulnerable avian populations. Toxicantscan have significant impacts on avian reproduction, including reduced fertility, abnormal egg development, altered embryonic development, hormonal disruption, nesting habitat impairment, and reduced offspring survival.

Immunotoxicity

Toxicants can suppress the immune system of birds, making them more susceptible to diseases and infections. Heavy metals, pesticides, and certain industrial pollutants can compromise the avian immune response, leading to decreased resistance to pathogens.Toxicants, including pesticides, heavy metals, industrial pollutants, and other environmental contaminants, can have detrimental effects on the immune system of avian species. The immune system plays a crucial role in protecting birds from pathogens, and diseases, and maintaining overall health. Exposure to toxicants can weaken the immune response, compromising avian immune function and increasing susceptibility to infections and other health challenges. The effects of toxicants on avian immunity include the following:

Suppression of Immune Response:

Certain toxicants can suppress or impair the avian immune response. Prolonged exposure to pesticides or industrial pollutants can disrupt the production and activity of immune cells, such as lymphocytes and macrophages. This suppression weakens the ability of the immune system to recognize and eliminate pathogens, leaving birds more vulnerable to infections and diseases.

Increased Susceptibility to Infections: Toxicants can compromise the avian immune system's ability to fight off infections effectively. Weakened immune responses can result in increased susceptibility to viral, bacterial, and fungal infections. Avian species exposed to toxicants may experience higher infection rates, longer recovery times, and more severe disease outcomes.

Altered Inflammatory Responses:

Toxicants can disrupt the balance of inflammatory responses in avian species. Inflammation is a natural immune response that helps eliminate pathogens and initiate healing. However, excessive or prolonged inflammation can be detrimental. Some toxicants can either suppress or exaggerate the inflammatory response, leading to chronic inflammation or impaired wound healing in birds.

Immunotoxic Effects on Antioxidant Systems:

Many toxicants can induce oxidative stress in avian species. Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the avian antioxidant defense system. Toxicants can generate ROS and impair the antioxidant systems, leading to cellular damage and suppressed immune function.

Impaired Humoral and Cellular Immunity:

Toxicant exposure can impact both humoral and cellular components of avian immunity. Humoral immunity involves the production of antibodies to neutralize pathogens, while cellular immunity involves the activation of immune cells to directly eliminate infected cells. Toxicants can disrupt the production of antibodies and compromise the activation and functioning of immune cells, impairing the overall immune response in avian species.

Reduced Vaccine Efficacy:

Vaccination is an essential tool in preventing infectious diseases in avian species. However, exposure to certain toxicants can reduce the efficacy of vaccines by compromising the immune response.

Weakened immune systems may not mount a robust response to vaccination, resulting in reduced protection against targeted pathogens.Efforts to mitigate the toxicant effects on avian immunity include reducing the use of toxic chemicals, implementing sustainable agricultural practices, and improving waste management to minimize environmental contamination. Creating protected habitats and minimizing stressors can also help enhance avian immune function. Additionally, monitoring avian health and implementing vaccination programs can aid in disease prevention in populations exposed to toxicants.Toxicantscan have detrimental effects on the immune system of avian species, leading to suppressed immune responses, increased susceptibility to infections, altered inflammatory responses, impaired antioxidant systems, and reduced vaccine efficacy. Protecting avian habitats, reducing toxicant exposure, and promoting overall environmental health is crucial for maintaining robust immune function in avian populations and ensuring their long-term survival.

Bioaccumulation

Some toxicants, particularly those that are persistent and fat-soluble, can accumulate in bird tissues over time. This bioaccumulation can lead to increased concentrations of toxicants in higher trophic level birds, such as raptors, with potentially adverse effects on their health and reproductive success.Toxicants, including pesticides, heavy metals, industrial pollutants, and other environmental contaminants, can have detrimental effects on the immune system of avian species. The immune system plays a crucial role in protecting birds from pathogens, and diseases, and maintaining overall health. Exposure to toxicants can weaken the immune response, compromising avian immune function and increasing susceptibility to infections and other health challenges. The effects of toxicants on avian immunity include the following:

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Ecological implications

The presence of toxicants in avian populations can have significant ecological implications. The decline of bird populations due to toxicant exposure can disrupt ecosystems by affecting pollination, seed dispersal, and nutrient cycling. Additionally, the loss of certain bird species can have cascading effects on other organisms, including increased insect populations or altered plant communities.The presence of toxicants in avian populations can have significant ecological implications. Toxicants, including pesticides, heavy metals, industrial pollutants, and other environmental contaminants, can accumulate in avian species and disrupt their physiology, behavior, and overall ecological interactions. The effects of toxicants on avian populations extend beyond individual birds and can impact entire ecosystems, as discussed below.

Disruption of Trophic Interactions:

Avian species play critical roles in various trophic levels within ecosystems. They act as predators, prey, and seed dispersers, contributing to the balance and functioning of food webs. When toxicants accumulate in avian populations, they can disrupt these trophic interactions. For example, if a predatory bird bioaccumulates high levels of toxicants, it may suffer

reproductive impairments or increased mortality, leading to imbalances in prey populations and potentially cascading effects on the entire food web.

Impacts on Biodiversity:

Avian species are essential components of biodiversity, contributing to ecosystem stability and resilience. The presence of toxicants in avian populations can negatively impact biodiversity. Birds that are particularly susceptible to toxicants or face higher exposure due to their feeding habits may experience reduced reproductive success or increased mortality. This can lead to declines or local extinctions of certain avian species, disrupting the natural diversity and functioning of ecosystems.

Altered Nutrient Cycling:

Avian species play a role in nutrient cycling within ecosystems through their feeding habits and subsequent excretion. By consuming and dispersing seeds, birds facilitate plant regeneration and contribute to nutrient cycling. However, the presence of toxicants in avian populations can affect their foraging behavior, reproduction, and survival, potentially disrupting nutrient cycling processes. Reduced seed dispersal or altered nutrient inputs can have cascading effects on vegetation composition and ecosystem dynamics.

Pollination Disruptions: Avian species, such as hummingbirds and certain bird species in tropical regions, play a crucial role in pollination. They transfer pollen between flowers, facilitating plant reproduction and contributing to the diversity of plant species. Toxicants can disrupt avian reproductive capabilities, affecting their ability to visit flowers and transfer pollen. This can lead to reduced plant reproduction, decreased genetic diversity, and potential shifts in plant community structure.

Ecological Resilience: Toxicants can reduce the ecological resilience of avian populations and their associated ecosystems. Resilience refers to the ability of an ecosystem to withstand and recover from disturbances. When toxicants accumulate in avian populations, it can decrease their ability to adapt to environmental changes, cope with additional stressors, or recover from population declines. This can make avian populations more susceptible to further disruptions, compromising the overall resilience of the ecosystems they inhabit.Efforts to mitigate the ecological implications of toxicants in avian populations involve comprehensive approaches. These include reducing toxicant release into the environment, implementing sustainable land and resource management practices, and conserving and restoring avian habitats. Additionally, monitoring avian populations, assessing the presence and impacts

of toxicants, and implementing conservation strategies targeted at vulnerable species can help safeguard avian populations and maintain ecological balance. Thepresence of toxicants in avian populations can have significant ecological implications. These include the disruption of trophic interactions, impacts on biodiversity, altered nutrient cycling, disruptions to pollination processes, and decreased ecological resilience. Understanding and mitigating the effects of toxicants on avian populations are crucial for maintaining healthy ecosystems and preserving the biodiversity and functioning of our natural environment

Conservation and mitigation efforts

Avian species face numerous threats to their populations and habitats, including habitat loss, climate change, pollution, and other anthropogenic activities. To safeguard avian species and ensure their long-term survival, various conservation and mitigation efforts have beenimplemented. These efforts aim to protect avian habitats, mitigate threats, and promote sustainable practices. Some key conservation and mitigation strategies for avian species include:

Protected Areas:

Establishing protected areas, such as national parks, wildlife sanctuaries, and nature reserves, plays a crucial role in avian conservation. These areas provide safe havens for avian species, ensuring the preservation of their habitats and promoting biodiversity. Protected areas often have regulations in place to minimize human disturbances and protect critical nesting, foraging, and breeding sites for avian populations.

Habitat Restoration and Management:

Protecting and restoring avian habitats is essential for their conservation. Efforts include reforestation, wetland restoration, and grassland management to create suitable habitats for different avian species. Implementing sustainable land-use practices, such as responsible forestry and agriculture, can help minimize habitat destruction and maintain essential ecological processes.

Threatened Species Recovery Programs:

For critically endangered avian species, recovery programs are implemented to prevent their extinction. These programs involve captive breeding and reintroduction efforts, habitat restoration, and targeted conservation actions to increase population sizes and improve genetic diversity.

Recovery programs often require collaboration between government agencies, conservation organizations, and local communities.

Conservation Breeding And Genetic Management:

In situations where avian species face severe population declines, conservation breeding programs can be established. These programs involve breeding and managing populations in captivity with the aim of reintroducing individuals into the wild. Genetic management is a crucial component of such programs to maintain genetic diversity and prevent inbreeding.

International Conservation Initiatives:

Avian conservation efforts often require international cooperation, particularly for migratory species that cross multiple countries during their annual cycles. International initiatives, such as the Convention on Migratory Species and the Ramsar Convention on Wetlands, promote collaboration among nations to protect important habitats, conserve critical flyways, and mitigate threats to avian species on a global scale.

Education and Public Awareness:

Raising public awareness about the importance of avian conservation is essential for fostering a culture of environmental stewardship. Education programs, public outreach campaigns, and citizen science initiatives can help engage communities in avian conservation efforts. Understanding the ecological value of avian species and their habitats encourages responsible behavior and support for conservation initiatives.

Policy and legislative measures

Governments play a crucial role in avian conservation by enacting and enforcing legislation and policies that protect avian species and their habitats. These measures may include habitat protection regulations, pollution control policies, and restrictions on harmful practices such as illegal hunting and trade of endangered species. International agreements, such as the Convention on Biological Diversity, provide frameworks for governments to develop and implement conservation strategies.

Research and monitoring

Continuous research and monitoring are fundamental for understanding avian populations, their habitats, and the impacts of threats. Monitoring avian populations allows for the early detection of declines and the identification of conservation priorities. Research provides valuable insights into the ecology, behavior, and conservation needs of avian species, guiding targeted conservation efforts.Conservationand mitigation efforts for avian species involve a combination of habitat protection, restoration, captive breeding, international collaboration, public awareness, policy development, and research. By implementing these strategies, we can work towards safeguarding avian species, preserving their habitats, and promoting the overall health and biodiversity of ecosystems. It requires the collective effort of governments, conservation organizations, scientists, local communities, and individuals to ensure a sustainable future for avian populations.Recognizing the importance of avian species and the threats they face from toxicants, conservation efforts are underway to minimize their exposure and mitigate the effects. Governments and environmental agencies have implemented regulations to restrict the use of certain toxic substances, such as DDT and lead ammunition, which have proven harmful to bird populations.Preserving and restoring habitats that are critical for bird populations can help reduce their exposure to toxicants. Wetland conservation, for example, provides important breeding grounds for numerous bird species.Raising awareness among the public about the impacts of toxicants on avian species is crucial. By promoting responsible pesticide use, proper waste disposal, and supporting conservation initiatives, individuals can contribute to the protection of bird populations.

Conclusion

Toxicants pose a significant threat to avian species worldwide, impacting their health, reproduction, and overall ecological role. By understanding the sources, mechanisms of toxicity, and ecological implications of toxicant exposure, we can work towards mitigating these threats and ensuring the long-term survival of our feathered friends. Through concerted conservation efforts and responsible environmental practices, we can strive to create a safer and healthier environment for avian species to thrive.In conclusion, toxicants pose a significant threat to avian species worldwide, with far-reaching impacts on their health, reproduction, and ecological role within ecosystems. The accumulation of toxicants in avian populations can lead to a range of adverse effects, including neurological impairments, reproductive disorders, weakened immune responses, and bioaccumulation in various organs

and tissues. These effects can disrupt avian populations and have ecological implications such as altered trophic interactions, biodiversity loss, nutrient cycling disruptions, and reduced ecological resilience.

The widespread presence of toxicants in the environment necessitates urgent action to mitigate their harmful effects on avian species. Conservation efforts should prioritize reducing the use and release of toxic substances, implementing sustainable agricultural practices, improving waste management, and promoting environmental regulations to limit toxicant pollution. Protecting and restoring avian habitats is crucial to provide safe and healthy environments for avian populations to thrive.Furthermore, comprehensive research and monitoring programs are needed to understand the extent of toxicant exposure, identify vulnerable avian species and populations, and assess the effectiveness of conservation measures. Public awareness and education play a vital role in fostering a sense of responsibility and encouraging individuals, communities, and governments to take action in protecting avian species from toxicant threats.

Preserving avian species is not only crucial for their intrinsic value but also for the health and balance of ecosystems. Avian species play key roles in pollination, seed dispersal, and pest control, contributing to ecosystem functioning and resilience. By addressing the threat of toxicants, we can help safeguard avian populations, maintain biodiversity, and protect the intricate web of ecological interactions that support life on our planet.

Ultimately, it is our collective responsibility to prioritize the conservation and well-being of avian species. By recognizing and addressing the detrimental effects of toxicants, we can strive towards a healthier environment where avian species can thrive, ensuring a sustainable future for both avian populations and the ecosystems they inhabit.

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Fish, fisheries, and food: exploring the nexus of sustainable resource management and nutritional security

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Abstract

Fish and fisheries play a crucial role in global food security, providing a significant source of animal protein, essential nutrients, and economic livelihoods for millions of people worldwide. This abstract explores the intricate relationship between fish, fisheries, and food, highlighting the importance of sustainable resource management practices and their impact on nutritional security. The paper first examines the growing global demand for fish as a vital food source, driven by population growth, changing dietary preferences, and the nutritional benefits of fish consumption. It discusses the diverse range of fish species and their contribution to the nutritional needs of different populations, emphasizing the importance of a varied and balanced diet. Next, the abstract delves into the significance of sustainable fisheries management in ensuring the long-term availability of fish resources. It highlights the importance of science-based approaches, effective governance, and stakeholder engagement in maintaining fish stocks, preventing overfishing, and preserving marine ecosystems. The role of technology, such as satellite monitoring and data analysis, in improving fisheries management practices is also discussed. Furthermore, the abstract explores the concept of responsible aquaculture as a means to enhance fish production while minimizing environmental impacts. It discusses the potential of sustainable aquaculture systems, such as integrated multi-trophic aquaculture and recirculating aquaculture systems, to meet the growing demand for fish and reduce pressure on wild fish stocks.Additionally, the socioeconomic aspects of fisheries are examined, highlighting the role of fisheries in poverty alleviation, income generation, and the empowerment of local communities. The abstract emphasizes the need for inclusive and equitable approaches that prioritize the well-being of small-scale fishers and ensure their access to resources and markets.Finally, the abstract underscores the importance of integrating fish,

fisheries, and food into broader sustainable development frameworks. It emphasizes the need for interdisciplinary collaborations between fisheries scientists, nutritionists, policymakers, and other stakeholders to address the complex challenges facing the fish-food nexus. Overall, this abstract highlight the critical role of fish and fisheries in providing nutritious food, sustaining livelihoods, and promoting sustainable development. It emphasizes the need for comprehensive approaches that balance the social, economic, and environmental dimensions of fisheries management to ensure the availability of fish as a vital food resource for present and future generations.

Keywords: Fish, Fisheries, Food, Sustainable Resource Management, Nutritional Security, Sustainable Fisheries Management

Introduction

Seafood has played a significant role in human diets throughout history, and its consumption has evolved over time. Understanding the past, present, and future of seafood consumption provides valuable insights into the importance of sustainable practices, the challenges faced by the industry, and the potential for innovative solutions. In the past, seafood was a vital food source for coastal communities and societies situated near rivers and lakes. Fishing was primarily small-scale and localized, with communities relying on local marine resources for sustenance and trade. As societies developed and global trade expanded, seafood began to reach inland areas, thanks to improved transportation and preservation methods. The present scenario reflects a significant increase in seafood consumption, driven by factors such as population growth, changing dietary preferences, and increased globalization. Industrialization and technological advancements have transformed the fishing industry, allowing for large-scale commercial fishing operations and the development of aquaculture. These changes have enabled the supply of seafood to meet the growing demand, but they have also introduced sustainability challenges. Overfishing, habitat destruction, and environmental pollution have led to declining fish stocks and threatened the health of marine ecosystems.

Looking toward the future, the sustainable seafood movement is gaining momentum. Recognizing the importance of maintaining healthy fish populations and preserving marine ecosystems, stakeholders in the seafood industry are embracing practices that prioritize sustainability. This includes implementing science-based fisheries management, adopting responsible aquaculture practices, promoting traceability and certification programs, and raising awareness about the environmental and social impacts of seafood production. Innovative solutions are emerging to address the challenges of

seafood consumption. Alternative sources of seafood, such as plant-based and lab-grown alternatives, offer promising avenues for reducing the pressure on wild fish stocks and alleviating environmental concerns associated with traditional fishing methods. Additionally, advancements in technology, such as satellite monitoring, data analysis, and blockchain, are enhancing transparency, traceability, and accountability within the seafood supply chain.

The future of seafood consumption will depend on finding a balance between meeting global demand, preserving marine biodiversity, and ensuring food security. It will require collaboration between governments, industry stakeholders, scientists, and consumers to develop and implement sustainable practices that consider environmental, social, and economic aspects. Education and awareness campaigns can also play a vital role in empowering consumers to make informed choices and support sustainable seafood options. In conclusion, the past, present, and future of seafood consumption highlight the need for sustainable practices and responsible management. Balancing the nutritional benefits of seafood with the preservation of marine ecosystems is crucial to ensure the availability of seafood for future generations (Pauly, *et al.* 2017). By embracing innovative solutions, fostering collaboration, and promoting consumer awareness, we can shape a future where seafood is both a source of nourishment and a driver of environmental stewardship

Fish is not only a delectable and versatile food option but also a nutritional powerhouse. Its unique composition makes it a valuable source of essential nutrients that contribute to overall health and well-being. This essay explores the nutritional benefits of fish, highlighting its role in promoting heart health, brain development, and optimal growth. Fish is renowned for its high-quality protein content, making it an excellent dietary choice for individuals seeking to meet their protein needs. Protein is crucial for the growth, repair, and maintenance of body tissues, including muscles, organs, and skin. Compared to other animal proteins, fish protein is highly digestible and contains all the essential amino acids required by the body (FAO. 2018). One of the standout nutritional components of fish is its abundance of omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (Calder, 2015). These essential fatty acids are associated with numerous health benefits, particularly for cardiovascular health (Delgado, *et al.* 2012). Studies have shown that regular consumption of omega-3 fatty acids can reduce the risk of heart disease, lower blood pressure, and decrease triglyceride levels, ultimately promoting a healthy heart.Omega-3 fatty acids, specifically docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), have garnered significant attention for their potential benefits on cognition, behavior, and

mood. Clinical findings have suggested that omega-3 DHA and EPA supplementation may have positive effects on various aspects of brain function. These fatty acids are integral components of cell membrane phospholipids, which are crucial for maintaining the integrity and fluidity of brain cells. DHA, in particular, is highly concentrated in the brain, particularly in regions associated with memory and cognitive function (Kidd, 2007). Studies have indicated that DHA and EPA supplementation may improve cognitive performance, attention, and memory, as well as alleviate symptoms of mood disorders such as depression and anxiety. Furthermore, research has highlighted the structural-functional synergies between omega-3 fatty acids and cell membrane phospholipids, as these fatty acids support synaptic function, neuroplasticity, and anti-inflammatory processes in the brain. While more research is needed to fully elucidate the mechanisms underlying these effects, the evidence suggests that omega-3 DHA and EPA play a significant role in promoting optimal brain health and mental well-being.

Brain development and cognitive function

Omega-3 fatty acids, specifically DHA, are vital for brain development and function. They are integral to the structure and function of brain cell membranes and are essential for proper neuronal communication. Adequate DHA intake during pregnancy and early childhood are particularly important for optimal brain development and cognitive function. In adults, omega-3 fatty acids have been linked to a reduced risk of cognitive decline and neurodegenerative diseases like Alzheimer's.

Vitamins and minerals:

Fish is a rich source of various vitamins and minerals (Belton, & Thilsted, 2014) that are essential for overall health. It is an excellent source of vitamins D and B12, both of which are essential for bone health, nerve function, and red blood cell production. Fish also contains minerals such as iodine, selenium, zinc, and magnesium, which play crucial roles in metabolism, immune function, and various physiological processes.

Low in saturated fat and high in unsaturated fats:

Compared to many other animal protein sources, fish is relatively low in saturated fat and high in unsaturated fats. This composition makes fish an excellent choice for individuals aiming to maintain a healthy weight and reduce the risk of chronic diseases, such as obesity and type 2 diabetes. Unsaturated fats, especially monounsaturated and polyunsaturated fats, have been associated with a lower risk of heart disease and improved insulin sensitivity.

The diverse range of fish species plays a vital role in meeting the nutritional needs of different populations and promoting a varied and balanced diet. Fish are excellent sources of high-quality protein, essential fatty acids (including omega-3 fatty acids), vitamins, and minerals. They provide an array of nutrients that are beneficial for overall health, including cardiovascular health, brain function, and immune system support (De Young, & Charles, 2015).

Different fish species have varying nutritional profiles, which allows individuals to select fish that align with their dietary requirements and preferences. For example, fatty fish such as salmon, mackerel, and sardines are rich in omega-3 fatty acids, which are essential for brain development and function, reducing the risk of cardiovascular diseases, and supporting healthy aging (Bouwens, *et al.* 2016). White fish, like cod, haddock, and sole, are lower in fat but still provide important nutrients such as protein, vitamins, and minerals. Emphasizing the importance of a varied and balanced diet is crucial in maximizing the nutritional benefits of fish consumption. Incorporating different fish species into one's diet ensures a diverse intake of nutrients and reduces the risk of nutrient deficiencies. Furthermore, fish consumption complements other dietary components, such as fruits, vegetables, whole grains, and legumes, contributing to a holistic approach to nutrition. To ensure the long-term availability of fish resources, sustainable fisheries management is of utmost importance (Allison, *et al.* 2009). This approach focuses on maintaining fish stocks at levels that can support continued harvesting while preserving the health of marine ecosystems. Science-based approaches play a fundamental role in understanding fish populations, their habitats, and their interaction with the environment (Bogazzi, & Hentati 2018). By conducting research, monitoring fish populations, and assessing fishing practices, scientists can provide valuable insights into the sustainability of fish stocks and inform management decisions. Effective governance and stakeholder engagement are essential components of sustainable fisheries management (Cao, *et al.* 2019). It involves establishing regulations, policies, and enforcement mechanisms to prevent overfishing and protect vulnerable species. Collaborative efforts among governments, fishing communities, scientists, and conservation organizations are crucial for implementing and enforcing these measures. Stakeholder engagement ensures that different perspectives are considered, local knowledge is incorporated, and the social and economic aspects of fisheries are taken into account (Bush, *et al.* 2013).

Science-based approaches, effective governance, and stakeholder engagement are critical elements in maintaining fish stocks, preventing overfishing, and preserving marine ecosystems. These components work in

synergy to ensure the sustainable management of fisheries and promote the long-term health of marine environments. Science-based approaches involve using scientific research, data collection, and analysis to understand fish populations, their habitats, and the dynamics of marine ecosystems. By studying factors such as fish abundance, reproduction rates, and migration patterns, scientists can provide valuable insights into the status of fish stocks and inform management decisions. Scientific assessments help determine appropriate catch limits, fishing seasons, and other regulations to prevent overexploitation and ensure the sustainable harvest of fish (Golden, *et al.* 2018).

Effective governance is essential for implementing and enforcing fisheries management measures. Governments, international organizations, and regulatory bodies play a crucial role in developing policies, regulations, and laws that guide fishing activities. Clear guidelines and enforcement mechanisms help control fishing efforts, monitor compliance, and deter illegal, unreported, and unregulated (IUU) fishing. Well-defined property rights and access rights frameworks also contribute to effective governance by providing incentives for responsible fishing practices.

Stakeholder engagement is vital for successful fisheries management. Engaging with various stakeholders, including fishing communities, scientists, conservation organizations, and local communities, ensure that management decisions consider diverse perspectives, local knowledge, and the social and economic aspects of fisheries. Collaboration and dialogue foster understanding, trust, and cooperation, leading to more effective and socially acceptable management measures.

Technology, such as satellite monitoring and data analysis, has revolutionized fisheries management practices. Satellite-based technologies allow for remote monitoring of fishing activities, including vessel tracking, fishing effort estimation, and identification of potential IUU fishing hotspots. This real-time information helps authorities detect and address illegal fishing, enforce regulations, and improve the overall transparency and accountability of fishing activities. Data analysis plays a crucial role in understanding the status of fish stocks and assessing the effectiveness of management measures. Advanced statistical models and computer algorithms help analyze large datasets, enabling scientists to make accurate predictions, evaluate the impacts of different fishing strategies, and adjust management approaches as needed. This data-driven decision-making enhances the efficiency and effectiveness of

fisheries management, contributing to the preservation of fish stocks and ecosystems.

Responsible aquaculture offers a complementary approach to enhancing fish production while minimizing environmental impacts. It involves the cultivation of fish in controlled environments, such as ponds, tanks, or offshore structures. Responsible aquaculture focuses on sustainable feed sources, efficient use of resources, waste management, and minimizing the escape of farmed fish into the wild. By adopting responsible aquaculture practices, fish production can be increased to meet the growing demand while reducing the pressure on wild fish stocks and minimizing negative ecological consequences. Science-based approaches, effective governance, stakeholder engagement, and technological advancements are crucial for maintaining fish stocks, preventing overfishing, preserving marine ecosystems, and promoting responsible aquaculture practices. These elements work together to ensure the sustainable management of fisheries, protect biodiversity, and support the long-term viability of fish resources for present and future generations.

Prey fish sustainability is a critical concern under the influence of multiple stressors. Prey fish species, such as small pelagic fish and forage fish, play a crucial role in marine ecosystems as a primary food source for larger predatory fish, marine mammals, and seabirds. However, these prey fish populations face various stressors, including overfishing, habitat degradation, climate change, and pollution. The combined impacts of these stressors can lead to significant declines in prey fish abundance, compromising the stability and health of entire marine food webs. To ensure the sustainability of prey fish populations, it is essential to implement science-based fisheries management approaches that account for ecosystem dynamics, set appropriate catch limits, protect critical habitats, and consider the interactions between prey and predator species (Golden, *et al.* 2018). Additionally, mitigating climate change, reducing pollution, and promoting ecosystem resilience are crucial steps in safeguarding prey fish sustainability and maintaining the overall health and productivity of marine ecosystems.

Reflections on the success of traditional fisheries management reveal valuable insights into the effectiveness of long-standing approaches in sustaining fish populations and supporting fishing communities. Traditional fisheries management systems often rely on local knowledge, customary practices, and community-based governance structures. These systems have demonstrated their ability to adapt to local ecological conditions and the social dynamics of fishing communities over generations. By employing techniques

such as seasonal fishing closures, gear restrictions, and community-based monitoring, traditional management approaches have successfully maintained fish stocks and prevented overfishing in many cases (Hilborn, & Ovando, 2014). Furthermore, the involvement of local communities in decision-making processes has fostered a sense of stewardship and responsibility for marine resources, leading to more sustainable use of fisheries. The success of traditional fisheries management highlights the importance of integrating local knowledge and engaging fishing communities in modern management strategies to promote sustainable fishing practices and conserve fish populations for future generations.

Effective fisheries management plays a crucial role in improving fish stock status by implementing measures to regulate fishing activities, prevent overexploitation, and promote sustainable practices. Through science-based assessments and monitoring programs, fisheries management authorities can gather essential data on fish populations, fishing efforts, and ecological conditions. This information enables them to set appropriate catch limits, implement fishing quotas, and establish fishing seasons to ensure that fishing activities are conducted within sustainable levels. Additionally, measures such as gear restrictions, closed areas, and size limits contribute to protecting spawning grounds, nursery areas, and vulnerable species, allowing fish populations to recover and thrive (Hilborn, *et al.* 2020). By implementing effective fisheries management strategies, it is possible to strike a balance between the economic interests of fishing communities and the long-term conservation of fish stocks. Such efforts contribute to maintaining the ecological integrity of marine ecosystems, providing food security, and sustaining livelihoods dependent on fisheries.

Preserving marine ecosystems is another critical aspect of sustainable fisheries management. Healthy ecosystems provide the necessary habitats and resources for fish populations to thrive. By protecting critical habitats, reducing bycatch and discards, and implementing ecosystem-based approaches, fisheries management can safeguard the delicate balance of marine ecosystems, ensuring the long-term availability of fish resources. The diverse range of fish species contributes significantly to meeting the nutritional needs of different populations. A varied and balanced diet that includes different fish species provides essential nutrients and promotes overall health. Sustainable fisheries management, with its focus on science-based approaches, effective governance, and stakeholder engagement, plays a vital role in ensuring the long-term availability of fish resources while preventing overfishing and preserving marine ecosystems. By embracing sustainable practices, we can

maintain fish stocks, support food security, and protect the biodiversity and health of our oceans.

There are several highly demanded fish species in the market known for their exceptional taste and culinary appeal. These fish are sought after by consumers and chefs alike for their delicate flavors, succulent texture, and versatility in various cuisines.

Here are some of the popular highly demanded fish species in the market for their taste:

Salmon:

Salmon is renowned for its rich, buttery flavor and tender, flaky flesh. It is highly versatile and can be prepared in various ways, such as grilling, baking, or smoking. The high-fat content of salmon gives it a luscious texture and contributes to its distinctive taste. Wild-caught Pacific salmon, including Chinook (King), Sockeye (Red), and Coho (Silver), are highly prized for their exceptional flavor. Salmon is highly demanded for various reasons, including its exceptional taste, nutritional value, versatility in cooking, and cultural significance. Salmon is known for its rich, buttery flavor, which is highly sought after by seafood enthusiasts. Its taste is often described as succulent, delicate, and slightly sweet. The unique flavor profile of salmon makes it a favorite among consumers and chefs alike.

Salmon is a nutritional powerhouse, packed with essential nutrients that promote overall health. It is an excellent source of high-quality protein, omega-3 fatty acids (including EPA and DHA), vitamins (such as vitamin D and B vitamins), and minerals (including selenium and potassium). The abundance of omega-3 fatty acids in salmon makes it particularly beneficial for heart health, brain function, and reducing inflammation.As consumers become increasingly health-conscious, salmon's nutritional benefits have made it a preferred choice. Its low saturated fat content, high omega-3 fatty acid content, and rich nutrient profile align with dietary preferences focused on promoting heart health, maintaining brain function, and supporting overall well-being. The rise of salmon aquaculture has helped meet the growing demand for salmon while also addressing concerns about overfishing wild populations.

Sustainable salmon farming practices, such as responsible feed sourcing, low-impact farming systems, and environmental monitoring, have increased consumer confidence in the sustainability of farmed salmon. Salmon is widely available in supermarkets, fish markets, and restaurants, contributing to its consistent demand. Its accessibility, both fresh and frozen, allows

consumers to enjoy salmon throughout the year, regardless of seasonal variations. The combination of its exquisite taste, nutritional benefits, culinary versatility, and cultural significance has made salmon a highly sought-after fish in the market. Sustainable fishing and farming practices play a crucial role in ensuring the long-term availability of salmon and maintaining its desirability in the global market.

Tuna:

Tuna is a firm-fleshed fish with a meaty texture and a robust flavor. It is popularly consumed raw in sushi and sashimi dishes, where its mild, slightly sweet taste shines. Yellowfin tuna and Bluefin tuna, especially the prized Toro (fatty belly) cuts, are highly sought after for their exceptional taste and tenderness. Tuna is highly valued for its nutritional profile. It is an excellent source of high-quality protein, low in saturated fat, and packed with essential nutrients. Tuna is particularly rich in omega-3 fatty acids, which promote heart health, reduce inflammation, and support brain function. Its nutrient density makes it an attractive choice for health-conscious individuals.

Sea Bass:

Sea bass, including species like Chilean sea bass (Patagonian toothfish) and European sea bass, is highly regarded for its mild, delicate flavor and moist, tender flesh. It has a buttery texture that melts in the mouth, making it a favorite among seafood enthusiasts. Sea bass is versatile and can be prepared by grilling, steaming, or pan-searing to enhance its natural flavors.

Halibut:

Halibut is a lean, white fish with a firm, meaty texture, and a sweet, delicate flavor. It is prized for its versatility in cooking and its ability to hold up well to various cooking methods. Halibut's mild taste makes it an excellent canvas for different flavor profiles and sauces. Pacific halibut, specifically Alaskan halibut, is highly valued for its superior flavor and sustainability.

Mahi-Mahi:

Mahi-Mahi, also known as dorado or dolphin fish, is a tropical fish with a mild, slightly sweet flavor and a firm, flaky texture. It has a distinctively white flesh that turns opaque and moist when cooked. Mahi-Mahi's mild taste pairs well with a variety of seasonings and is often grilled, baked, or pan-seared to showcase its natural flavors.

Cod:

Cod is a popular fish known for its mild, clean taste and delicate texture. It has a slightly sweet flavor and a lean, flaky flesh that lends itself well to a wide range of preparations, including frying, baking, or poaching. Atlantic cod and Pacific cod are both highly regarded for their culinary appeal.

Pomfret:

Pomfret is a nutritious fish, providing an array of essential nutrients. It is a good source of high-quality protein, omega-3 fatty acids, vitamins (such as vitamin D, vitamin B12, and niacin), and minerals (including iodine and selenium). The omega-3 fatty acids found in pomfret offer various health benefits, such as promoting heart health and supporting brain function.

Hilsa:

Hilsa is not only delicious but also a good source of essential nutrients. It is rich in omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are beneficial for heart health and brain function. Hilsa is also a good source of high-quality protein, vitamins (such as vitamin A, vitamin D, and vitamin B12), and minerals (including iron and calcium).

Fish eggs :

Fish eggs, also known as roe, are highly sought after in the culinary world and have a significant demand for several reasons. The demand for fish eggs can be attributed to their unique flavor, culinary versatility, nutritional value, and cultural significance. Fish eggs come in various forms, such as caviar (sturgeon roe), ikura (salmon roe), tobiko (flying fish roe), and masago (capelin roe). Each type of fish egg offers a distinct flavor profile ranging from buttery and creamy to briny and salty. The delicate, bursting texture of fish eggs adds a unique experience to culinary preparations, making them a sought-after delicacy.Fish eggs are nutrient-dense and packed with essential vitamins, minerals, and healthy fats. They are a rich source of omega-3 fatty acids, which are known for their numerous health benefits, including supporting heart health, reducing inflammation, and promoting brain function. Fish eggs are also high in protein, providing essential amino acids for muscle growth and repair.

Fish eggs hold cultural significance in various cuisines around the world. Caviar, in particular, is renowned and associated with luxury and special occasions. In countries like Russia, Iran, and Japan, caviar has a long-standing

tradition and is considered a delicacy reserved for celebrations and high-end dining experiences. Certain types of fish eggs, such as sturgeon caviar, are highly sought after due to their limited availability. The time-consuming and meticulous process of harvesting fish eggs, along with the specific species requirements, contributes to their exclusivity and high price. This limited availability adds to the desirability and demand for fish eggs.

Importance of Fish Fisheries:

Fisheries contribute significantly to the global food supply, employing millions of people and supporting coastal communities. Fish is a valuable source of animal protein, especially in regions where alternative sources of protein are scarce or expensive. It provides essential nutrients that are crucial for human health and development, including omega-3 fatty acids, which are beneficial for cardiovascular health and brain function. Fisheries also have economic implications, as they generate income and export opportunities for many countries. Small-scale fisheries, in particular, play a vital role in the livelihoods of local communities, providing employment and food security. Additionally, fishery products contribute to international trade, promoting economic growth and development.

Challenges in fish fisheries

Despite the significance of fish fisheries, they face several challenges that threaten their sustainability and the availability of fish as a food source.

Overfishing: Overfishing occurs when fish are harvested at a rate that exceeds their natural reproduction capacity. This can deplete fish populations, disrupt marine ecosystems, and jeopardize the long-term viability of fisheries.

Illegal, Unreported, and Unregulated (IUU) Fishing: IUU fishing undermines conservation and management efforts by operating outside of established regulations. It depletes fish stocks, damages marine habitats, and compromises the sustainability of fisheries.

Habitat Destruction: The destruction of coastal and marine habitats, such as coral reefs and mangroves, has a detrimental impact on fish populations. These habitats serve as breeding grounds, nurseries, and feeding areas for many species. Their loss disrupts the natural life cycle of fish and diminishes their overall abundance.

Pollution and Climate Change: Pollution from industrial and agricultural activities, as well as climate change, poses significant threats to fish and their habitats. Chemical pollutants can accumulate in fish, making them unsafe for

human consumption. Climate change affects ocean temperatures, acidity levels, and food availability, altering the distribution and behavior of fish species.

Promoting Sustainable Fish Fisheries:

To ensure the long-term viability of fish fisheries and maintain fish as a reliable food source, sustainable practices are essential. Governments, international organizations, and fishing communities must collaborate to implement the following measures:

Fisheries Management: Effective fisheries management involves setting catch limits, implementing fishing quotas, and establishing protected areas to allow fish populations to recover. Scientific research and data collection are critical for informed decision-making. Fisheries management refers to the process of regulating and controlling the extraction of fish from marine or freshwater ecosystems in a sustainable and responsible manner. It involves implementing policies, regulations, and practices to ensure the long-term viability of fish populations, protect marine habitats, and support the livelihoods of those dependent on fisheries. Effective fisheries management is crucial to maintaining the ecological balance of marine ecosystems, promoting food security, and sustaining the economic and social benefits derived from fishing activities. The primary objective of fisheries management is to ensure the sustainability of fish stocks. This involves setting catch limits and establishing fishing seasons or closures based on scientific assessments of fish populations (Cashion, *et al.* 2017). By preventing overfishing and allowing fish populations to reproduce and replenish, fisheries management aims to maintain healthy fish stocks for present and future generations.

Ecosystem-Based Approach: Fisheries management recognizes the interconnectedness of marine ecosystems and the need to consider the broader ecological impacts of fishing activities. An ecosystem-based approach takes into account the interactions between target species, their predators, prey, and the overall ecosystem health. It considers the conservation and management of habitats, the protection of biodiversity, and the mitigation of negative impacts on non-target species. The ecosystem-based approach in fisheries management recognizes that fisheries operate within complex ecosystems and emphasizes the need to consider ecological interactions and processes when making management decisions. It takes into account the interconnectedness of species, habitats, and ecosystem functions, and aims to maintain the health and integrity of marine ecosystems while sustaining fisheries.Here are key aspects of the ecosystem-based approach in fisheries management:

Ecological Interactions: The ecosystem-based approach recognizes that fish populations are influenced by a range of ecological interactions, including predator-prey relationships, competition, and habitat availability. It considers the impacts of fishing on these interactions and seeks to minimize negative effects on non-target species and ecosystem structure and function.

Conservation of Biodiversity: Maintaining biodiversity is a central objective of the ecosystem-based approach. It acknowledges the importance of protecting a wide range of species, including non-target fish species, endangered or threatened species, and other components of the marine ecosystem. Conservation measures may include the establishment of protected areas, habitat restoration, and the mitigation of bycatch.

Habitat Protection and Restoration: The ecosystem-based approach recognizes the significance of habitats for fish populations and ecosystem functioning. It focuses on the conservation and restoration of critical habitats such as coral reefs, seagrass beds, mangroves, and spawning grounds. Protecting and restoring habitats ensures the availability of suitable environments for fish reproduction, foraging, and shelter.

Precautionary Approach: The ecosystem-based approach adopts a precautionary approach to fisheries management. It acknowledges the uncertainty associated with ecological dynamics and the potential for unexpected impacts. Precautionary measures, such as setting conservative catch limits and implementing ecosystem-based reference points, help avoid irreversible damage to fish stocks and ecosystems.

Adaptive Management: The ecosystem-based approach promotes adaptive management, which involves regular monitoring, evaluation, and adjustment of management measures based on new information and feedback from stakeholders. This allows for flexibility and the ability to respond to changing environmental conditions, emerging threats, and evolving scientific knowledge.

Stakeholder Engagement: Stakeholder engagement is a crucial component of the ecosystem-based approach. It recognizes the importance of involving various stakeholders, including fishermen, scientists, conservation organizations, indigenous communities, and the broader public, in decision-making processes. Stakeholder input helps ensure that management measures consider diverse perspectives and incorporate local knowledge and values.

Integrated Management: The ecosystem-based approach encourages integrated management that considers multiple sectors and activities that interact with fisheries, such as coastal development, pollution control, and

climate change adaptation. It recognizes that effective fisheries management cannot be achieved in isolation but requires coordination and cooperation with other sectors to address cumulative impacts on ecosystems.By adopting an ecosystem-based approach, fisheries management seeks to balance the sustainable utilization of fishery resources with the conservation and protection of marine ecosystems. It recognizes the interconnectedness of species, habitats, and ecological processes, and strives to maintain the long-term health and resilience of ecosystems, ensuring the continued provision of ecosystem services and benefits for both present and future generations

Conservation of Habitat: Protecting and conserving critical fish habitats, such as coral reefs, seagrass beds, and spawning grounds, is a key aspect of fisheries management. By identifying and safeguarding essential habitats, fisheries management aims to maintain the ecological integrity and productivity of marine ecosystems, which directly impact the abundance and diversity of fish populations.

Monitoring and Data Collection: Fisheries management relies on accurate and up-to-date data to inform decision-making processes. Monitoring the size and composition of fish populations, tracking fishing efforts and catch data, and assessing the health of marine ecosystems provide crucial information for setting regulations, assessing the effectiveness of management measures, and making informed management decisions.

Collaboration and Stakeholder Engagement: Successful fisheries management involves collaboration among various stakeholders, including government agencies, fishermen, scientists, conservation organizations, and local communities. Engaging stakeholders in the decision-making process, considering their knowledge and perspectives, and fostering cooperation and dialogue are essential for implementing effective and socially acceptable management measures.

Enforcement and Compliance: Establishing and enforcing regulations is a critical component of fisheries management. This includes monitoring fishing activities, implementing licensing systems, enforcing catch limits and gear restrictions, and addressing illegal, unreported, and unregulated (IUU) fishing. Effective enforcement mechanisms help ensure that fishing activities are conducted in accordance with management measures and contribute to sustainable fisheries.

Adaptive Management: Fisheries management is an ongoing and dynamic process that requires regular evaluation and adaptation. Adapting management measures based on new scientific information, monitoring results, and

feedback from stakeholders helps to address emerging challenges and changing environmental conditions. Adaptive management ensures that management approaches remain responsive and effective over time.

Combating Illegal Fishing: Strengthening monitoring and surveillance efforts, enforcing strict regulations, and promoting traceability in the seafood supply chain are crucial steps in curbing illegal fishing activities.

Protection of Marine Habitats: Conserving and restoring critical coastal and marine habitats, such as coral reefs and mangroves, will enhance the resilience of fish populations and preserve the overall health of marine ecosystems.

Sustainable Aquaculture: Expanding sustainable aquaculture practices can help alleviate pressure on wild fish stocks. Responsible aquaculture methods include minimizing environmental impacts, using sustainable feed sources, and avoiding the use of antibiotics and chemicals.

Consumer Awareness: Educating consumers about sustainable fishing practices and responsible seafood choices empowers them to make informed decisions. Certifications, such as the Marine Stewardship Council (MSC) label, help identify sustainably sourced fish products.

Fish is a valuable source of high-quality protein, essential nutrients, and beneficial omega-3 fatty acids that contribute to overall human health. However, concerns have arisen regarding the potential risks associated with fish consumption due to the presence of environmental contaminants, such as heavy metals, industrial pollutants, and microplastics. This article aims to evaluate the risks and benefits of fish intake on human health, considering the potential exposure to contaminants and the overall nutritional value provided by fish. Fish is widely recognized for its numerous health benefits. It is a rich source of lean protein, containing essential amino acids necessary for muscle growth, repair, and overall cellular function. Furthermore, fish, particularly fatty fish like salmon, mackerel, and sardines, is a primary dietary source of long-chain omega-3 fatty acids, including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These omega-3 fatty acids are associated with a range of health benefits, including cardiovascular health, brain function, and anti-inflammatory effects (Mozaffarian, & Rimm, 2006).

Evaluating the risks of contaminant exposure

While the nutritional benefits of fish consumption are well-established, concerns regarding contaminants have raised questions about the safety of fish intake. Fish can accumulate environmental contaminants through their diet and habitat, particularly in polluted waters. Heavy metals, such as mercury, lead,

and cadmium, as well as persistent organic pollutants (POPs), including polychlorinated biphenyls (PCBs) and dioxins, are among the most commonly discussed contaminants found in fish. Mercury is a neurotoxic metal that can accumulate in certain predatory fish species. It primarily enters aquatic systems through industrial activities, such as coal combustion and gold mining. High levels of mercury exposure, especially in vulnerable populations such as pregnant women and young children, can lead to adverse neurological effects. However, it is important to note that not all fish species contain significant levels of mercury, and the benefits of consuming low-mercury fish outweigh the potential risks.

Similarly, PCBs and dioxins are persistent organic pollutants that can accumulate in the fatty tissues of fish. These contaminants are byproducts of industrial processes and have been linked to various health concerns, including cancer and reproductive issues. Regulatory measures have been implemented to control the release of these pollutants into the environment, resulting in a decline in their levels in fish over time. Regular monitoring and adherence to recommended consumption guidelines can help mitigate the potential risks associated with PCBs and dioxins.

Assessing the Balance: Risks vs. Benefits:

Evaluating the risks and benefits of fish intake requires considering the levels of contaminants in specific fish species and balancing them against the nutritional advantages. It is essential to distinguish between different fish species, their habitats, and their dietary preferences, as these factors significantly influence their contamination levels. Government agencies and health organizations provide guidelines and advisories regarding fish consumption, particularly for vulnerable populations. These guidelines recommend limiting the intake of high-mercury fish, such as shark, swordfish, king mackerel, and tilefish, while encouraging the consumption of low-mercury options like salmon, trout, and sardines. By following these guidelines, individuals can reap the nutritional benefits of fish while minimizing the potential risks associated with contaminants.

Promoting Sustainable and Safe Fishing Practices:

The importance of sustainable fishing practices cannot be overlooked in the context of fish consumption and human health. Overfishing, destructive fishing methods, and habitat destruction can disrupt marine ecosystems, leading to a decline in fish populations and the disruption of natural food chains. Sustainable fisheries management practices, including catch limits, gear restrictions, and marine protected areas, are crucial for preserving fish stocks

and ensuring the long-term availability of fish resources. Furthermore, addressing the issue of environmental contamination requires proactive measures to reduce pollution sources, monitor water quality, and enforce regulations on industries that contribute to contamination. Efforts to mitigate and prevent pollution can help reduce the levels of contaminants in fish and ultimately safeguard human health.

Fisheries in the anthropocene

Fisheries in the Anthropocene face unprecedented challenges and complexities as human activities have become the dominant force shaping marine ecosystems. The Anthropocene, an epoch characterized by significant human impact on the Earth's systems, has led to overfishing, habitat destruction, pollution, and climate change, all of which have profound implications for fisheries. The intensification of fishing practices, driven by increased global demand for seafood, has led to the depletion of fish stocks and the degradation of marine habitats. Additionally, climate change-induced alterations in ocean temperatures and currents affect the distribution and abundance of fish species. To address these challenges, fisheries in the Anthropocene require innovative and adaptive management approaches that incorporate ecosystem-based management principles, stakeholder engagement, and the use of scientific data and technology (Pauly, *et al.* 2013). Embracing sustainable fishing practices, protecting critical habitats, and reducing greenhouse gas emissions is imperative for the resilience and future viability of fisheries in the Anthropocene.

Aquaculture, also known as fish farming, plays a crucial role in adding resilience to the global food system. As the world's population continues to grow, there is an increasing need to find sustainable and efficient ways to produce food. Aquaculture offers several advantages that contribute to the resilience of the global food system.Firstly, aquaculture provides a significant source of protein-rich food. Fish and seafood are highly nutritious, containing essential amino acids, omega-3 fatty acids, vitamins, and minerals. With the decline of wild fish stocks due to overfishing and habitat degradation, aquaculture serves as a reliable and sustainable means of meeting the growing demand for seafood.

Furthermore, aquaculture reduces pressure on wild fish populations. By cultivating fish in controlled environments, aquaculture reduces the need for capturing wild fish for consumption. This helps to conserve marine biodiversity and maintain the ecological balance of aquatic ecosystems. Aquaculture systems can be established in various locations, including land-

based facilities, coastal areas, and even offshore locations. This flexibility allows for the production of fish and seafood in areas where traditional fishing may not be feasible or sustainable. Additionally, inland aquaculture systems can be established closer to urban areas, reducing transportation costs and the carbon footprint associated with long-distance seafood supply chains.

Another aspect that adds resilience to the global food system is the ability of aquaculture to provide employment and economic opportunities, particularly in rural and coastal communities. Fish farming operations create jobs in production, processing, and distribution, contributing to local economies and reducing rural-urban migration. This socioeconomic aspect helps to improve food security, reduce poverty, and enhance resilience within communities. Aquaculture also offers the potential for innovation and technological advancements. Through research and development, improvements in feed formulations, disease management, and water quality control have led to more efficient and environmentally friendly practices. This continuous innovation contributes to the long-term sustainability and resilience of aquaculture operations.

Moreover, aquaculture can contribute to food security by providing a consistent and reliable food source. Unlike traditional fishing, which can be influenced by factors such as weather conditions and fluctuating fish stocks, aquaculture allows for consistent production and a more predictable food supply. This stability helps to mitigate the risks associated with food production and contributes to overall food system resilience. However, it is important to note that responsible and sustainable aquaculture practices are essential for maximizing its benefits and minimizing potential negative environmental impacts. This includes addressing concerns such as the use of antibiotics and chemicals, effluent management, and the potential for escaped farmed fish to interact with wild populations (Troell, *et al.* 2014). Proper regulations, monitoring, and certification programs are necessary to ensure that aquaculture operations adhere to environmental and social sustainability standards. Aquaculture plays a vital role in adding resilience to the global food system. By providing a sustainable and nutritious source of food, reducing pressure on wild fish populations, generating economic opportunities, and promoting innovation, aquaculture contributes to the long-term stability and security of the global food supply. With responsible practices and ongoing research, aquaculture has the potential to further enhance resilience and contribute to a sustainable and food-secure future.

Conclusion

Fish consumption offers numerous nutritional benefits and contributes to a healthy and balanced diet. While concerns about environmental contaminants exist, the risks can be managed through informed choices and adherence to recommended guidelines. By selecting low-mercury fish species and promoting sustainable fishing practices, individuals can enjoy the nutritional advantages of fish while minimizing potential exposure to contaminants. Regular monitoring, research, and collaborative efforts between government agencies, health organizations, and the fishing industry are vital in ensuring the continued evaluation of risks and benefits associated with fish intake, with the ultimate goal of safeguarding human health and preserving marine ecosystems.

In conclusion, fish and fisheries play a significant role in our lives, providing a valuable source of nutrition, economic livelihoods, and cultural significance. The diverse species of fish available in our oceans, rivers, and lakes offer a wide range of flavors, textures, and nutritional benefits. From popular choices like salmon, tuna, and hilsa to lesser-known varieties, each fish species brings its unique qualities to the table.

Fisheries, both wild-caught and aquaculture-based, contribute to meeting the growing global demand for fish. Sustainable fishing practices, responsible aquaculture techniques, and effective management are crucial for maintaining fish stocks, protecting marine ecosystems, and ensuring the long-term viability of the industry. Consumers have a role to play in supporting sustainable fishing and making informed choices. By selecting sustainably sourced fish, understanding seafood labeling and certifications, and promoting responsible consumption, individuals can contribute to the preservation of fish populations and the health of our oceans. Furthermore, the importance of fisheries extends beyond food production. They serve as economic drivers, supporting the livelihoods of millions of people worldwide, particularly in coastal communities. Fishing activities provide employment opportunities, contribute to local economies, and preserve cultural traditions tied to fishing practices. However, challenges such as overfishing, habitat destruction, pollution, and climate change pose significant threats to fish and fisheries. It is imperative to adopt science-based management strategies, promote sustainable fishing practices, and invest in research and conservation efforts to ensure the future sustainability of fish populations and the fishing industry. In conclusion, fish and fisheries are not only a vital source of nutrition and economic value but also hold cultural significance. By embracing sustainable practices and

recognizing the importance of responsible consumption, we can safeguard fish populations and promote the long-term health of our oceans, ensuring that future generations can continue to enjoy the benefits and pleasures that fish provide. Fish fisheries play a crucial role in global food security, providing vital nutrients and supporting coastal. Fish is a nutritional powerhouse, offering a wide range of health benefits due to its unique composition. Its high-quality protein content, abundance of omega-3 fatty acids, and essential vitamins and minerals make it an essential component of a healthy diet. Regular consumption of fish can promote heart health, support brain development and cognitive function, and provide essential nutrients necessary for overall growth and well-being. Embracing fish as a regular part of one's diet can contribute significantly to a balanced and nutritious eating pattern, enhancing overall health and vitality. Fisheries play a vital role in providing food for millions of people around the world. Fish is not only a rich source of high-quality protein but also contains essential omega-3 fatty acids, vitamins, and minerals that contribute to a healthy and balanced diet. This chapter explores the significance of fish fisheries in meeting global food demand, the challenges they face, and the sustainable practices necessary for the future of fish as a primary food source. The demand for fish eggs is driven by their exquisite flavor, culinary versatility, nutritional value, cultural significance, exclusivity, and gourmet appeal. While fish eggs add a touch of luxury to culinary experiences, it is essential to balance the demand with sustainable practices to protect fish populations and maintain the health of our oceans.

In conclusion, fisheries management plays a vital role in maintaining the sustainability of fish stocks, protecting marine habitats, and supporting the socio-economic well-being of fishing communities. By employing science-based approaches, considering ecosystem dynamics, and engaging stakeholders, fisheries management aims to balance the extraction of fish resources with the conservation of marine ecosystems for the benefit of present and future generations.

Fish and fisheries play a critical role in addressing global challenges related to food security, livelihoods, and sustainable development. Recognizing their importance, it is essential to adopt comprehensive approaches that consider the social, economic, and environmental dimensions of fisheries management.First and foremost, fish are a valuable source of highly nutritious food, providing essential proteins, omega-3 fatty acids, vitamins, and minerals. They contribute to a balanced and healthy diet, particularly for populations that rely heavily on fish as a primary source of animal protein. The nutritional benefits of fish are

especially crucial in combating malnutrition and promoting overall well-being, particularly in vulnerable communities.

In addition to food security, fisheries support livelihoods and economic development worldwide. Fishing communities, both coastal and inland, rely on fish as a source of income and employment. The fishing industry provides jobs in various sectors, including fishing operations, processing, transportation, and marketing. Sustainable fisheries management not only ensures the availability of fish resources but also contributes to the social and economic well-being of these communities.

Moreover, fisheries play a significant role in supporting sustainable development goals. Sustainable fishing practices promote ecosystem health and biodiversity conservation. By preserving marine habitats and maintaining healthy fish populations, fisheries management contributes to the sustainability of marine ecosystems and the services they provide, such as carbon sequestration, water filtration, and coastal protection. Furthermore, sustainable fisheries management aligns with the principles of responsible stewardship, promoting social equity, resilience, and the preservation of cultural heritage associated with fishing communities.To ensure the availability of fish as a vital food resource for present and future generations, comprehensive approaches to fisheries management are crucial. These approaches should consider the social, economic, and environmental dimensions to strike a balance between meeting human needs, protecting the environment, and sustaining livelihoods.

Science-based approaches are fundamental in understanding fish populations, their dynamics, and the impacts of fishing practices. By collecting and analyzing data on fish stocks, habitat conditions, and fishing efforts, scientists and fisheries managers can develop informed strategies to prevent overfishing, promote sustainable harvesting, and protect vulnerable species.Effective governance and regulatory frameworks are essential to enforce sustainable fishing practices. Governments, in collaboration with stakeholders, should establish and enforce policies, regulations, and monitoring systems that promote responsible fishing, prevent illegal, unreported, and unregulated (IUU) fishing, and ensure compliance with sustainability standards. Engaging fishing communities, indigenous groups, and other stakeholders in decision-making processes fosters ownership and facilitates the adoption of sustainable practices.Innovation and technology play a significant role in improving fisheries management practices. Advancements such as satellite monitoring, data analysis, and fishery modeling systems enhance the accuracy of stock assessments, enable real-time monitoring of fishing

activities, and support adaptive management approaches. Embracing technological solutions can lead to more efficient and sustainable fishing practices.

Education and awareness programs are crucial in promoting sustainable fishing practices and fostering a culture of responsible fishing. By educating fishers, consumers, and the wider public about the importance of sustainable fisheries management, the impacts of overfishing, and the benefits of responsible consumption, behavioral changes can be encouraged that support the long-term sustainability of fish resources.

In conclusion, the critical role of fish and fisheries in providing nutritious food, sustaining livelihoods, and promoting sustainable development cannot be overstated. Comprehensive approaches that balance the social, economic, and environmental dimensions of fisheries management are essential. By adopting science-based approaches, effective governance, stakeholder engagement, and embracing technological advancements, we can ensure the availability of fish as a vital food resource for present and future generations, while safeguarding the health of marine ecosystems and the well-being of fishing communities.

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Organoprotection during extracorporeal circulation

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Abstract

Background: In many cases, surgical correction of congenital heart malformations or aortocoronary bypass surgery involves the use of cardiopulmonary bypass (CPB). However, the possible negative effects of CPB on internal organs such as the brain, kidney, lungs, and liver cannot be ignored. Typically, CPB triggers a systemic inflammatory response syndrome (SIRS), which is thought to be caused by blood components coming into contact with the surface of the CPB tube. Furthermore, during CPB, the heart typically experiences a period of cold ischemia, while other peripheral organs experience overall hypoperfusion with low flow. As a result, a large number of pro-inflammatory mediators and cytokines are released and various biochemical pathways are activated, which can eventually lead to the occurrence of micro thrombus formation, micro embolism, coagulation factor deficiency, and bleeding diathesis in addition to typical ischemia-reperfusion injury.

Conclusion: In our review, we focus on possible pharmacological interventions for patients to reduce adverse effects of CPB and improve postoperative outcomes related to the heart and other organs such as the brain, kidney or lungs.

Keywords: Cardiopulmonary bypass, organoprotection, cardioplegia, CPB

Introduction

In the early 2th century, most congenital heart defect could not be treated with open-heart surgery due to the lack of medical equipment to move blood through the body. In 1885 two physicians invented a “Ventilation

system" that could be considered a prototype of the heart-lung machine: Maximilian von Frey and his colleague Maxcampus von Gruber, both at the Carl Ludwig Institute in Leipzig, developed a machine, which can be aimed at perfusion and oxygenation of respiratory isolated organs (von Frey and Gruber,1885). However, the machine is intended for basic research in open heart surgery. Nearly 70 years later in 1954, Gibbon designed a device that bypasses the heart and lungs, and he was the first heart surgeon to use it for open-heart surgery.

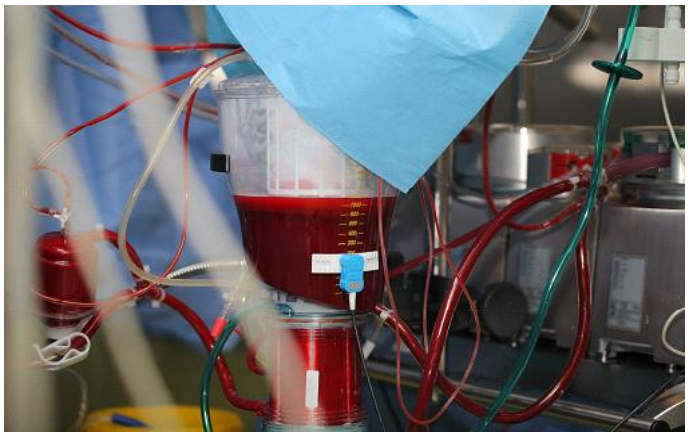

Figure 1

A reservoir consisting an oxygenator for converting the deoxygenated blood from the venous system to oxygenated blood to the aortic system . A bubble detector for detecting the bubbles seen in figure 1

This heart-lung machine – the so-called cardiopulmonary bypass (CPB) – along with the superficial hypothermia developed by Bigelow (1954), was a milestone in cardiac surgery. Both medical developments were giant leaps in cardiac surgery and the beginnings of modern cardiac surgery. While heart-lung machines have now become indispensable and allow for very complex heart surgery, such as the correction of congenital heart defects such as Fallot disease or hyperplastic left heart syndrome, the technology can be harmful to sensitive organs such as the brain and kidney, hence side effect cannot be ignored. There are several reports of adverse effects of cardiopulmonary bypass (CPB) on brain development, especially in children, and some brain regions, including the hippocampus, are particularly sensitive to ischemia and reperfusion injury.

Damage to the hippocampus, which is involved in learning and memory processes, is known to lead to cognitive impairments such as learning disability, memory deficits, behaviour disturbance, and hyperactivity. Although neurologic assessment of new-born and young children is inherently difficult, multiple lines of evidence suggest that the potential side effect of CPB on developing brain is subtle and that neurologic deficits often emerge years after successful surgical correction. Indeed, there are several clinical studies of children with complex cardiac malformation who underwent surgery in early childhood that CPB may negatively affect later neurologic outcomes.

The airflow produce by a heart-lung machine typically has a constant and mostly laminar distribution. This is in contrast to our own cardiovascular system, which produce pulsating blood flow. This does not adversely affect cerebral perfusion, which remains constant over a wide pressure range (50-150mmHg) due to an auto regulatory process. However, there is evidence that physiologic pulsatile flow may be superior to the non-pulsatile flow commonly used during CPB (Kusch et al., 2001). Other organs such as the kidney, liver and intestines are less self- regulating and thus may also be affected by CPB, epically in young organisms.

However, more than two- thirds of cardiac surgeries are not related to congenital heart defects in younger patients, but to aortocoronary bypass surgery and valve replacement in older patients. These patients are also at high risk of serious injuries such as neurological complications (disorientation, transient ischemic attack, and stoke), kidney failure requiring dialysis, or lung disease requiring prolonged mechanical ventilation.

It should be noted that strokes and TIAs can be attributed to thromboembolic median cerebral artery regions, whereas disorientation may be the result of globe low-flow ischemia affecting the Hippocampus attachment area.

It’s worth nothing that despite adequate “cardiac output” through heart-lung machines and body cooling, organ damage can still occur, compromising postoperative outcomes. Furthermore, both bypass organs, the heart and the lungs, are subjected to ischemia and reperfusion injury, which also negatively affects postoperative outcomes.

Typically, CPB triggers a systemic inflammatory response (SIRS), which is thought to be caused by blood components coming into contact with the surface of the CPB tube. This activates leukocytes, monocytes, endothelial cells, platelets, and the complement system, leading to the release of numerous pro-inflammatory mediators and cytokines.

Figure 2

The Cardiopulmonary Bypass Circuit is provided with PVC and Silicone tubing which produces the inflammatory response caused by blood components coming into contact with the surface of the CPB tube seen in figure 2.

Activation of various biochemical signalling pathways can lead to micro thrombosis, micro embolism, coagulation factor depletion, and the development of bleeding diathesis (Murphy and Angeline, 2004).

At the cellular level, ischemia and reperfusion induce multiple signalling cascades, including translocation of many transcription factors [Z]. PARP activation (poly-ADP- ribose polymerase), and formation of reactive oxygen and nitrogen species. These signalling cascades involve regulatory mechanisms of cell survival and cell death, ultimately leading to underlying organ dysfunction.

In recent, several protective strategies have been employed to ensure greater safety during CPB: bubble traps and mesh filters to reduce the risk of embolism, lung-protective mechanical ventilation to prevent respiratory distress syndrome, improved pH, Temperature and fluid management, and pulsatile flow (which has been shown to improve renal function and regional cerebral oxygen saturation) or pharmacological approaches to minimize organ damage. Various drugs have been tested – mainly in different animal models – to reduce organ dysfunction: drugs targeting Na+/H+ exchangers or IKATP channels, MMPs inhibitors, PARP inhibitors, antioxidants, guanylate cyclase stimulators, or anti-inflammatory drugs.

Cardioplegia

Cardiac protection during CPB has been controversial because the heart is not perfused during cardiopulmonary arrest, implying a period of absolute

myocardial ischemia. Surface cooling and induction of cardioplegia are critical for the survival of myocardial tissue. While the previously described procedures are intended to protect the heart and peripheral organs, the cardioplegia changes are primarily intended to protect the cardiac organ.

To achieve cold cardioplegia several cardioplegia are used, the most famous of which are St Thomas' Hospital's "extracellular" mixture, which is rich in potassium and magnesium, and Bret Schneider cardioplegia, the so-called "cellular" Inner" low sodium, low calcium, high potassium solution. Both crystalloid solutions are used in cold cardiac arrest.

A third technique known as "Calafiore blood cardioplegia" is also used in clinical settings during CPB. In this technique, oxygenated blood that has been supplemented with high potassium and magnesium levels is given through the aortic root until cardiac arrest. According to Calafiore and colleagues, warm blood cardioplegia has an advantage over cold blood cardioplegia in that patients' postoperative outcomes were better and myocardium-specific enzyme levels were lower in the group receiving warm blood cardioplegia (Calafiore et al., 1995). Different outcomes were found by other writers. Poling et al. (2006) discovered a marginally superior outcome for patients with cold cardioplegia, particularly in individual with long clamping periods, in a later trial with cold and warm cardioplegia arrest. Unfortunately, only 17 patients from each group participated in their trial, which was relatively small.

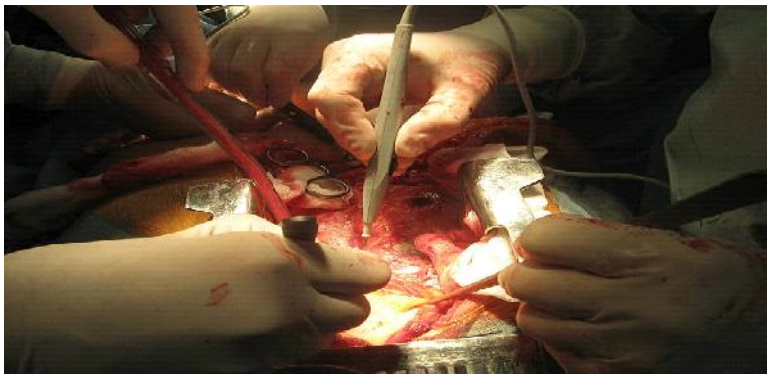

Figure 3

Surgeons assessing the defect in the heart by providing the blood from the heart to the extracorporeal system using aortic and venous cannula.

In general, it may be said that the question of whether cold, warm, blood, or crystalloid solutions world be ideal for cardioplegia during a particular heart operation has not yet been answered. Nonetheless, a number of additives have been tested in an effort to reduce ischemia/reperfusion damage and better maintain the energy balance of the solution (=Custodial) was supplemented with L- arginine, N- acetyl-L-histidine deferoxamine, and LK-614 (an iron chelator). It was found that the Custodial – N group's ATP content was significantly higher and it levels of myeloperoxidase. Also, the rat's cardiac function improved when the novel Custodial-N solution showed protective properties.

Unlike decades before, when CPB's organ protective effects were mostly focused on cardio protection, recent years have seen an increase in attention paid to the harmful effects of CPB on other organs such the kidney,brain,lung, and liver. Consequently, many cardioplegia treatments and protocols, such as pulsatile flow protocols, hypothermic arrest, and warm blood cardioplegia, were tested in the early decades by scientists and surgeons. More recently, novel tactics that frequently target the biochemical pathways that are activated by the ischemia-reperfusion injury linked to CPB were focused on protecting the brain, kidney, lung, and liver. Therefore, it has been demonstrated that CPB acutely causes an ischemia – reperfusion injury in the kidney, lung, and brain. To varying degrees, this injury can be treated using anti-oxidant and anti-apoptotic drugs, MPTP inhibition, NHE blockade, PARP inhibition, and MPTP inhibition.

PARP inhibitors

DNA strand breaks mainly occur during reperfusion phase with elevated oxygen levels. Reactive oxygen species(ROS) and Peroxyntrite (formed in the presence of NO) diffuses into the nucleus and induce destruction of genetic material. The resulting of single -stranded DNA nick is recognised by PARP and marked with a PAR strand. These in turn signal for other DNA repairenzymes, such asDNA ligases and DNA polymerases beta. After repair, the PAR chain degenerates. Hyperactivation of PARP depletes NAD+ stores and eventually leads to lowered ATP levels, ultimately with disastrous consequences for cells. In addition, the PAR chain can cause the release of AIF (apoptosis- inducing factor) from the mitochondria into the cytoplasm. AIF migrates to the nucleus and triggers so called par Thanatos, which are irreversible and lead to cell death.

Inhibitors of the PARP signalling pathway such as minocycline can prevent ATP deficiency and maintain intracellular ATP levels. Minocycline is a broad-spectrum antibiotic belonging to the tetracycline class. It has bacteriostatic properties and is often used to treat acne vulgaris or Lyme disease. In addition, it has neuroprotective and anti-inflammatory properties. In a rat model of hypothermic cardiac arrest,it is able to demonstrate that minocycline reduced ischemia- induced increases in brain.

Typically, plasma concentrations in patients receiving minocycline for medical reasons are in the range of 1-2Mmol/l. This is more than 10-old higher than the concentration reported for sufficient inhibition of PARP. It seems reasonable to consider the use of minocycline during Cardiopulmonary Bypass in a clinical setting, but patient studies demonstrating a protective effect of minocycline are lacking. Another tetracycline with a similar chemical structure of minocycline is doxycycline, and there is evidence that this tetracycline derivative else has cytoprotective effects of the two tetracycline derivatives to these, as the other derivatives tested did not show any positive effect on ischemia/reperfusion injury.

Collagen-dissolving actors were first discovered by Gross and Lapiere in 1962 while studying how tadpoles lose,they’re during metamorphosis. This factor was later named MMP-1, and more than 20 different MMPs have been discovered so far. MMPs are zinc-dependent endoprosteases involved in the degradation of the extracellular matrix, the cleavage of cell surface receptors, and the regulation proliferation, apoptosis and migration. Furthermore, they affect cytokines processing, such as the activation of TNF or IL, thereby regulating leukocytes recruitment and inflammatory processes. Multiple cardiovascular diseases are associated with MMP dysfunction. Aortic aneurysm development due to MMP-17 deficiency or MMP-2 overactivation, plague susceptibility in angina patients, and impaired wound healing in diabetes.

Conclusion

CPB induces a systemic inflammatory response. So, the obvious idea is to suppress inflammation by using corticosteroids. McBride showed in a small patient study that subclinical renal impairment was reduced in a group of patients treated with methylprednisolone, although renal dysfunction was not prevented. In another study of neonates undergoing arterial switch surgery, dexamethasone was administered prior to CPB and levels of inflammatory molecules in myocardial tissue were measured.

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Emerging Applications of Nanotechnology in Neurological Disorders

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Abstract

The main health concerns in the modern world are neurological disorders like Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease, stroke, epilepsy, brain tumours, multiple sclerosis, etc. The central nervous system (CNS) has intracellular and extracellular barriers that make it difficult to transfer drugs to the CNS, which is why traditional therapies have not yet been successful in treating these illnesses. Nanotechnology has the potential to make significant improvements in the treatment of these debilitating neurological human illnesses and has already showed great promise in resolving issues with traditional treatment modalities. Gold nanoparticles, micelles, quantum dots, polymeric nanoparticles, liposomes, microparticles, carbon nanotubes, and fullerenes are just a few of the nanoscale materials that have been created and put to use for a variety of tasks, such as improving diagnosis, delivering neurotherapeutic agents, determining treatment response, etc. These barriers are crossed by the nanomaterials, which also target certain cells or signalling pathways, react to endogenous stimuli, carry genes, and assist nerve regeneration. Such frameworks may function as efficient drug delivery systems and open the door to efficient neurological disease treatments. It has been discovered that medications enclosed in nanoparticles are more effective at curing diseases than bulk materials utilised in traditional treatments. However, there are a number of fundamental obstacles with the therapeutic application of nanotechnology, including health risks and other complications due to the extremely small size of nanomaterials. The CNS defences, effective drug delivery systems using nanomaterials, their synthesis, mechanisms of action, nanoformulations of various neuroprotective drugs, nano-neurotoxicity, and future views are the main focuses of this review.

Key words: blood-brain barrier, nanomaterials, neuronal disorders, therapeutic drugs.

Introduction

The phrase "neurological disorders" refers to illnesses of the brain, spinal cord, cranial nerves, peripheral nerves, nerve roots, autonomic nervous system (ANS), neuromuscular junction, and muscles that affect the central and peripheral nervous systems. These conditions include stroke, neuroinfections, autism spectrum disorder, Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis, brain tumours, and schizophrenia (Chhabra et al., 2015). Regrettably, numerous potent neuropharmaceuticals designed to treat these illnesses failed in extensive clinical trials. The failure of drugs to reach their intended place of action within the body is, at least in part, to blame. Many neurological illnesses have been studied using a large range of possible medications, but their therapeutic success is still restricted due to a variety of difficulties (Sahoo et al., 2017).

Specifically, the blood-brain barrier (BBB) and the blood-cerebrospinal fluid barrier, which are peripheral barriers, are difficult to pass. The major obstacle to getting therapeutic substances including drugs, proteins, nucleic acids, imaging agents, and other macromolecules into the central nervous system is the blood-brain barrier (BBB), in particular (Sahoo et al., 2017). Using nanotechnology as a delivery method for these neurotherapeutics across BBB is a novel and intriguing idea. Although the creation and application of nanoscale particles have occurred for a long time, nanomedicine was first formed as an interdisciplinary field in the 1990s. The nanotechnological method was originally developed in the 1950s, and soon the driving power to establish nanomedicine as a crucial area in science and medical treatments acquired prominence (Krukemeyer et al., 2015 Sohail et al., 2020).

Drugs loaded inside nanoparticles (Table 1) have demonstrated great potentials for effective drug delivery to the central nervous system over the past few decades due to their nano-size range, unique physico-chemical properties, and capacity to exploit surface engineered biocompatible and biodegradable nanomaterials (Aso et al., 2019). These nanoparticles can be created using a variety of methods, as shown in Table 2. Nanotechnology will become more significant in the medical field during the next ten years because it can help individuals with neurological problems live better lives (Sohail et al., 2020).The field of neural circuits has expanded tremendously since the

tactics in nanotechnology were successfully put into practise (Sohail et al., 2020).

Table 1. Preparation of nanoparticles

Sr. No.	Techniques Used	Preparation Procedure	Types of Nanoparticles
1.	Solvent Evaporation	The polymer solutions are prepared in water-non-miscible, Organic volatile solvents ($CHCl_3$, $CHCl_2$, and C_4H8O_2). The Emulsion (o/w, w/o/w) undergoes evaporation of the solvent. The NPs are collected, washed, and lyophilized after ultracentrifugation	Poly (lactic-co-glycolic acid) (PLGA) nanoparticle isprepared by this method (Reis et al., 2006)
2.	Nanoprecipitation	A solution is prepared by dissolving polymer in water miscible organic solvent. For formation of colloidal suspension and its precipitation pipetting is done in stirring aqueous medium	Preparation of cyclosporine A loadedNPs (Allemann et al., 1998)
3.	Emulsification	The polymer is dissolved in partially water-soluble solvent in the presence of excess of water. This is then dissolved in aqueous solution having surfactant. Nano spheres or Nano capsules are produced depending on the concentration of oil and polymer	Doxorubicin (anti-cancer drug) loaded PLGA NPs is done by this method (Yoo et al., 1999)
4.	Salting Out	Drug and polymer are dissolved in a solvent(acetone). This is dissolved in an aqueous solution containing as calcium chloride or sucrose which acts as salting out agent and polyvinyl pyrrolidone acting as stabilizing agent. This forms o/w emulsion that is then diluted in excess water resulting in the production of Nano spheres	This technique is employed in formation of lipophilic drugs (Memisoglu et al., 2003)
5.	Supercritical Fluid Technology	In this process, rapid expansion of supercritical solution into liquid solvent (RESOLV) and rapid expansion of super critical fluids (RESS) was used	Submicron particles of cyclosporine, water insoluble drug (Young et al., 2000)
6.	Emulsion Polymerization	The monomer is dispersed in aqueous or organic non-soluble solvent followed by addition of surfactant. Polymerization is established either by adding an initiation molecule such as a free radical or by producing the radical by the monomer itself with the aid of radiation	Poly (styrene-methyl methacrylate) /SiO_2composite NPs (Mahdavian et al., 2007)

Table 2. Nano approaches towards CNS drug delivery

Sr No.	Nanoparticles	Description	Uses
1.	Micelles	Micelles are the vesicles ranging from10 to 100 nm with outer hydrophilic portion and inner hydrophobic core (generally polypropylene glycols, phospholipids, fatty acids). They may be made up of either amphiphilic surfactants (non-polymeric micelles) or amphiphilic copolymers (polymeric micelles)	They help in the loading of hydrophobic drugsfor CNS delivery (Torchilin, 2007)
2.	Polymeric Nanoparticles	Polymeric nanoparticles (10-100 nm) are solid colloidal dispersion of biocompatible, biodegradable polymers. These have a core of dense polymer and a hydrophilic outer covering to provide steric stability	*Encapsulates lipophilic* drugs which may be encapsulated, adsorbed or chemically attached to the surface (Sahoo et al., 2017)
3.	Solid Lipid Nanoparticles (SLN)	They are aqueous colloidal nano-carrier system composed of lipids (triglycerides, fatty acids, steroids, etc.), introduced aqueous surfactant solution or water and enerally solidify on cooling	Quercetin loaded to treat AD, Atazanavir loaded against HIV-encephalitis (Chattopadhyay et al., 2008)
4.	Nano Emulsions	Nano emulsions (100-500nm) are o/w or w/o colloidal particulate systems which are made up of edible oils, surfactants and water.	Modification of nano emulsions helps in overcoming the BBB, helping in rapid distribution of drugs to peripheral sites, mainly the brain (Shah et al., 2013)
5.	Dendrimers	Dendrimers have 3-dimensional symmetrical structure having an inner core from which there is a number of hyper branches, ('generations') with functional groups at the peripheral terminal surface to be easily functionalized with many ligands	Dendrimers are used for hydrophobic and hydrophilic drug delivery (Tripathy and Das, 2013; Sohail et al., 2020)
6.	Carbon Nanotubes and Fullerenes	These are carbon allotropes which are characterized by a hollow structure and striking thermal, electrical and mechanical properties. Fullerenes are of two types- Spherical Fullerenes and Cylindrical Fullerenes or Nanotubes	These are successfully used in neuronal disorders like AD, PD, and ischemic stroke and in vivo in many diseases like bone ants, rheumatoid arthritis, osteoporosis, and cancer (Boridy et al., 2009)

Research on nanotechnology has exploded in recent years, opening up new opportunities for medication delivery, theranostics, tissue engineering, magnetofection, and gene therapy (Krukemeyer et al., 2015). Nanotechnology's efficacy is now well established, and it has paved the way for new, highly effective medication delivery techniques, even to the most inaccessible areas like the CNS (Kumar and Singh, 2015). By highlighting the important ideas, concepts, and methods in this review, we aim to clarify how nanotechnology can be used to treat neurological illnesses. This will help people better understand the subject and encourage additional study (Naqvi et al., 2020).

Blood Cerebrospinal Fluid Barrier (BCSFB) and Blood Brain Barrier (BBB):

The average distance between blood capillaries in the brain is roughly 40 microns, which indicates that each brain cell may have its own capillary. The brain has a very dense microvasculature (Duvernoy et al., 1983). About 10–20 nm separate the closest capillary from a neuron in terms of diffusion distance (Schlageter et al., 1999). Tight connections are found in the epithelial cells of the choroid plexus (CP), which prevent chemicals from the circulation from penetrating into the CSF.

There are, however, few chemicals that enter the CSF from the circulation because of its low resistance (Saito, 1983). For instance, azidothymidine (AZT) is strongly limited at the BBB after entering the CSF through the choroid plexus epithelium. A substance's penetration into the brain parenchyma could not be possible after it enters the CSF. The distinct presence of ependymal and glial cells distinguishes the circumventricular organs from the rest of the brain (Abbott et al., 2006), and diffusion facilitates the penetration of chemicals from CSF to brain parenchyma. The great separations provide a diffusion barrier that is sometimes called the CSF-brain barrier (CBB). The subarachnoid space, which is filled with CSF and surrounds the brain and spinal cord, contains arachnoid barrier (AB) cells, which may serve as a barrier and limit the penetration of chemicals into the CSF (Yasuda et al., 2013; Sohail et al., 2020).

Methods for Drug Delivery into the CNS:

Invasive drug delivery procedures include a multitude of negative side effects, including immune system inflammation, nervous system injury, and many others. Contrarily, non-invasive methods like nano drug delivery ensure that drugs are delivered without compromising BBB (Jain, 2007). By encapsulating the drug into a carrier system, namely nanoparticles, using the technique of nanotechnology, the targeted drug delivery in the needed quantity

might be achieved in this procedure. The nanoparticles must possess enough tensile strength to withstand prolonged circulation without deteriorating.Either a polymer-based or lipid-based delivery method is possible (Naqvi et al., 2020).

Using nanomaterials to release drugs: the mechanism of action

The negative surface charge of the endothelial cells found in the brain electrostatically interacts with the positive surface charge of nanomaterials, and the lipophilic characteristic of nano-carriers enhances the adsorption process. After typical endocytosis and transcytosis, the nanoparticles enter the brain capillary endothelial cells and bind to low density lipoprotein receptors. Once again entering the bloodstream after desorption, the drug-loaded nano carrier releases the drug that has been encapsulated or adsorbed on the blood brain barrier and diffuses into the brain parenchyma. Selective entrance into the brain can occur via passive, gradient-dependent (passive targeting), or active, energy-dependent (active targeting) routes (Figure 1). Transcellular conveyance is used for nanocarriers smaller than 500 Da (Georgieva et al., 2014).

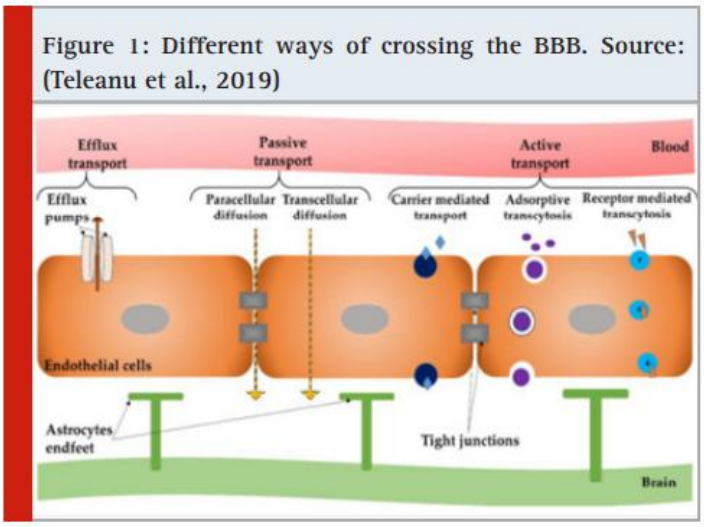

Figure 1: Different ways of crossing the BBB. Source: (Teleanu et al., 2019)

Clathrin-Mediated Endocytosis:

All mammalian cells use this process. In order to produce an inward budding that engulfs the cargo, the nano-carrier connects with a particular plasma membrane receptor, inducing the polymerization of the cytoplasmic protein clathrin-1 just below the plasma membrane (Rappoport, 2008).The inward budding is stopped by the GTPase activity of dynamin, which causes

clathrin-coated vesicles to form. Actin aids in clathrin coat shedding, which results in the development of early endosomes that deliver their material to late endosomes and then to the lysosomes where it is broken down. The pH gradually drops during the transition from late endosomes to lysosomes, resulting in the drug's release from the nano-vehicle and eventual release at the target site (Georgieva et al., 2014).

(ii) The brain's caveolar pathway for delivery:

This mechanism is distinct from the clathrin-mediated system because it avoids lysosomal delivery.Three isoforms of the caveolin protein, caveolin-1, caveolin-2, and caveolin-3, are present in mammalian cells and aid in transportation through this channel. Caveolae are flask-shaped invaginations in the plasma membrane.After attaching to the caveolar receptor, the Nano carriers are internalised, creating a vesicular structure known as a cavicle. The cavicle is then propelled by actin-derived energy and united with caveosomes, which have a neutral pH, before moving towards the endoplasmic reticulum by piercing into the cytoplasm and eventually entering the nucleus through the nuclear pore complex (Rappoport, 2008).

Uses of Nanotechnology in CNS Disorders:

In Alzheimer's disease, polyethylene glycol (PEG) stabilized\snanomicelles made up of phospholipids block Abaggregation and mitigate Ab-induced neurotoxicity in SHSY-5Y human neuroblastoma cell line in vitro.The potential of microemulsion nanoparticles laden with the copper chelator d-penicillamine to traverse the BBB and dissolve the pre-existing Ab clumps in vitro was discovered (Vinogradow et al., 2004). Curcumin-containing nanoliposomes not only prevent Ab from aggregating, but they also increase its bioavailability.In addition, fullerene has a neuroprotective effect, the capacity to prevent Ab-induced cognitive deficits following intraventricular delivery, and the ability to inhibit Ab peptide fibrillization (Taylor et al., 2011).

The PEG and polyethylenimine nano gel complexes with antisense oligonucleotides may effectively pass the blood-brain barrier in vitro in Parkinson's disease. The oligonucleotides supply the brain more effectively when administered intravenously, especially when the gels were functionalized with insulin (Mohanraj et al., 2013). L-Dopa-encapsulated nanoparticles and polybutylcyanoacrylate (PBCA) nanoparticles attached to nerve growth factor (NGF) penetrate the blood-brain barrier (Siddiqi et al, 2018).Fullerenols can remove free radicals and lessen oxidative stress on cells in Huntington's disease.

Macropinocytosis and phagocytosis mechanisms for medication transport into the brain are shown in Figure 2. (Hillaireau and Couvreur, 2009).

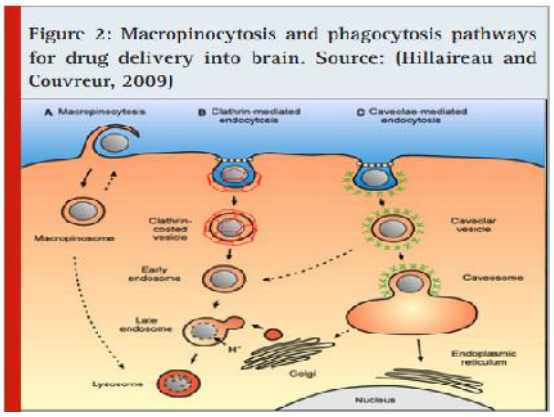

Figure 2: Macropinocytosis and phagocytosis pathways for drug delivery into brain. Source: (Hillaireau and Couvreur, 2009)

SLN-encapsulated nitrendipine demonstrated greater drug absorption than bulk nitrendipine. Huntingtin (HTT) mRNA expression is decreased by short-interfering RNA (siRNA) encapsulated cyclodextrin nanoparticles both in vivo and in vitro (Huang et al., 2012). The interaction of stem cells and carbon nanotubes in multiple sclerosis offers a means for tissue engineering to investigate and enhance cell behaviour. Ciliary neurotrophic factor (CNTF) loaded microcapsules showed in situ sustained administration of CNTF upon encapsulation into polymers in preclinical research. This has no cytotoxic or immune-modulating effects (Godinho et al., 2013). A superoxide dismutase (SOD)-coated gold nanoparticle and SOD1 aggregates are employed as a colorimetric detection technique for the diagnosis of amyotrophic lateral sclerosis.

It is occasionally possible to employ carboxyfullerene nanotubes with SOD. It is possible to use carbon NPs to efficiently and precisely administer the glutamate inhibitor riluzole to the troubled areas (Klyachko et al., 2013; Alexander et al., 2019).As comparison to free medications, nanoformulations such as PBCA nanoparticles containing methotrexate and temozolamide have boosted intracerebral drug concentration in brain tumours. In vitro, etoposide and paclitaxel solid lipid nanoparticles (SLNs) were shown to have an improved inhibitory effect on glioma cell line proliferation compared to the free drug alone (Kohane et al., 2002). Effective treatments for epilepsy include carbamazepine-filled SLNs and b-carotene-loaded PLGA nanoparticles. Liposomal muscimol formulation is found to reduce histological changes while suppressing focal seizures in a rat model (Brioschi et al., 2012). In rat models, xenon gas laden liposomes were successful when given for up to 5 hours after

the onset of stroke, with a tolerable dosage range of 7–14 mg/kg (Peng et al., 2013). Using poly (hexylcyanoacrylate) NPs, increased targeted delivery of azidothymidine (AZT) to macrophages is conceivable in neuro-AIDS. Using poly (hexylcyanoacrylate) NPs, saquinavir can also be delivered to human monocytes or macrophages (Chhabra et al., 2015; Alexander et al., 2019).

Nanotechnology-Based Neuroprotective Drug Delivery: Curcumin (diferuloylmethane), a physiologically active and important phenolic component of turmeric that is derived from the rhizomes of the Curcuma longa plant, has demonstrated significant therapeutic value in treating a number of ailments (Chattopadhyay et al., 2008). Curcumin is a naturally occurring antioxidant that has been shown in preclinical and clinical research to have a wide range of pharmacological properties, including anti-inflammatory, antibacterial, anticancer, and the neuroprotective effect in neurological illnesses. Despite curcumin's numerous medical uses, its clinical implications are limited by low solubility, physico-chemical instability, poor bioavailability, and rapid metabolism (Chattopadhyay et al., 2008). Yet, by creating effective delivery systems with the use of a nanotechnological approach, these issues can be remedied. Curcumin-loaded polysorbate 80 supplemented with some (CPC) nanoparticles also shown greater stability, a longer circulation time, and a higher permeation of curcumin nanoformulation as compared to bulk curcumin (Naksuriya et al., 2014; Alexander et al., 2019).

Nerve Growth Factors (NGFs) offer the greatest therapeutic promise among growth factors for a variety of CNS diseases.

By encouraging neurogenesis and cerebral angiogenesis, vascular endothelial growth factor (VEGF) has been demonstrated to contribute to the process of post-ischemic brain healing. Treatment with modified liposomes containing transferrin-loaded VEGF has therefore proved successful in promoting vascular regeneration and neuroprotection in the ischemic brain. The well-known lipophilic medication edaravone (EDR) is utilised as a free radical scavenger for cancer, cardiovascular illness, and neurological disease (Hudson et al., 2013). EDR has demonstrated excellent efficacy in preclinical tests when administered orally to treat AD and cerebral aneurysms, although its oral bioavailability is relatively low (Cruz, 2018). By enhancing the oral bioavailability, the lipid-based nanosystem (LNS) loaded with EDR was created to support its successful oral delivery (Alexander et al., 2019).

Nano-Neurotoxicity: The neurotoxicity of nanomaterials

Doors are opened for both medication transport and toxicity while invading the neuronal network's defences. The difficulty in determining

nanotoxicology is partially due to the scope and scale of toxic events. They interact strongly with elements and systems in both the physiological system and the cell's biochemical environment (Karmakar et al., 2014). Metal oxide nanoparticles are very beneficial in many industries, including engineering and medical.

Due to their small size and substantial surface area, these NPs are highly poisonous and chemically reactive. These NPs can build up in the brain's cortex and cerebellum, among other areas (Valavanidis and Vlachogianni, 2016). Studies have suggested a significant level of genotoxicity (DNA interference) associated with the use of multi walled carbon nanotubes (MWCNTs) as scaffolds, which is indicative of a larger issue brought on by the usage of nanomaterials. Thus, according to Kumar et al. (2017) and Alexander et al. (2019), nanotoxicology profiling is an essential part of investigations of nanomaterials.

Conclusion

The development of brain-targeted medicine delivery devices has received a lot of interest recently.Over the past ten years, numerous fields have discovered applications for nanotechnology, including drug delivery, biological sensing, biomedical imaging, targeted anticancer treatments, and antibiotic carriers. Nanotechnology has made its way into the field of medicine, enhancing not only drug delivery but also the necessary surgical procedures, as demonstrated in the instance of brain tumours. New polymeric implants are favourable because they offer enhanced bioavailability with little to no neuroinflammation, in contrast to conventional implants that, because of the rigidity of the material, may cause neuroinflammation.

Although several nanoformulations have demonstrated excellent performance in preclinical and clinical research, there are still a number of fundamental issues that need to be resolved in the future for nanoformulations to successfully enter the clinical setting. In addition to being easily biodegradable, the nanomaterials used in brain-targeted medication delivery systems should be efficient and safe. Eco-friendly methods should be used in the development of nanomaterials. To create efficient medication delivery systems that target specific areas of the brain, it is important to thoroughly assess the physico-chemical features associated with nanomaterials. It is important to develop a non-invasive alternative drug delivery strategy to prevent the problems associated with invasive approaches. To increase the likelihood of using nanoparticles in therapeutic settings, more basic research is necessary.

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Non-anesthetic benefits of Lignocaine - A game changer

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Abstract

Lignocaine, also known as Lidocaine which comes under the class of local anesthetic drug of the amino amide typeand commonly sold under the brand name Xylocaine. Lidocaine is the most common local anesthetic agent which is used in almost all medical specialties. It is in the class of the local amide anesthetics, which, compared to the ester-type local anesthetics, which is usually well tolerated with only rare occasions of allergic reactions. Lidocaine mixtures may also be applied directly to the skin or mucous membranes to numb the area. It is often used mixed with a small amount of adrenaline to prolong its local effects and to decrease bleeding, but it is contraindicated to administrate at the distal part of limbs. Lignocaine has many special positive

effects such as analgesic, anti-arrhythmic effect, etc… In this review we focused on non-anesthetic benefits of lignocaine during clinical practice.

Keywords: Lignocaine, Lidocaine, local anesthetics, anti-arrhythmic, cardioplegia.

Introduction

Lignocaine, also known as Lidocainewhich comes under the class oflocal anesthetic drug of the amino amide typeand commonly sold under the brand name Xylocaine.Lidocaine is a local anesthetic drug, when the drug is injected or applied in proximity to neural tissue it produces transient loss of sensory, motor, and autonomic function. It is the most common local anesthetic agent which is used in almost all medical specialties[1].

It is also commonly used as an antiarrhythmic agent to depress pulseless ventricular arrhythmias. Infusions of lidocaine have been used to supplement general anesthetic techniques, as they are capable of reducing the minimum alveolar concentration of volatile anesthetics by up to 40%, as well as providing pain relief in the peri-operative phase[2].

It is in the class of the local amide anesthetics, which, compared to the ester-type local anesthetics, which is usually well tolerated with only rare occasions of allergic reactions.Lidocaine mixtures may also be applied directly to the skin or mucous membranes to numb the area. It is often used mixed with a small amount of adrenaline to prolong itslocal effects and to decrease bleeding, but it is contraindicated to administrate at the distal part of limbs[3].

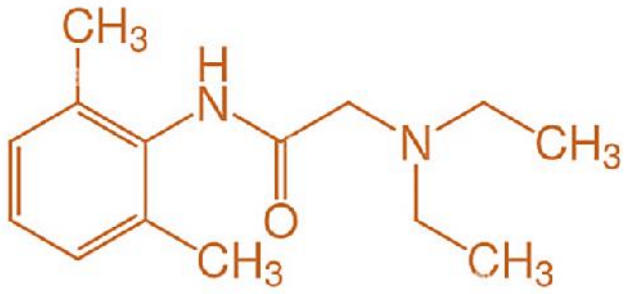

Figure 1

Figure 1 represents the chemical formula of lignocaine

General Mechanism of Action

The mechanism of action of lidocaine is at Na+ channels on the internal surface of nerve cell membranes. The uncharged Na+ ions diffuse via neural sheaths into the axoplasm before ionizing by combining with hydrogen ions. The resulting cation binds reversibly to sodium channels from the intracellular level, arresting them in the open state and preventing nerve depolarization[4].

Lidocaine has a more rapid onset of action than other local anesthetics with higher pKa values because as lidocaine is a weak base with a dissociation constant (pKa) of 7.7, approximately 25% of molecules will be un-ionized at a physiological pH of 7.4 and will be available to translocate inside the nerve cells[5].

Due to acidosis decreasing the proportion of un-ionized lidocaine molecules, efficacy decreases in the presence of inflammation, which can be a faster decrease in lidocaine concentration due to increased blood flow, and potentially also through increased production of inflammatory mediators like Peroxyntrite, which act directly on sodium channels[6].

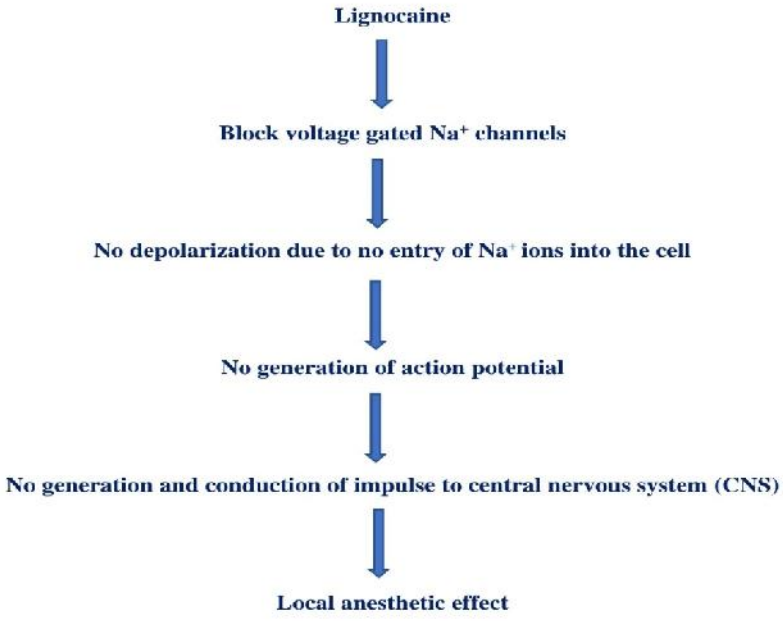

Figure 2

Figure 2 represents the mechanism of action of lignocaine as a local anesthetic agent

Forms of lignocaine for various uses

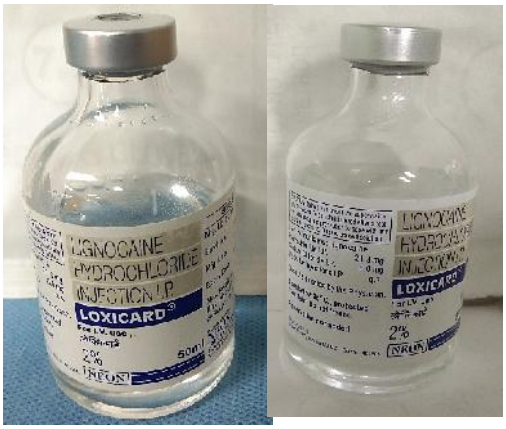

Figure 3

Figure 3 represents the vial of lignocaine(21.3mg/ml) as ananti-arrhythmic agent

Apart from its anesthetic use, it is used as a multipurpose drug in other fields. Lidocaine also comes under the class of antiarrhythmic drug of class 1b type, which works by blocking sodium channels and thus decreasing the rate of contractions of the heart. Lignocaine blocks the signals conducting via the nerve to brain, when injected near the nerves[7].

It is used intravenously for the treatment of refractory ventricular fibrillation (VF), pulseless ventricular tachycardia (pVT), Cardiac arrest from VF or VT Wide complex tachycardia. Continuous infusion after return of spontaneous circulation (ROSC) from VF/pVT 2nd line agent if amiodarone is unavailable[8].

Recommended dose for antiarrhythmic effect

For cardiac arrest 1 to 1.5 mg/kg IV/IO bolus may repeat twice at a half dose every 5-10 minutes to total of 3 mg/kg; followed by a continuous infusion of 1-4 mg per minute Continuous infusion should begin with the post-ROSC from VF/pVT: For wide complex tachycardia with pulse: Administer 0.5-1.5 mg/kg IV; may repeat treatment twice at half dose every 5-10 minutes for a total dose of 3 mg/kg; followed by a continuous infusion of 1 to 4 mg per minute[8].

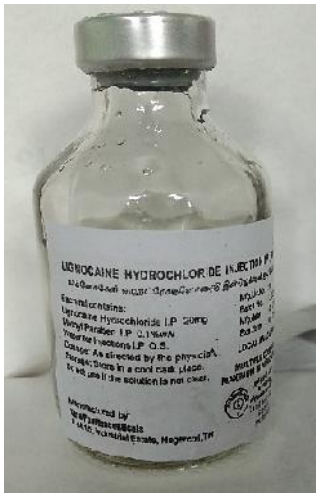

Figure 4

Figure 4 represents thevial of lignocaine (20 mg/ml) as alocal anesthetic agent

Chronic pain and acute surgical pain can be treated via infusing intravenous lidocaine infusions which is also used as an opiate sparing technique. Inhaled lidocaine can act peripherally to reduce the cough reflex, so it is also be used as a cough suppressor. As lignocaine reduces the incidence of coughing and prevents tracheal damage, so it can be considered as a safety and comfort measure for patients who have to be intubated during emerging from Anesthesia[9].

Administration of intravenous Lignocaine infusion is considered as an adjunctive intervention in patients with severe acute tenderness, during and post laparotomy, following major trauma or burns and for acute cancer pain flares or neuropathic pain that has not responded to other interventions[10].

Prescription lidocaine transdermal comes as a 5% patch and as a 1.8% topical system to apply to the skin. Prescription lidocaine transdermal is should be applied only once a day. Surprisingly lidocaine is used to relieve nerve pain called as post-herpetic neuralgia[11].

Figure 5

Figure 5 represents the transdermal lignocainehypochloride gel, as a local anesthetic agent

Currently iv lidocaine is used as a perioperative analgesic across a wide number of areas including the operation theatre, intensive care units, surgical wards and recovery room. Lidocaine has anti-nociceptive, anti-inflammatory actions and it is presumably these actions, rather than a local anesthetic effect, which explain the apparent prolonged effect hours after an infusion has been completed[12].

Plain lignocaine (21.3mg/ml) is used as a major component in cardioplegiawhich is chemical solution made up of combination of drugs such as potassium, sodium bicarbonate, lignocaine, mannitol, etc..., This cardioplegia is completely handled by the highly trained healthcare professionals, who are called perfusionist, use this solution to induce diastolic cardiac arrest of heart during the cardio thoracic surgery[13].

Many of the study suggests that lidocaine containing cardioplegia appears to be safe in adults undergoing cardiac procedure when administered for the first 60 minutes of aortic cross clamping. Higher CK-MB levels did not translate into adverse clinical outcomes[14].

Mechanism of lignocaine in cardioplegia solution

Lidocaine is a sodium channel blocker and class 1b antiarrhythmic agent, which increases the myocyte refractory period and it prevents the negative effect of hyperkalemic depolarized arrest by polarizing the cell to some degree and reducing intracellular sodium and calcium influx[15].

Conclusion

This review concluded the non-anesthetic benefits of lignocaine during clinical practice, apart from local anesthetic effect, lignocaine has multiple positive effects in cardiovascular system such as anti-arrhythmic effect and cardioplegic effects, so lignocaine may open a new era in cardiovascular health.

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A Review on role of earthworm gut microbes in improving soil fertility and plant growth

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Abstract

Hazardous agricultural chemicals cause serious issues with the environment and with human health. Organic farming may eventually replace the utilization of synthetic pesticides and fertilizers. Earthworms have long been known to improve soil fertility and aid in the decomposition process. In essence, decomposition and the creation of humus in soil are enzyme-mediated processes that heavily rely on soil microbes. Earthworms' guts are home to a variety of microbes. Moreover, these bacteria may have a key effect on the quicker germination of seeds, lentils, and paddy plants. The earthworm gut microbes can be used as biofertilizers and can be effectively used in a variety of organic agricultural techniques.

Keywords: Earthworm, Earthworm gut microbes, utilization of gut microbes by soil and plant.

1. Introduction

Earthworms have many microorganisms in their gut that they utilize in an extensive wide range of ways. Earthworm castings have been shown to contain far more nutrients than the surrounding soil. On cow dung, vegetable waste, chicken droppings, slaughterhouse waste, coffee grounds, kitchen waste, sewage sludge, kitchen mill waste, septic tank sludge, leaf litter, agro-industrial sludge, and other agro wastes, L. RUBELLUS may be farmed quite successfully. These species are frequently employed for the decomposition of organic

wastes, such as fruit and vegetable wastes (Suthar, 2004; Adi Noor, 2009; Suthar 2010 and Singh ET AL., 2010).

According to Norgrove and Hauser (2000), earthworms generate considerably higher quality casts on poorer soil. They get most of their nourishment from microbes. Teotia ET AL. (1950) discovered a much higher microbial population in earthworm castings than in surrounding soil. Plant development can be aided by soil microbes by improving soil organic matter conversions, mobilising inorganic nutrients, generating plant growth regulators (PGRs), and a variety of other processes (Siddiqui, 2005). The use of chemical fertilisers reduces the overall yield of the crops, and over time the soil becomes sterile and unusable for farming techniques (Bhawalkar, 1996). Earthworms are largely divided into the three types of epigeic, anecics, and endogeics (Bouche, 1977) based on their eating and burrowing habits.

Certain species of earthworms exhibit the existence of gut bacteria unique to ecological groups (Lavelle ET AL., 1994). In the L. TERRESTRIS hindgut, several physical connections between bacterial cells and epithelium were discovered (Jolly ET AL., 1993). Many of the bacteria that travel through an earthworm's gut seem to be temporary, and the worm merely eats them to get nutrition (Drake ET AL., 2007). According to several research, the microbial composition of soil and food sources and the bacteria in earthworms' guts are related (McLean ET AL., 2006; Drake ET AL., 2007; Knapp ET AL., 2008).

2. Role of earthworm gut microbes in improving soil fertility and plant growth

2.1. Gut microbes in earthworms and their activity

Farmers consider earthworms in high esteem as their companions and as nature's ploughman (Darwin, 1881). In their gut, earthworms keep a variety of microbes that they use in different ways. Their main source of nourishment comes from microbes. With enhanced nutrient intake, improved soil physical characteristics, greater soil mixing, and increased water penetration rates, earthworm activity can boost crop development (Kladivko and Timmenga, 1990). The vermicompost is an organic material that has been aerobically digested and chemically disintegrated by enzyme activity in earthworms' guts as well as by related microbial populations. The granular aggregate known as "worm cast" is sustained by an earthworm and microbial mucosal polysaccharide covering (Anand ET AL, 1995 and Kumar ET AL, 2010).

From the gut of *Lumbricus terrestris*, Bassalik (1913) isolated more than fifty different types of bacteria, and all of these bacteria were also present in the soil environment. According to Parle (1963a), there were many microorganisms in the soil and plant detritus surrounding three Lumbricid species' alimentary canals. 50 Although earthworm castings have far higher bacterial counts than the surrounding soil, it is generally known that the earthworm's stomach offers favourable conditions for the growth of bacterial colonies (Senapati, 1993). Earthworms have been shown to increase the amount of microorganisms in soil by up to five times, according to Atlavinyte and Lugauskas (1971). In pasture soil, microfungi connected to the degradation of the tissue of *Lampito mauritii* and *Octochae tonasurensis* were described by Dash ET AL. in 1979. Considering that these earthworms frequently consume organically rich materials, where microbial colonisation is already substantial, extended gut transit times may allow for microbial proliferation (Kristufek ET AL., 1992).

In their 1980 study, Dash ET AL. examined the impact of a population of the worm LAMPITOMAURITII on four functionally distinct classes of nematodes, including parasitic forms, other feeders, microbial feeders, and predators. The microorganisms in the stomach may cause the breakdown of organic materials, making the castings more nutrient-rich for plants (Crossley ET AL., 1995). Lignin oxidation and humus production may occur in the intestines of earthworms. Large volumes of dirt are consumed by earthworms, and their digestive tracts are constantly exposed to toxins (Morgan ET AL., 2004). The gums that cement the castings into water-resistant aggregates are produced by the gut bacteria of earthworms. The breakdown of organic matter and the release of mineral nutrients into the soil are greatly influenced by the interactions between earthworms and microorganisms (Scheu ET AL., 2002).

More than fifty different bacterial species were extracted by Bassalik (1913) from the gut of Lumbricus terrestris, and every single one of these bacteria was also discovered in the soil environment. According to Parle (1963a), there were many microorganisms in the soil and plant detritus surrounding three LUMBRICID species' alimentary canals. Although earthworm castings have far higher bacterial counts than the surrounding soil, it is generally known that the earthworm's stomach offers favourable conditions for the growth of bacterial colonies (Senapati, 1993). The vermicast contains a wealth of macro and micronutrients, vitamins, enzymes, antibiotics, growth hormones, and immobilised microflora, all of which are quickly soluble in water (Sudha and Chandini, 2003).

In an undisturbed forest floor in the Sirumalai Hills, South India, Karmegam and Daniel (2000-e) studied a selected microbial population of the earthworm casts, *Pontoscolex corethrurus* (Muller), and surrounding soil. The study revealed a higher rate and range of microflora in the casts than in the surrounding soil. Earthworms have been shown to increase the amount of microorganisms in soil by up to five times, according to Atlavinyte and Lugauskas (1971). According to Teotia et al. (1950), a much higher number of microorganisms were discovered in the earthworm castings than in the nearby soil. According to Stochli (1928), as bacteria travelled through the Lumbricid gut, their populations of soil Actinomycetes, pigmented bacteria, and Bacillus cereus group bacteria increased. In L. terrestris, *Aporrectodea caliginosa*, and A. *longa*, bacteria and actinomycetes grow quickly as they move through the stomach, according to Parle (1963a). He discovered in 1959 that *L. terrestris's* hind intestine had roughly 1000 times as many actinomycetes and bacteria as its foregut.

It has been discovered that earthworm guts preferentially induce particular microbes to be harboured there. According to Marialigeti (1979), several strains of the gram-negative, facultatively anaerobic Vibrio sp. made up 73% of the bacteria recovered from the intestine of the wood-eating earthworm E. lucens. He concluded that these bacteria play a significant part in wood indigestion because they can ferment glucose, arabinose, xylose, and some sucrose, which suggests a symbiotic connection. Many bacterial species, such as Bacillus spp., Azotobacter spp., Azospirillum spp., Beijerinckia SPP., and Pseudomonas spp., are capable of fixing nitrogen (Kristufek ET AL., 1994). Mulberry trees have been treated with nitrogen-fixing bacteria as foliar sprays (Sudhakar et al., 2000).

Streptomyces lipmanii, a rare species, was found in the intestine of *E. lucens* in 122 out of 145 isolates, or roughly 90%, according to Contreas (1980). According to Gest and Favinger (1992), the earthworm intestines had an abundance of several kinds of purple photosynthetic bacteria (Rhodospirillaceae). The earthworm's intestines and castings include bacteria including *Staphylococcus aureus*, *Proteus mirabiis*, Klebsiella species, and *E. coli*, as well as fungus like *Aspergillus flavus*, *Aspergillus terms*, *Aspergillu sniger*, Alternaria species, and Penicillium species. Large amounts of cast, finely fractured, and processed organic waste are consumed by earthworms. Casts typically have more microorganisms than the nearby soil does (Bohlen and Edwards, 1995).

In Indian earthworm species, gut microbes like Bacillus SP, Aeromonas sp and bacillus subtilis were commonly identified (Uma Bharathi ET AL. 2021)

2.2. Gut microbes tolerance against heavy metals

Inorganic phosphate solubilization of a few species, including *Aspergillus awamori, ASpergillus niger, Penicillium digitatum, Bacillus polymyxa, B. megaterium, B.circulans, B. pulvifaciens, Escherichia coli,* and *Pseudomonas striata,* was discovered by Arora and Gaur in 1978. On the other hand, Day (1950) discovered that their numbers significantly fell when the *Bacillus cereus* var. mycoides-inoculated soil moved through the stomach of *L. terrestris*. When *L. terrestris* ate the infected soil, other bacteria *Serratia marcescens* were destroyed. Similar findings were made by Briisewitz (1959), who discovered that Escherechia coli were likewise eliminated by *L. terrestris* when infected soil was consumed (Edwards and Bohlen, 1996).

Wani et al. studied how physiological parameters affected the P-solubilizing activity of four phosphor-microbes, namely *Bacillus polymyxa, Pseudomonas striata, Aspergillus awamori,* and *Penecillium digitatum* (1979). 14 cultures of several Bacillus spp. were tested by Bardiya and Gaur (1972) for P-solubilization on Mussourie and Singhbum rock phosphates. Phosphates were solubilized by all of the isolates, and this solubilization was consistently linked with a fall in medium pH. *Aspergillus carbonum, Aspergillus flavus, Aspergillus fumigatus, Aspergillus wentii,* and Bacillus species were isolated from Mussourie, Jhamarkotra, and Maton rock phosphates and studied for their phosphorous solubilization. Gaur et al. (1973) found that the pH decreased as the amount of organic P was solubilized more.

In some studies, the research had proved that the gut microbes can tolerate heavy metals such as copper, lead, cadmium and zinc etc.

2.3. Nitrogen fixation by gut microbes present in earthworms

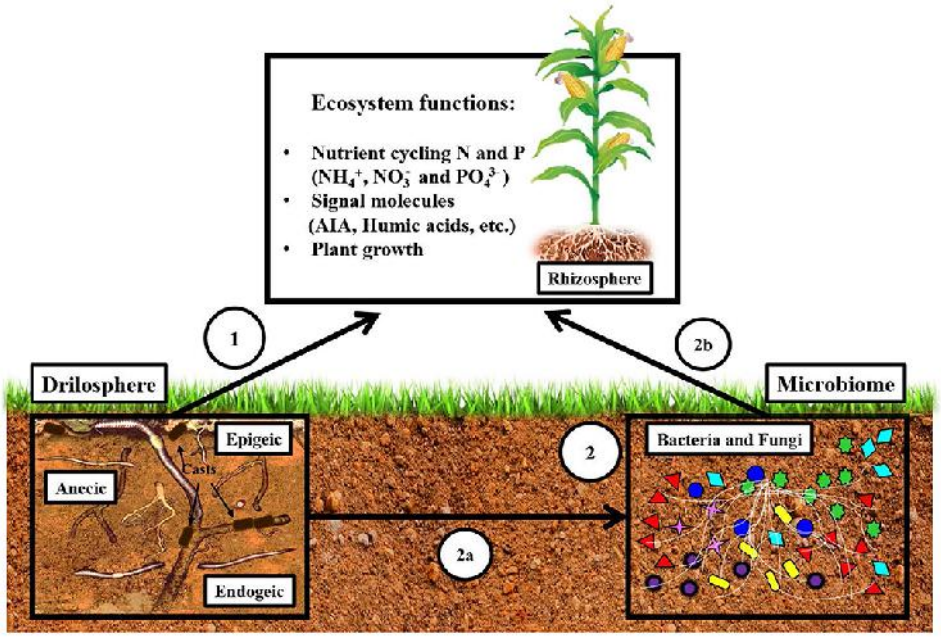
A thorough understanding of microbial successions is crucial for every composting process that is used (Taiwo and Oso, 2004). Bess (1999) asserts that a standard analysis for microbial content in composting must be established through the concentration of six functional categories of microorganisms, including fungus, Actinomycetes, Pseudomonads, aerobic bacteria, anaerobic bacteria, and nitrogen-fixing bacteria. There are now methods for determining the concentrations of these organisms in the final

compost, and those may be used as an interpretive guide to establish the compost's quality as a soil microorganism inoculant. According to Marcus ET AL. (2003), the intestines of *Apporectodea caloginosa*, *Allolobophora chlorotica*, *L. terrestris*, and *L. rubellus* constitute the perfect environment for microbes that produce N2O when swallowed. Some of the helpful bacteria may proliferate and participate in the digestion of earthworms by becoming dominant (Contreas, 1980).

2.4. Gut microbes that regulate plant growth

Regulators of plant growth are chemical compounds that, at extremely low concentrations, affect the physiology and growth of plants. Growing evidence suggests that phytohormones including auxins, gibberellins, and cytokinins are produced by plant growth-promoting rhizobacteria (PGPR), which then affect plant growth and development (Ortiz-Castro ET AL, 2008) In an experiment, the bacterial cultures of plant growth-promoting rhizobacteria (PGPR) Bacillus subtilis and *Pseudomonas aeruginosa* were inoculated with the plant species *Solanum lycopersicum* L. (tomato), *Abelmoschus esculentus* (okra), and Amarcmthus SP. (African spinach).

Figure.1: Role of earthworms on plant development and nutrient cycling (Regina ET AL., 2019).



Vermicasts have a large population of microorganisms, according to several research (Lee, 1985 and Parthasarathi and Ranganathan, 1999). In addition to acting as a carrier material for biofertilizers like *Azotobacter chroococcum*, *Bacillus megaterium*, *Rhizobium leguminosarum*, and Rhizobium and phosphate solubilizing bacteria, earthworm casts provide a suitable base for free-living beneficial microbes whose activity is necessary for the release of nutrients to plants (Ross and Cairns, 1982). (Manivannan and Daniel, 2007).

According to Kim ET AL. (2004), several microbial communities have colonised the earthworm's stomach. Many Pseudomonas, Bacillus, Arthrobacter, Azospirillum, Klebsiella, and Enterobacter plant growth-promoting rhizobacteria (PGPR) have been isolated from the rhizosphere of diverse crops, and synergistic effects on plant development have been shown (Egamberdiyeva and Hoflich, 2001).

Conclusion

All of the preceding studies suggest that although dangerous bacteria are selectively eliminated by earthworms, certain beneficial bacteria are chosen to multiply in abundance. And the helpful bacteria assist in numerous ways, such as maintaining soil fertility and enhancing plant development. Earthworms' accelerated microbial activity in the organic matter could produce large amounts of plant growth regulators like indole acetic acid, gibberellins, and cytokinins (Edwards, 1998).

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Oral dysbiosis – A potential decoder of systemic diseases

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Introduction

The significant role of microbes in day-to-day human life been evidenced since their discovery dates back from the 17th Century (Gao et al, 2018). Common microbial inhabitants of our body constitute the microbiome (Deo et al, 2019). The term microbiome was coined by Joshua Lederberg and the credit of first recognition of oral microbiome belongs to Antonie Van Leeuwenhoek (Yamashita et al, 2017).
Oral microbiome:

Construction of oral microbiome in a normal healthy individual has the presence of more than 100 species including archaea, bacteria, viruses, fungi and protozoans. (B. Sampaio-Maia et al, 2016). Oral bacterial members include a wide range of Gram positive and Gram negative bacteria such as *Abiotrophia*, *Peptostreptococcus*, *Streptococcus*, *Stomatococcus*, *Actinomyces*, *Bifidobacterium*, *Corynebacterium*, *Eubacterium*, *Lactobacillus*, *Propionibacterium*, *Pseudoramibacter*, *Rothia*, *Veillonella*, *Moraxella*, *Neisseria*, *Capnocytophaga*, *Campylobacter*, *Desulfobacter*, *Desulfovibrio*, *Eikenella*, *Fusobacterium*, *Haemophilus*, *Leptotrichia*, *Prevotella*, *Selenomonas*, *Simonsiella*, *Treponema*, *Wolinella* (Philip D. Marsh, 2000). The commonly encountered genera among oral fungal members includes *Aspergillus*, *Aureobasidium*, *Candida*, *Cladosporium*, *Cryptococcus*, *Fusarium*, *Gibberella*, *Penicillium*, *Rhodotorula*, *Saccharomycetales* and *Schizophyllum*. Most commonly reported oral viral infections are found to be

caused by human herpes viruses and human papilloma viruses. Frequently documented oral protozoans include *Entamoeba gingivalis* and *Trichomonas tenax* (Xinyi et al, 2011) (April Martinez et al, 2000).

Significance of the Oral Microbiome:

The human oral cavity serves as the reservoir of diverse microbial community predominantly colonised by bacteria (Kilian et al, 2016). inhabiting various sites such as teeth, gingival surface, tongue, cheeks, palate and tonsils (Dewhirst et al, 2010). This constitutes the most important and complex oral microbiome in the human body (Peng et al, 2022). Researches on the oral microbiome composition and their significant relatedness with the general health have drawn attention in the recent years (Willis et al, 2020).

Oral dysbiosis:

Symbiotic eccentricity within the bacterial population found in the oral cavity (Sudhakara et al, 2018). may be attributed to various predisposing factors such as stress, consumption of tobacco, diet, smoking, alcohol leading to an imbalance causing oral dysbiosis (Lee et al, 2021). State of oral dysbiosis unveils the most important contributing factor to the commonly encountered oral infections among humans (Kumar, 2016). Variations within the oral microbiome can be mediated by chief pathogens called as “keystone pathogens” commonly implicated in periodontitis and are significantly associated with systemic infections involving heart, lungs and brain, diabetes mellitus, inflammation of the joints and adverse outcomes of pregnancy (Sudhakara et al, 2018) (Jia et al, 2018). Oral dysbiosis is not only responsible for oral cancer but also linked with malignant state of pancreas, colorectum and oesophagus (Ahn et al. 2012)

Impact of oral dysbiosis results in carcinogenesis involving the generation of mediators of inflammation. This assists in the process of mutagenesis, uncontrolled proliferation of cells, angiogenesis and degeneration of cells accounting to neurodegenerative disorders and cancers. (Giusy Rita Maria La Rosa et al, 2020).

Conclusion

The oral microbiome constitutes a multifaceted community of microbiomes. The link between the oral microbiome with the host is bidirectional. i.e., they play a major role in the maintenance of health status and diseased condition of the host. Dysbiosis of the oral microbiome is responsible for oral infections like caries and periodontitis and also influences other systemic diseases. Hence, dysbiosis of the oral microbiome may serve as a potential decoder of systemic infections and could be useful in their diagnosis and treatment (Thomas et al, 2021)

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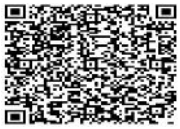

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Mosquito control – A green Approach

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Abstract

Mosquitoes serve as the primary vector for a wide range of illnesses and parasites that affect both humans and animals. The prolonged utilization of synthetic pesticides to control mosquitoes has caused resistance to evolve, damaged natural biological control mechanisms and brought back mosquito populations. Besides that, it has caused detrimental impact on non-target creatures and created problems on the environment and human health which prompted a quest for alternate control methods.Interrupting disease transmission is one strategy for controlling the mosquito-borne diseases. It can be done by using repellents to stop mosquitoes from biting people or by using chemicals to cause large-scale larval mortality at the breeding grounds of these vectors having direct or indirect negative environmental effects. The plant-derived chemicals is may be useful for decreasing mosquito populations since they are target-specific and biodegradable. As plants are abundant in bioactive chemicals, they can serve as a substitute source for insect repellents. Phytocompoundshas the ability to kill mosquito larvae may differ greatly depending on the species, plant parts employed, age (young or old), maturity (mature or senes), and extraction solvent.The phytochemicals activity connected to plants can either be exploited as insecticides for killing larval or adult mosquitoes or as repellents for protection against mosquito bites.The greatest larvicidal potential of green based silver nanoparticles AgNPs against the third instar larvae of *Anopheles stephensi, Aedes aegypti,* and *Culex*

quinquefasciatus was reported in this study compared to its pure leaf extract.In light of the aforementioned, the study showed that plant extracts might be used to control mosquitoes successfully.

Key words: Mosquito control, Plant extract, Phytochemical activity, Nano Particles, Larvicidal Activity.

Introduction

Mosquitoes (Culicidae family) are by far most researched insects. It is highly probable to have greater impact on human health and well-being around the world than any other arthropod, owing to their role in both transmitting a variety of dreadful diseases (such as malaria, filariasis, dengue, Japanese encephalitis, Rift valley fever, Chikungunya, and West Nile virus) and causing major public health issues. Among the various species of bloodsucking insects, mosquitoes of the genera Culex, Aedes, and Anopheles are the most important arthropods in terms of medicine, accounting for about 10% of all human illnesses. Despite the fact that there are over 3500 species on the planet. However, there are only about 100 species in eight genera. However, only fewer than 100 species under eight genera only are vectors of diseases. These vectors are organized in two of the three subfamilies, Anophelinae and Culicinae, while the third subfamily Toxorhynchitinae has members with mouthparts suited to feed on plant sap only. Mosquitoes are cosmopolitan in distribution and are found in all climatic zones and zoogeographical regions(WHO 2012).

Aedes aegypti

The *Aedes aegypti* mosquito is a tiny, dark insect with white lyre-shaped patterns on its body and banded legs. They prefer to bite humans and prefer to bite indoors. These mosquitoes may lay their eggs in both natural settings (such as tree holes and plant axils) and manmade containers with water. They lay eggs in water containing organic material (decomposing leaves, algae, etc.) in containers with large openings during the day, preferring dark-colored containers in the shade. The major vector of dengue fever, dengue hemorrhagic fever, and yellow fever, *Aedes aegypti*, is found over much of the tropics and subtropics. According to the World Health Organization (WHO), around 40% of the world's population is now at danger of dengue virus transmission, and the only option to prevent dengue virus transmission is to

combat disease-carrying mosquitoes (WHO, 2012). According to official figures from India's Union Health Ministry, the country experienced a major surge in dengue illness in 2012. (Taubitz *et al*., 2007).

Culex quinquefasciatus

Culex quinquefasciatus, the main vector of filariasis, is a global mosquito that can be found in human habitations across the world's tropics and subtropics. *Cx. quinquefasciatus*, the most medically important species, breeds in waters polluted with organic material such as rooted plants, household waste, and excreta. These vector species' larvae are usually found in partially clogged drains and ditches, soak away pits, septic tanks, and village pots, particularly abandoned ones with filthy and unfit-for-drinking water. Mosquitoes are linked to urbanization and municipalities with poor or insufficient drainage and sanitation. Its population rapidly grows under these circumstances. Many Culex species, including *Cx. quinquefasciatus*, attack people and other hosts at night. *Cx. Quinquefasciatus* frequently rests indoors before and after feeding, although they also seek shelter in natural areas (Service, 2000). *Cx. quinquefasciatus* is a vector of lymphatic filariasis, a tropical illness that affects roughly 120 million people globally, with 44 million experiencing persistent symptoms (Bernhard *et al*., 2003).

Vector control:

Vector control is a major concern in developing countries like India due to a lack of widespread awareness, the development of resistance, and socioeconomic factors. Each year, one or more vector-borne diseases impact a considerable portion of the population. Any mosquito control programs must include vector control, which includes both antilarval and antiadult techniques. The primary necessity for creating an effective vector control strategy is control, whether by biological or chemical means. Malaria, filariasis, Japanese encephalitis, yellow fever, dengue, and chikungunya are all diseases spread by vector mosquitos. As a result, it has become a major public health issue around the world, with significant social and economic consequences, particularly in tropical areas. Mosquito-borne diseases are common in over 100 countries, claiming the lives of approximately two million people each year and killing at least one million children, putting as many as 2100 million people at danger worldwide. Mosquitoes of the Aedes, Anopheles, and Culex species are significant vectors of human diseases in India. The rapid growth in human

population, inadequate funding for mosquito control programmes, and a lack of public knowledge, combined with environmental change and vector mosquito adaptability, resulted in an increase in mosquito-transmitted diseases. As a result, mosquito control efforts remain an important technique for preventing mosquito-borne diseases. Low case reporting is due to a lack of awareness about the disease, its focused distribution, and the fact that it primarily affects disadvantaged rural areas. Now, steady progress is being made in developing diagnostic tools, understanding how infection spreads, and developing therapy and prevention, all of which offer the potential of improved disease management.

Plant based larvicides

Plant based pesticides are a viable alternative to synthetic pesticides because of their minimal environmental contamination, low toxicity to humans, and other advantages, (Liu *et al.,* 2000). A concerted effort has recently been made to promote the use of botanical pesticides (as a possible alternative to synthetic chemical insecticides), which give a pest-specific, cost-effective, easy-to-use, readily biodegradable, and environmentally benign technique (Shaalana, *et al.,* 2005). As a result, alternate pesticides should be sought. Plants include a wealth of bioactive compounds that can be exploited to create ecologically friendly vectors and pest-control treatments. A number of plants and microorganisms have been found to be selective, causing little or no harm to non-target organisms or the environment (Govindarajan and Sivakumar, 2011; Govindarajan *et al.,* 2008a). One of the most effective alternative approaches under the biological control programme. Exploring floral biodiversity and entering the field of employing safer insecticides of botanical origin as a simple and sustainable means of biological control programme. Furthermore, unlike traditional insecticides, which are made up of a single active component, plant-derived insecticides are made up of botanical blends of chemical compounds that work together to affect both behavioural and physiological processes. As a result, pests are unlikely to acquire resistance to such compounds. Identification of efficient bio-insecticides that are also compatible and adaptable to ecological settings is critical for sustained effective vector control management. Botanicals offer a wide range of insecticidal qualities and will surely become a new weapon in the arsenal of synthetic pesticides, as well as a viable alternative solution to combat mosquito-borne diseases in the future. Because of the well-known downsides of synthetic insecticides, mosquito control programmes have turned to using

environmentally beneficial, biodegradable, and microbial plant chemicals that have mosquitocidal properties.

Natural compounds derived from plants are often favoured because to their lower toxicity to non-target organisms and inherent biodegradability. Medicinal herbs have been documented to exhibit a variety of bioactivities, including insecticidal, antifungal, and nematicidal properties, which could make them a viable mosquito control option. Due to their eco-safety, target specificity, low resistance, reduced number of applications, higher acceptability, and suitability for rural regions, the use of botanicals as mosquito control agents has been demonstrated to be effective in eliminating these negative aspects. Many studies have found that extracts from various plants can be utilized as effective and cost-efficient alternatives to synthetic insecticides, or in combination with other insecticides, in integrated vector management programmes for mosquito control. An analysis of 120 plants divulged the larvicidal efficiency of 7 species, notably *Allium sativum L., Ricinus communis L., Zingiber officinale Roscoe, Citrus reticulata Blanco, Pimenta dioica(L.) Merr, Adenocalym maalliaceum (Lam.) Miers, and Saritaea magnifica (W. Bull) Dugand*. As the effectiveness of *Adenocalymma alliaceum, Pimentadioica,* and*Saritaeamagnifica* in reducing mosquito vectors has not previously been demonstrated, thorough studies on these plants were attempted. In addition to having larvicidal effects, smoke is also effective in keeping mosquito vectors away, albeit the results of this test are not presented in the thesis. Flavonoids and terpenoids have been identified as the components responsible for larvicidal activity in relation to *Adenocalymmaalliaceum*; phenols and flavonoids in *Pimentadioica*; and flavonoids, alkaloids and terpenoids in *Saritaea magnifica* (Rathy 2017).And other plant species that is carried out in different mosquito species are given in table 1.

Table 1. Plant species used for phytoextracts and its impact on mosquito species showing LC_{50} and LC_{90} values of 2019.

Scientific name of plant species	Solvent used / Secondary metabolites	Mosquito species	LC50	LC90	Reference
Curcuma zedoaria	Essential oil	*Culex quinquefasciatus* deltamethrin-susceptible strain	36.32 ppm (24 hours)	-	Suttanont *et al* (2019)
Curcuma zedoaria	Essential oil	*Culex quinquefasciatus* deltamethrin-resistant strain	37.29 ppm (24 hours)	-	Suttanont *et al* (2019)
Carica papaya	Methanol crude (72 hours)	Dengue virus type 2	13.09 µg/mL	-	Bere*et al* (2021)
Carica papaya	Aqueous crude (72 hours)	Dengue virus type 2	182.10 µg/mL	-	Bere *et al* (2021)
Solanum Mammosum	Aqueous crude	*Aedes aegypti*	1631.27 Ppm	4756.20 ppm	Pilaquinga *et al* (2019)

Nanoparticles in green synthesis

According to recent studies, it is simple to achieve a quick green synthesis of metal nanoparticles utilizing metabolites from bacteria, fungi, and plants. Due to its higher rate of synthesis and potential to minimise the stages in downstream processing, plant-mediated synthesis has been used particularly well for the creation of silver nanoparticles (Huang et al. 2007; Salam et al. 2012).Nanotechnology is widely used in vector control, including Nano sensors for pest detection and Nano capsules for managing pests and vectors and delivering herbicides(Scrinis*et al* 2007). New insecticides and insect

repellents are also created with the use of synthesized silver or gold nanoparticles. By synthesizing silver/gold nanoparticles from ecologically friendly plant extract and eco-friendly reducing and capping agents, applications of nanotechnology have been expanded in the field of mosquito control.

Synthesis of nanoparticles using biological compound

Salunkhe et al. 2011 have described the larvicidal potential of silver nanoparticles produced utilising the fungus *Cochliobolus lunatus* against two species of mosquitoes, *Aedes aegypti* and *Anopheles stephensi Liston*. Metallic nanoparticles such as platinum, gold, palladium, silver, and titanium nanoparticles (Govindhan *et al* 2016, Kanninen *et al* 2017, Skrabalak *et al* 2008, Wyszogrodzka *et al* 2016, Xiong *et al* 2007, Karimi *et al* 2017, Nari *et al* 2007, Coelho *et al* 2016 and Mahmoud *et al* 2017) have been investigated and reported on for a variety of fantastic uses. The most significant aspects of studying the nature and consequences of nanoparticles are their reactivity, stability, bioavailability, and behaviour (Pettitt*et al* 2013). AgNPs exhibit mosquito larvicidal properties against the dengue vector mosquito *Aedes aegypti*; the nanoparticles can also degrade commercial colours. Silver nanoparticles are expected to find widespread use in the biomedical, catalysis, and pharmaceutical sectors in the near future. Silver and gold nanoparticles derived from *Chrysosporium tropicum* were investigated as a larvicide against *Aedes aegypti* larvae (Soni and Prakash 2012). They discovered that silver nanoparticles were more efficient than gold nanoparticles against mosquito larval stages. The silver nanoparticles synthesized with *Nelumbo nucifera* leaf extract have been tested against the malaria and filariasis vectors (Santhoshkumar et al. 2011)Silver nanoparticles derived from the leaves of *Nelumbo nucifera* have been tested against malaria and filariasis vectors (Santhoshkumar et al. 2011).

Nanoparticles control mosquito larva

Antifungal (Kim et al 2009), anti-inflammatory (Nadworny et al. 2008), and anti-viral action has been demonstrated for AgNPs (Rogers et al. 2008). The idea of Ag leaking or being released into water systems is particularly concerning, given that several studies have shown that ionic Ag is highly poisonous to a variety of freshwater aquatic species, with varied fatal amounts depending on the species (Dethloff et al. 2007; Naddy et al. 2007). Green AgNPs have been manufactured utilising natural products such as

Azadirachtaindica (Tripathi et al. 2009), *Glycine max* (Vivekanandhan et al. 2009), *Cinnamon zeylanicum* (Sathishkumar et al. 2009), and *Camellia sinensis* (Begum et al. 2009). According to Elumalai et al. (2010), AgNPs were created using the aqueous extract of *Euphorbia hirta*leaves that had been shade dried and tested for their antibacterial properties. *Asteraceae* plant *Eclipta prostrata* was used to make synthetic AgNPs, which were tested against the fourth instar larvae of the filariasis vector *C. quinquefasciatus* Say and the malaria vector *A. subpictus* (Rajkumar and Rahuman 2011). Mycosynthesized AgNPs' larvicidal effects against the vectors *A. aegypti* and *A. stephensi* that transmit illnesses important to public health have been assessed (Salunkhe et al. 2011).

The effectiveness of produced silver nanoparticles against the larvae of *A. subpictus*, *C. quinquefasciatus*, and *Rhipicephalus microplus* has been assessed using the aqueous leaf extract of *Mimosa pudica* (Marimuthu et al. 2010). *Tinospora cordifolia's* aqueous leaf extract was used to create the silver nanoparticles, which have been shown to have pediculocidal and larvicidal effects on human capitis and fourth-instar larvae of *A. subpictus* and *C. quinquefasciatus* (Jayaseelan et al. 2011).Silica nanoparticles, however, have been tested on the larvae and pupae of *A. stephensi*, *C. quinquefasciatus*, and *A. aegypti* (Barik et al. 2012). Silver nanoparticles created using *E. hirta* have been tested against the larvae of *A. stephensi* for their ability to be biolarvicidal and pupicidal (Priyadarshini et al. 2012) The *A. aegypti*, *A. stephensi*, and nontarget fish *Poecilliareticulata* have all been tested for the larvicidal activity of silver nanoparticles made from *Pergulariadaemia* plant latex (Patil et al. 2012).

Table 2. Showing plant species used for green synthesis of Ag Nano particle and its impact on mosquito species showing LC50 and LC90 values from 2019.

Scientific name of plant species	Solvent used / Secondary metabolites	Mosquito species	LC_{50}	LC_{90}	Reference
Carica papaya	Methanol extract	Dengue virus type 2	9.20 µg/mL	-	Bere *et al* (2021)
Carica papaya	Aqueous extract	Dengue virus type 2	126.20 µg/mL	-	Bere *et al* (2021)
Annona glabra	Aqueous extract (1:10)	*Aedes aegypti*	5.29 mg/L (24hrs)	-	Amarasinghe *et al* (2020)
Annona glabra	Aqueous	*Aedes*	1.5	-	Amarasinghe

	extract (1:10)	*albopictus*	mg/L (24hrs)		*et al* (2020)
Annona glabra	Aqueous extract (1:20)	*Aedes aegypti*	3.02 mg/L (24hrs)	-	Amarasinghe *et al* (2020)
Annona globra	Aqueous extract (1:20)	*Aedes albopictus*	1.14 mg/L (24hrs)	-	Amarasinghe *et al* (2020)
Curcuma Zedoaria	Essential oil	*Culex quinquefasciatus*deltamethrin-susceptible strain	0.57 ppm (24hrs)	-	Suttanont *et al* (2019)
Curcuma Zedoaria	Essential oil	*Culex quinquefasciatus*deltamethrin-resistant strain	0.64 ppm (24hrs)	-	Suttanont *et al* (2019)
Annona reticulate	Flavonoids, triterpenoids, polyphenols.	*Aedes aegypti*	4.43 µg/mL	13.96 µg/mL	Parthiban *et al* (2019)
Annona reticulate	Tannins, alkaloids, phenols, glycosides, flavonoids, steroids.	*Aedes aegypti*	2.38 Ppm	2.81 Ppm	Malathi *et al* (2019)
Curcuma zedoaria	Alkanes, alkenes, sesquiterpenes, monoterpenes, carboxylic acids, essential oil	*Culexquinquefasciatus*	0.64 Ppm	8.88 Ppm	Sutthanont *et al* (2019)
Chomelia Asiatica	Phenols, alkanes, aromatic compounds	*Aedesaegypti*	7.15 µg/mL	20.86 µg/mL	Aina *et al* (2019)

Conclusion

In order to reduce the mosquito population, biological control can therefore offer a practical and environmentally responsible strategy. Research papers on NPs synthesised using living organisms like plant extracts, fungi, and bacteria were carefully examined and discussed in terms of the type of nanoparticles, test species, exposure medium, and suitable concentration in order to understand the current research trends of nanoparticles in mosquito control. Even when utilising the identical nanoparticles, the studies showed a broad range of outcomes. This was due to the idea that the test medium, surface coating, and particle size all affected the outcomes. Consequently, in the future, study may be done taking into account the aforementioned criteria.

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Pharmacological Activities and phytochemical constituents of *Pergularia daemia*

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Abstract

Pergularia daemia is a plant that traditionally has been used as an antihelmintic, laxative, antipyretic expectorant, and to treat infantile diarrhoea and intermittent malarial fevers. It is extensively dispersed throughout the world's tropical and subtropical climates. Many phytochemicals have been isolated and identified from the different portions of the plant, including terpenoids, flavonoids, sterols, and cardenolids (leaves, stems, shoots, roots, seeds and fruits). Several tribal people in India's Western Ghats employ *P. daemia* to cure a number of illnesses, albeit mostly liver disease and jaundice are treated using the plant's roots.

Keywords: *Pergularia daemia*, pharmacological activities, phytochemistry

Introduction

Pergularia daemia

Scientific classification:

Kingdom	Plantae – Plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida – Dicotyledons
Order	Gentianales
Family	Asclepiadaceae – Milkweed family
Genus	*Pergularia*
Species	*P.daemia* (Forsk.) Chiov.

Common and local names:

Tamil	Uttamani, and Veliparuthi
English	Trellis-vine, Hariknot plant and Pergularia
Kannada	Juttuve and Talavaranaballi
Hindi	Utaran and Akasan
Malayalam	Veliparatti
Sanskrit	Kurutakah and Visanika
Telugu	Jittupaku and Dustapuchettu

The plant *P.daemia* has historically been used as an expectorant, anthelmintic, laxative, antipyretic, and to treat infantile diarrhoea and malarial intermittent fevers. It also has stomachic, laxative, and diuretic effects that are beneficial for cough, biliousness, and sore eyes (Pandey M et.al, 2013). According to studies, this plant exhibits hepatoprotective (Shad AA, et.al., 2014), anti-fertility (Santosh MKet.al., 2013), antidiabetic (Jain C, et.al., 2019), wound-healing (Patwardhan B, et.al., 2005), antibacterial (Frawley D, et.al., 2007), and anti-inflammatory (P (Meena AK, et.al, 2009).The plant extract helps with parturition and disorders of the uterus and menstruation. When combined with lime, the leaf juice is administered to rheumatic swellings and asthmatic flare-ups. It has been stated that the ethanol extract of *Pergulariadaemia* (Forsk.) Chiovaerial .'s parts has anti-inflammatory, antipyretic, and analgesic properties (Meena AK,. et.al, 2009). Presence of triterpenes and saponinscardenolides and alkaloids were reported. According to Aanjaneyulu et al., several triterpenes and steroidal substances were present (Pandey MM, et.al, 2008). To evaluate the therapeutic potential of this plant, the ethanolic, pet ether, ethyl acetate, and n-butanol extracts of *P.daemia* were tested for diuretic activities.

Botanical description:

P.daemia is abundant across the tropical and subtropical regions, especially in India, Africa, Arabia, Malaya, Pakistan, Afghanistan, and some areas of south east Asia (Fig. 1). It is typically found in India's hedges at altitudes between 900 and 1000 metres in Southern India and the Himalaya. *P.daemia* is a milky sap-producing perennial twining plant. The stems are up to 4 metres long and coated in delicate hairs. The thin, heart-shaped, broadly ovate, glabrous, or ciliate-hairy leaves are 5–10 cm long, 3.8–9 cm wide, and have petioles that are 2-6.3 cm long and pubescent. The flowers are on long peduncled axillary pseudo umbells. Pendulous debuts at night.

Phytochemicals in *P.daemia:*

The therapeutic and pharmacological potential of the specific plants is primarily due to secondary metabolites derived from the medicinal and aromatic plant extract [Ananth DA, et. al, 2016]. Occasionally, people treat a variety of ailments with the crude extracts of medicinal herbs. On the other hand, it is crucial to isolate and identify the bioactive substances as well as to extract, purify, and understand how the purified chemical works. In order to uncover bioactive chemicals from medicinal plants as well as to validate previously claimed therapeutic properties, researchers have recently concentrated on this topic. For the validation of bioactive phytochemicals, both

qualitative and quantitative methods of analysis are crucial.The qualitative study of phytochemicals Alkaloids, flavonoids, terpenoids, tannins, steroids, glucosides, carbohydrates, proteins, amino acids, saponins, glycosides, fixed oils, gums, and mucilage have all been found to be present in *P.daemia* extract. The first stage in using phytochemicals to create dietary supplements, pharmaceuticals, and other goods is the extraction of bioactive compounds from plant materials. Plant samples that are fresh or dried can be used to obtain phytocompounds. When compared to dried powdered extraction, the freeze drying extraction technique typically maintains higher levels of phenolic content in plant samples [Abascal K, et al, 2016]. Due to their simplicity, effectiveness, and broad applicability, solvent extractions are the method that is most frequently used to make extracts from plant materials.Supercritical extraction (SCE), solid-liquid extraction (SLE), microwave extraction (ME), conventional extraction (CE), and ultrasound extraction (USE), among other techniques, are just a few of the recent innovations. [M. Naczk et al., 2014]. Chromatographic methods are frequently employed to identify bioactive substances in plant preparations. High performance thin layer chromatography (HPTLC), gas chromatography (GC), high performance liquid chromatography (HPLC), with diode array detection (DAD), and mass spectrometry (MS) detection, are the most commonly used analytical techniques for the separation of polyphenolic compounds.This combination of methods is currently one of the most popular and extensively used for the separation, identification, and quantification of polyphenolic compounds [Downey MO, et al, 2008]. MS is a well-known and effective method for determining the mass and revealing the structural details of proteins [Dai J, et. al, 2015]. The primary applications of mass spectrometry (MS) are in the quantitative and qualitative study of biomolecules. The foundation of this technique is the separation of the petrol phase ions according to their mass-to-charge ratios (m/z). MS is a well-known and effective method for determining a biomolecule's mass and revealing its molecular details.For the majority of tasks in plant metabolite analysis and drug discovery, HPLC coupled with MS is the analytical method of preference [Hamburger M, et. al., 1998; Fang N et. al., 2002; Ye M et. al., 2005; Seeram NP et. al., 2006].

Plant extract from the entire plant, including the leaves, stem, and base, contains a variety of chemical elements. The extract from the leaves and roots of *P.daemia* includes -sitosterol, lupeol, oleanolic acid, calactin, calotropin, corotoxigenin, daucosterol, sucrose, -amyrin, -amyrin, and its acetate [Karthishwaran K, et.al., 2010, Bhaskar V, et.al., 2009, An (Fig. 3a). Additionally, from the complete plant extract, phytocompounds like betaine,

hentriacontane, pentacosanoic acid polypeptide, and glucoside of Daemiaextensa (also known as *P.daemia*) were found [Bhaskar V, et. al., 2014, Raman SP, et. al, 1958]. According to Bhaskar V. et al. (2014), *P.daemia* seed extract contains phytocompounds like protouscharin, uscharidin, calactin, calotropin, calotropigenin, corotoxigenin, dihydrocalotropigenin, and uscharin.Akin to this, [Rakhit S et.al, 1954] discovered several cardenolides in seed extract, including uscharidin and calotoxin. They also discovered additional related chemicals in the stem extract, including coroglaucigenin, corotoxigenin, uscharidin, and uzarigenin. During a qualitative study, it was discovered that flavonoids were the most significant and significant phytochemicals extracted from *P.daemia*aerial parts.According to Subramanian SS et al. (1968), the vegetative portions of *P.daemia* contain flavonoids and saponins in the fresh shoots and flowers as well as hyperoside (a flavonol) in the dried stem. The presence of hyperoside (a flavonol) in dried stem extracts was also found by Sinha and Dogra [Sinha S et al, 1985]. Numerous studies have shown that polyphenolic substances like flavonoids and phenolic acids may have medicinal effects. Phenols, flavonoids, phenolic glycosides, saponins, and cyanogenic glycosides are instances of well-known phytocompounds [Shahidi F, 2000; Shahidi F et al, 2008].According to Aqil F et al. (2006), flavonoids like flavones, isoflavones, flavonoids, anthocyanin, coumarinlignans, catechins, and isocatechins are particularly responsible for the plants' antioxidant action. Fresh fruit juices and green leafy veggies are excellent sources of polyphenolic substances like flavonoids and phenolic acids. Atherosclerosis, stroke, diabetes, Alzheimer's disease, cancer, and other anti-inflammatory disorders are all prevented by these herbal-based antioxidant compounds or medications [ShahidiF et al, 2008]. Importantly, phytocompounds' anti-inflammatory properties have been mentioned in previous studies, and some of them are currently undergoing preclinical testing [Subramanya S et al., 2018]. These days, a lot of people favour natural remedies in addition to their advantages of affordability and safety.

The primary phytocompound in the *P.daemia* preparations is flavonoids, with concentrations ranging from 72.549 0.449 to 400.196 0.339 mg/ml. When compared to other plant sections, leaf and stem extract showed a high content of flavonoids. At a concentration of 10 mg/ml, the equivalent amounts of quercetin in n-hexane, ethyl acetate, and water are 338.725 mg/g, 388.627 mg/g, and 400.196 mg/g, respectively [Dosumu OO et al., 2019]. The most well-known and widely-distributed class of plant phenolics is called flavonoids. Anthocyanidins, monomeric flavanols, flavanones, flavones, and flavanols are among them.The pro-inflammatory mediators and other

inflammatory agents may be inhibited by these polyphenols. Using a complete Freund's adjuvant (CFA)-induced rat model, Ananth et al. (2016) discovered and reported that *P.daemia* extracts contain five flavonoids (formononetin, qurecetin, chrysoeriol, taxifolin, and naringenin) that have anti-arthritic action. Antioxidant, antimicrobial, anti-inflammatory, and immunomodulatory action are just a few of the health-promoting qualities that flavonoids possess.Flavanols, flavanones, isoflavones, flavones, and anthocyanidins are some of the significant subclasses of flavonoids [Saito K et al,2019, Lin J-K et al,2006, López-Lázaro M,2009]. On the other hand, there are numerous therapeutic plants with significant active ingredients that have not yet been identified. One of those was *P.daemia*, which was discovered to be a trustworthy supply of flavonoids and other bioactive substances. Due to people's trust in newly developed natural therapeutics, quercetin, kaempferol, myricetin, and morin are common therapeutics.

Antioxidant activity:

According to recent findings, oxidative stress and its linked effects seriously harm people's health. During the stress situation, reactive oxygen species (ROS) and reactive nitrogen species (RNS) were overexpressed. According to studies by Ambriz-Pérez DL et al. (2016), Emerit J et al. (2004), and Kumar KR et al. (2012), these reactive species encourage degenerative illnesses. As a byproduct of the electron transport system and regular cellular metabolism, ROS such as superoxide anion (O), nitric oxide (NO) radicals, hydrogen peroxide (H_2O_2), peroxyl radicals (ROO), and reactive hydroxyl radicals (OH) are continually produced [Phaniendra A et al., 2015]. The failure of the defence mechanism caused by excessive ROS/RNS production results in the release of oxidants. By interfering with the oxidation process, chelating catalytic metals, and acting as oxygen scavengers, antioxidants can neutralise free radicals [Jayaprakash G, et al., 2001]. According to reports from Ambriz-Pérez DL et al. (2016), these chemicals are said to reduce the chance of producing a variety of degenerative diseases and disorders by preventing free radical-mediated oxidative damage. Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), albumin, transferrin, ceruloplasmin, lipid and water-soluble antioxidants like tocopherol, quinines, ascorbic acid, uric acid, and vitamin E are all present in our blood plasma in nature.Antioxidants work to stop biological system damage by converting ROS/RNS into a stable molecule. Today, synthetic antioxidants like butylatedhydroxyanisole (BHA), butylatedhydroxytoluene (BHT), propyl gallate (PG), and tert-butylhydroquinone (TBHQ) are frequently employed in the food and pharmaceutical industries. These substances have toxic effects on the victims

that are quite harmful. While having little to no negative side effects, a variety of isolated chemicals from medicinal plants have strong antioxidant activity. By inhibiting two different synthetic free radicals, namely 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) and 1,1-diphenyl-2-picrylhydrazyl, the in vitro antioxidant capacity of *P.daemia*preparations was investigated (DPPH). Comparable to gallic acid, the methanolic extract of *P.daemia* areal portion was extremely effective in scavenging ABTS, DPPH, and nitric oxide free radicals.*P.daemia* extract's ABTS IC50 concentration was 19.72 mg/ml, which was almost greater than the concentration of gallic acid (14.55 mg/ml). Similar to this, the IC50 value for gallic acid and extract for DPPH scavenging activity was 33.36 and 34.12 mg/ml, respectively. When compared to the gallic acid standard, *P.daemia* extract had outstanding nitric oxide scavenging action (IC50-32.37 mg/ml) [Cook NC, et al., 1996]. A 70% ethanolic extract of *P.daemia* leaf, however, demonstrated considerable DPPH free radical scavenging action comparable to industry standards like ascorbic acid and BHT. The EC50 values for leaf extract were 0.149, 0.699, and 2.608 mg/ml, respectively, and curiously, these lower EC50 values also demonstrated greater antioxidant activity.Moreover, ethanolic extract successfully prevented peroxide and hydrogen peroxide generation. Significantly, *P.daemia* extract has the capacity to convert ferrous (Fe2+) iron from ferric (Fe3+) iron, and the EC50 values for extract, ascorbic acid, and BHT were 17.78, 0.5239, and 0.2065 mg/ml, respectively. Dosumu et al. [Dosumu OO,et.al,2019] observed an inhibitory percentage in *P.daemia* leaf extract over DPPH radical scavenging activity ranging from 34.65% to 84.90%. The IC50 values were determined to be 6.27 g/ml for ethanol, 17.78 g/ml for ethyl acetate, 22.49 g/ml for n-hexane, and 5.67 g/ml for extracts of standard ascorbic acid, respectively. The IC50 values for *P.daemia* stem extract were 10.19 and 26.99 g/ml for ethyl acetate, and then 58.20 g/ml for n-hexane.The reported antioxidant effects may be caused by phytochemicals contained in the leaf extract, including phenols, alkaloids, flavonoids, phytosterols, saponins, tannins, and triterpenes [Dosumu OO, et.al., 2019, Karthishwaran K, et.al., 2012, and Sarcodie J, et.al., 2015].

Anti-inflammatory and analgesic activity:

To defend the tissue from damage, inflammation is a common biological process that reacts to external molecules, including bacteria. Normally, inflammation is a quick and self-contained process, but under abnormal pathological conditions, it produces excessive ROS and RNS, which can result in persistent inflammation. According to Calder PC, et. al. (2009) and Libby P. et. al. (2007), this chronic inflammation is associated to major inflammatory disorders such as arthritis, cancer, neurological, metabolic, and

cardiovascular diseases. To control this chronic inflammatory condition, researchers have previously created steroidal and non-steroidal anti-inflammatory medications. These medications successfully lessen the intensity of the illness, but they also have a number of negative effects. *P.daemia*, a medicinal plant, has curative properties with the fewest negative effects [Ananth DA, et al., 2016].Rats' paw edoema was significantly reduced by *P.daemia'*sethanolic extracts (p 0.001) when compared to carrageenan- and cotton pellet-induced techniques. These extracts, at a dosage of 200 mg/kg, demonstrated a reduction in granuloma development of up to 44.18% and 19.87%, respectively. At the same concentration, other extracts such as n-butanol, benzene, and chloroform displayed 16.83%, 13.96%, and 15.08%, respectively [Usman MRM et al, 2012]. Similar to this, Venkataraman et al. [Venkataraman S,et.al,2010] used entire plant extracts in chloroform and petroleum ether to study carrageenan-induced paw edoema in rats.Findings showed that the chloroform extract treated was significantly better than the control (p 0.01) in comparison. Recent research by Hina and Rose [Hina I, et. al, 2018] determined the in vitro anti-inflammatory activity of ethanolic extracts from the leaf and root of *P.daemia*. Additionally, they demonstrated membrane stabilization-based anti-inflammatory activity in ethanolic leaf (54.55%) and root (45.55%) extracts at a concentration of 300 g/ml, which produced the most notable stabilisation when compared to that of the reference drug, diclofenac sodium (72.73%) at a concentration of 100 g/ml. Plant extracts from *P.daemia*also shown potent analgesic properties. These extracts are being utilised as an alternative to painkillers.At a dosage of 1000 mg/kg, one study that assessed the analgesic effectiveness of *P.daemia* aqueous and alcoholic root extracts on the eddy's hot plate method revealed substantial (p 0.001) effects [Nikajoo LT, et al., 2009]. Using chloroform and the petroleum extract of *P.daemia*, similar analgesic effects were seen at a dosage of 100 mg/kg (p 0.01) [Venkataraman S, et al., 2010]. *P.daemia* may have strong analgesic and anti-inflammatory properties in large part due to the abundance of flavonoids and glycosides.

Anti-arthritic activity:

According to Ananth DA, et al. (2016), flavonoids are recognised to be potent phytocompounds for treating the anti-rheumatic state in animal models. Flavonoids such formononetin, qurecetin, chrysoeriol, taxifolin, and naringenin are present in *P.daemia* methanolic extracts. The paw inflammation in the methonolic extract-treated rat groups was successfully reduced, and serum biochemical markers such haemoglobin (11.84 0.42 g/dl) and red blood cells (RBC) (8.38 0.67 million/mm3) levels were markedly elevated. Whereas, other

arthritis indicator biomarkers including white blood cells (WBC) count (8.91 ± 0.38 thousands/mm3), rheumatoid factor (RF) (17.94 ± 0.45 IU/ml), erythrocyte sedimentation rate (ESR) (7.91 ± 0.12 mm/h) and C-reactive protein (CRP) (22.56 ± 0.26 mg/l) levels were significantly decreased when compared arthritic induced rat group [Hina I,et.al,2018].According to the study results, ethanolic extract of *P.daemia* leaf and root (300 g/ml) may have strong anti-arthritic effect. They verified using a membrane stabilisation assay, and they found that leaf activity was higher (54.55%) than root activity (45.55%). Similar to this, *P.daemia* root extracts shown 58.89% more inhibition than leaf extracts, which demonstrated 53.33%. In all instances, 100 g/ml of the reference medication diclofenac sodium was used to compare the results of the assays. By lowering the edoema and inflammation in the hind paws, petroleum ether extract of *P.daemia* leaf at 300 mg/kg improved the arthritis condition in arthritic rats [Sutar NG, et. al., 2014].Moreover, it is hypothesised that phytocompounds such flavonoids and sterols may be responsible for *P.daemia*'santi-rheumatic effects.

Anti-cancer activity:

Cancer is the riskiest and second-most significant cause of death worldwide. Secondary metabolites from plant extracts are used in herbal medicines that are recognised to treat cancer without having any negative side effects. According to Khorombi et al. [Khorombi TE,et.al, 2006], the entire plant extract's methanol dichloromethane (1:1 v/v) extract prevented the proliferation of malignant cells. The substance alpha-amyrin is in charge of stopping the growth of malignant cells, although its effectiveness was only between 15 and 50 g/ml. Another study found that *P.daemia* extract is a key component in the treatment of oral cancer.In compared to the methanolic extract, the ethyl acetate extract (300 mg/kg b.w.) particularly displayed excellent in vivo antioxidant activity. The effectiveness was evaluated in comparison to DMBA-induced hamster buccal pouch [Vaithiyanathan V, et al., 2016]. The cytotoxic action of leaf extract was demonstrated against the ovarian cancer cell lines PA-1 and OAW-42, with IC50 values of 30 and 120 mg/ml for each cell line, respectively. According to authors, polyphenolic chemicals, particularly triterpenoids, are crucial in the fight against the spread of cancer cells. A modest structural alteration of triterpenoids was also noted as having the potential to create an effective cancer treatment [Martin S, et al., 2017].

Anti -proliferative activity:

P. daemia methanolic extract showed an anti-proliferative effect against oral keratin-forming tumour cell line HeLa (KB) cells, according to a research by Mirunalini et al. [Mirunalini et al, 20014]. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide test was used to measure the activity. (MTT). For the purpose of confirming anti-proliferative action, ROS generation, antioxidant status, membrane (potential) potential, and cell cycle arrest were assessed. They verified the maximum cytotoxic impact of the *P.daemia* methanolic extract against oral KB cells at the highest concentration (160 g/ml). . 90% was the IC50 value of the methanolic extract when tested against cancer cell lines using the MTT method. When *P.daemia* extract was used to pre-treat KB cells, it greatly altered the cells' apoptotic morphology. This alteration was brought on by elevated ROS levels and a decrease in matrix metallopeptidases. (MMPs). In the intracellular area, the death of the cancer cell starts the production of ROS and lipid peroxidation (LPO), and it damages DNA by starting the apoptosis process in the KB cell [Mirunalini et al, 2014]. By encouraging apoptosis and halting growth in cancerous cells, *P.daemia*'spolyphenolics (phenolic acid and flavonoids) may be a key factor in helping to reverse this process.

Anti-diabetic activity:

Next to cancer and cardiovascular diseases, diabetes mellitus is emerging as the third "killer" condition in human history. It is a chronic metabolic condition that has an impact on both our body's physical and psychological processes. The potential for anti-hyperglycemic activity was found in the first study on *P.daemia* extract. According to Kumar and Ramesh [Kumar et al, 2014], *P.daemia* extracts at a concentration of 300 mg/kg substantially reduced the blood glucose level in diabetic rats that had been induced by streptozotocin (STZ). The diabetic animals were treated for 21 days with chloroform leaf extract, which resulted in blood glucose levels of 160.68 mg/dl, 132.61 ml/dl in ethanol, 152.80 mg/dl in water extract, 123.26 mg/dl in ethanol extract of the callus, and 194.6 mg/dl in glibenclamide (600 g/kg). [Wahi A et al, 2016] reported that alloxan (120 mg/kg; i.p.) was used to assess the effects of the administration of alcoholic and aqueous extracts from the entire plant of D. extensa on vitality. The blood glucose level (BGL) was significantly (P 0.01) decreased by alcohol extract in a single dosage after 1 hour. The anti-diabetic action was comparable to that of chlopropamide, a common medication. *P.daemia* extract has recently been shown to have anti-hyperglycaemic action against STZ-induced rat models, according to Sarkodie

et al, 2016. On a dose-dependent basis, the blood glucose level considerably dropped. Bioactive components in plants' hypoglycaemic action include flavonoids and their glycosides, phytosterols, saponins, phenols, alkaloids, triterpenes, tannins, and alkaloids [Sarkodie et al, 2016]..

Hepatoprotective activity:

The liver is a remarkable organ and the body's primary chemical laboratory. It is essential to the body's metabolism and detoxification of the many chemicals and toxins that reach it. The biochemical control of biomolecules like fats, carbohydrates, amino acids, and protein depends in large part on the distribution of exogenous toxins and therapeutic agents. Damage to the liver is greatly influenced by ROS. A common illness known as liver damage or injury can result from an overabundance of ROS being produced, which damages the liver's cells and tissue. Numerous substances, including carbon tetrachloride (CC14), -amanitin, acetaminophen, pyrrolizidine alkaloids, bromobenzene, ethanol, and polycyclic aromatics, as well as the toxin itself, create metabolites that harm the liver [Adesanoye et al, 2010]. Antioxidants a significant part in preventing CCl4-induced damage to the liver cells because they are efficient at scavenging free radicals [Hina I et al, 2018]. Recent studies suggested that natural antioxidants can guard against liver issues brought on by oxidative stress [Tan BL et al 2018, Dhanasekran D et al 2005, Wang BJ, 2004]. The ethanolic and aqueous extract of *P.daemia* has a significant (P 0.05) hepatoprotective impact against CCl4-induced hepatic rat model, according to Sureshkumar and Mishra [SureshKumar S et al,2010]. Aspartate aminotransferase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALKP), total bilirubin (TBL), and total cholesterol (CHL) levels were found to be decreased in rats treated with ethanolic extracts, while levels of total protein (TPTN) and total albumin (ALB) were found to be increased at a dose of 200 mg/kg. CCl4 produced a highly reactive trichloro free radical that is harmful to polyunsaturated fatty acids. because experimental animals' altered liver microsomal membrane hapatotoxicity was discovered [Shenoy et al 2001]. Aqueous and ethanolic extracts of *P.daemia* roots are also significantly protective against the rodent hepatotoxic effects of paracetamol and CCl4 [Suresh Kumar S et al,2010]. Similar to CCl4, paracetamol also led to a rise in serum liver enzymes like bilirubin and cholesterol. The biochemical indicators of SGOT and SGPT were significantly inhibited by both aqueous and ethanolic extracts at doses of 100 and 200 mg/kg. In rats treated with *P.daemia* extract, there was a reduction in LPO and malonaldehyde (MDA), and a rise in the serum protein antioxidant enzyme glutathione (GSH). Therefore, the bioactive substances found in these

preparations, such as flavonoids, terpenoids, glycosides, and saponins, may be what gives them their hepatoprotective properties. According to Sureshkumar and Mishra [SureshKumar et al, 2010], the ethanolic extract of *P.daemia* leaf that contains flavonoids and triterpenoids is what is most likely to be accountable for the hepatoprotective activity. Using quercetin-3-glucoside as a standard, HPTLC was used to validate the flavonoids from the ethanol extract and ethanol fraction in *P.daemia*. These findings suggested that the main bioactive compound for hepatoprotective action is flavonoids [Ananth et al, 2016, SureshKumar et al, 2010].

Diuretic activity:

Bhavina et al 2011studied the diuretic activity of the *P.daemia* extracts at a dose dependant manner by orally in rats. Lipschitzs test used for this study and furosemide used as a standard drug. Based on the results diuretic activity of *P.daemia* alcoholic extract showed a highest activity of 0.93 at 400 ml/kg concentration. Urine output of all tested extracts except the petroleum ether showed significant results ($P < 0.001$) in comparison to control.Importantly, plant compounds also have an impact on the excretion of urinary electrolytes. The excretion of sodium and potassium ions (Na+ and K+) in the urine was also enhanced by the addition of alcohol, ethyl acetate, and n-butanol extracts. Alcoholic extract was found to have a diuretic effect of 2.04 units, almost identical to that of normal furosemide (2.19 units). Alcoholic, ethyl acetate, n-butanol, and the common medication furosemide are examples of extracts that raised the levels of urinary Na+ and K+ ions and mildly acidified urine. These results firmly imply that *P.daemia* extracts have diuretic properties. Alkaloids, flavonoids, and steroids, among other secondary metabolites, may be the candidates for *P.daemia*'s diuretic action.

Anti-tuberculosis activity:

About 10.4 million cases of tuberculosis (TB) were recorded in 2016, and it was one of the leading causes of death, according to a 2017 WHO report. Plant extracts have been shown to have possible benefits in the Ayurvedic medical system for treating TB. The ameliorative action of *P.daemia* hydro alcoholic leaf extracts against anti-tuberculosis drugs (ATDs) induced liver injury was recently described by Mishra et al. [Mishra G et.al,2018]. Administration of ATDs substantially decreased the level of glucose and albumin. High amounts of bilirubin, triglycerides, aspartate aminotransferase, alkaline phosphatase, and cholesterol were also observed. Glutathione, peroxidase, glutathione reductase catalase, superoxide dismutase, glutathione, and glucose-6-phosphate dehydrogenase were all found to be reduced after

exposure to ATDs, and the amount of lipid peroxidation was also found to be increased.Therefore, compared to control, *P.daemia* extract substantially maintained these serum biochemical parameters and antioxidant components [Mishra G et al, 2018].

Anti-fertility activity:

P.daemia's steroidal fraction and ethanol extract both demonstrated possible anti-fertility properties. At the pre-implantation period, steroidal fraction of 200 mg/kg demonstrated significant activity against female mice. While ethanolic extracts had late-onset contraceptive action at 600 mg/kg. Within 48 hours of receiving the medication, the extract displayed 100% activity without any death. These findings suggest that the ethanolic and steroidal extracts of *P.daemia* may have an anti-fertility effect on female rodents [Sadik MG et al., 2001].

Anthelmintic activity:

According to Kumar et al. (2014), *P.daemia*'sethanolic extract exhibits greater anthelmintic potential than the water extract. With 100 mg/ml concentrations of the leaf extracts and albendazole as a standard treatment, they were tested against the round worm Ascarislumbricoides, the earthworm Eudrilluseugeniae, and the tapeworm Taeniasolium. For the round worm (20.86 0.54 and 61.84 0.54 min), earthworm (16.86 0.74 and 27.12 0.52 min), and tape warm (54.12 0.49 and 110.17 0.59 min), the paralysis and time of death were noted in the ethanolic extract, respectively. Aqueous extracts also demonstrated paralysis, and the times at which they died were 32.33, 0.67, and 76.19, 0.56 minutes for roundworms, 20.91, 0.31, and 30.89, 0.45 minutes for earthworms, and 64.44, 0.54, and 172.14, 0.81 minutes for tapeworms, respectively.With a concentration of 100 mg/ml, *P.daemia* extracts caused paralysis followed by death in the warms, showing (P 0.01) anthelmintic activity in comparison to that of standard medication.

Anti-ulcer activity:

Dehydration, ethanol's direct imposition of cytotoxic effects during the pathogenesis of ulcer development, and interference with mucosal cellular membranes all contributed to the progression of the inflammatory response [Park SW et al., 2008]. Meanwhile, alcohol unintentionally caused harmful effects through leukocytes, which cause inflammatory reactions, oxidative stress, and apoptosis. According to Sangiovanni E et al. (2013), NF-kappa B (NF-B) is crucial in this process for mediating the development of disease conditions. Numerous studies have shown that secondary compounds with anti-

ulcerogenic properties include triterpenes, flavonoids, and tannins [Borrelli F et al, 2000].These compounds are found in *P.daemia*, and they may be what gives the plant its anti-ulcer properties. *P.daemia* showed a healing impact on a rat ulcer caused by ethanol. The percentage of inhibition for the extracts (400 mg/kg) was 63.01, while the percentage for the group receiving the standard medication was 78.73%. In a dose-dependent way, Dhananjayan et al. (2014) hypothesised that ethanolic extracts of *P.daemia* leaf had excellent anti-ulcer activity.

Conclusion

One of the less researched and scientifically documented medicinal plants is *P.daemia*. We suggest that *P.daemia* demonstrated good pharmacological activity based on traditional accounts and literature reviews. From various parts of *P.daemia*, qualitative analysis of phytochemicals including flavonoids, terpenoids, phytosterols, proteins, amino acids, and saponins have been isolated and discovered. It is well known that medicinal plants are a natural supply of phytochemicals and bioactive substances. The significant bioactive components found in *P.daemia* extracts include natural flavonoids and cardenolides. Bioactive compounds engaged in pharmacological activities due to its antioxidant, anti-inflammatory and other related properties in human. By taking solvent extracts of *P.daemia*, you can avoid cancer, arthritis, and other illnesses that cause inflammation.It is noteworthy that *P.daemia*'s current phytochemistry and pharmacological state do not provide enough resources for herbal formulations. Clinical research and its methods of action, however, are unclear. Additional research is needed to determine the other *P.daemia* bioactive substances as well as their unique disease-management mechanisms. These investigations will help spread the use of herbal preparations based on *P.daemia*.

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Effect of pesticides uses on aquatic environments and fish diversity

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Introduction

Aquatic Toxicology is the study of the effectsof pollutants on the aquatic spectrum, such as pesticides, insecticides, etc. on the physical condition of fish species or other aquatic organisms (Pereira *et al*., 2009). Pesticides are used for various agriculture purposes to control pests mainly insects, aquatic weeds, different types of plants diseases, and aquatic snails that carry the cause of schistosomiasis. Pesticides have been found to be vastly noxious not only to fish species but also for other aquatic organisms, which constitute the tropic food chain. Pesticides are wide-ranging, are used very widely in various agriculture practices, in different forestry and in veterinary practices (Fabra *et al.*,1997; REBECA, 2007).

Pesticides are categorized into various types according to their objective use. Mainly pesticides are categorized into the three major types are herbicides (used for weed control), insecticides (used for insect control), and fungicides (use for mycotic control), but in comparison to all three types, insecticides are the more and acute toxic. Fishes species are the imperative wellsprings of proteins and lipids for humans and domestic animals, so the health of fish species is very essential for human beings. Insecticides are the synthetic compounds used to control various types of insects by killing or preventing them from engaging in undesirable behaviours or destructive.

Surface water contaminated by pesticides is notorious to impact on the aquatic and terrestrial ecosystem, the toxicant traveling from the lithosphere, hydrosphere and atmosphere shown in the Figure -1, To affect the survival and reproduction of the aquatic organism. Unfortunately, along with various advantages, of pesticides are threatening for the lasting survival of major ecosystems by interruption of ecological relationships between aquatic organisms and loss of biodiversity. Different types of pesticides used are organophosphate, carbamates, organochlorine, pyrethroids, and nicotinoids.

The residues of the pesticides used for intensive agriculture practices can contaminate the water (surface runoff and surface drainage) generally within a few weeks after the appliance. Use of insecticides results in a decrease in the rate of growth and also causes many metabolic and reproductive disorders. Especially in fish species, it may cause histopathological changes in gills, liver, hematopoietic tissue such as the spleen, kidney, and renal tubules, in endocrine tissues as well as brain, neurological, behavioural disorder and also cause genetic defect on exposure to insecticides. Some fish species are very sensitive to the environmental contamination of water (Maurya and Malik, 2016a). Hence, insecticides pollution in water may drastically damage in certain physiology and biochemical processes can cause serious mutilation

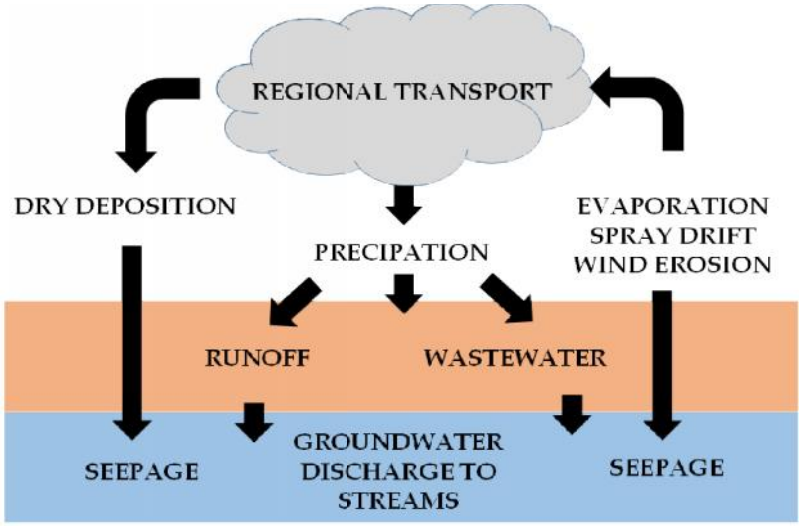

Figure -1. *Transportation of pesticides through atmospheric rotation.*

to physiological and health status as well as the structure of fish species. Aquaculture is solitary fastest growing fish food-producing sectors, supplying on an approximately 40-45% of the world's fish food (Mullen *et al*., 1997).

Besides all these benefits to society, the industry also faces various problems. Exposure of large quantities of pollutants might be an immediate effect as measured by mortality suddenly in largescale aquaculture, for example, fish mortality caused by pollution of waterways with agricultural insecticides. A small quantity of pollution discharge may result in the accumulation of pollutants in fish species and also by aquatic organisms. This paper presents the further in order to the concerning effects (acute, sub chronic and chronic) of the different types and different concentrations of insecticides

on some aspects of fish's biology, physiology, behaviour, the genetic and immune system of fish species. Also, when insecticides must choosing sensibly and are used in combination with various management tools, and also applied safely, in the result to avoid the surface water pollution and contamination of our aquatic life (Maurya *et al*., 2018).

Aquatic and fisheries resources in the form of lake, reservoir, ponds, rivers, seas, and oceans are supplying human with long term reimbursement. Those benefits can be the form of financial support which can provide employment, profit, water requirement, etc. to the humans. For example, the aquaculture and seafood industries provide jobs for commercial fisheries, wholesalers, and retailers. More round about, but equally important, benefits of fish and aquatic ecosystems include recreational activities like boating, sport fishing, swimming and natural beauty (Little *et al*., 1990; Malik and Maurya, 2015).

There are various occupational hazards and security concerns in the aquaculture industry. Some practices have caused environmental degradation. Community perception regarding the farmed fish species is that they are "cleaner" comparable to the wild fish species. On the other hand, various farmed fish have a much higher body burden of natural as well as man-made toxic production, e.g., in the form of antibiotics, insecticides, and pushy organic pollutants, than wild fish species. These types of contaminants in fish species can cause various health issues to unsuspecting consumers, mainly in pregnant or nursing women. The rule and regulations, as well as international oversight for the aquaculture industries, are very complex, in which various agencies indulge in aquaculture practices follow these regulation i.e. selection of site, control over pollution, quality of water, feed and also the safety of food. Different types of agricultural practices used insecticides results estrogenic and anti-estrogenic contaminants in the ecosystem can cause endocrine disruption and also effect on fish reproduction rate. Application of insecticides used for control a wide variety of insectivorous which would otherwise diminish both the quantity and quality of food production. Desolately, in spite of various advantages, the synthesized chemical compounds have significant drawbacks also threaten the long-lasting survival of major environmental disorder in relations between the aquatic organisms and also the loss of biodiversity. There are various major categories of insecticides that are habitually applied chlorinated hydrocarbons, carbamate, organophosphate, pyrethroids, and nicotinoids. Surface water contamination by insecticides is generally due to different agriculture practices combined with surface runoff and surface drainage, usually within a few weeks after application. Fish

species are chiefly sensitive to the environmental contamination of water. Hence, pollutants like insecticides may effect on various physiological and biochemical processes that types of insecticides can cause a serious threat to the health status of fishes (Maurya and Malik, 2016a). In modern agriculture activity, various types of chemical in the form of Pesticides, insecticides are used due to increased demand for productivity. Increased in productivity significantly increased the concentration of a chemical in food as well as in the ecosystem, which causes negative effects on human and other living organism health. (Richter, 2002) described that annually there are above million cases of pesticide poisonings worldwide. Moreover, with the progression of time, it may now better implicit that different pesticides have significant chronic health effects on the organism, including various types of cancer, nerve effects, diabetes, respiratory diseases, infant including fatal diseases, and genetic disorders. This type of health effects are different varied on the degree of exposure as well as the type of exposure. Normally, these effects are frequently for farmers, who are unswervingly exposed to pesticides, compared to the farmers living in rural areas who are less exposed to the following activities. Pesticides not only affect the farmer health but can also affect on consumer's health through residues of pesticide present in the food (Maurya and Malik, 2016b).

Regulation and use of Pesticides have long been controversial (Carson, 1962) in his famous publication made a popular observation in relation to risks associated with DDT (dichlorodiphenyltrichloroethane) and was followed by the US authorities for cancelation of this pesticide in agricultural uses. Various other examples of pesticide cancelation include EDB (ethylene dibromide) in 1983 and methyl bromide in 2005. It is now clear that a significant fraction of pesticides are carcinogenic; for instance, 18% of all insecticides and 90% of all fungicides were found to be carcinogenic (NAS, 1987), also it is well known that residues of the pesticide remain for long periods of time and that they are especially toxic to the young. Also, the uses of pesticides kill domestic animals, aquatic animals especially fishes and bees. Moreover, use of this type of chemical results in the development and evolution of pesticide resistance indifferent type insects, weeds and plant pathogens. All the same hundreds of different types of pesticides are used around the worldwide landscape, and some particular pesticides are used in some countries and not in other parts of countries. The main pesticide used for corn production in the various parts of US is atrazine, but this pesticide has been banned in the EU because of its heavy toxic effect since 2004 (Official Journal of the European Union 2004/248/CE). Public decisions concerning pesticides effects have long been

suspected of regulatory capture. Main reasons for transferring pesticides in 1970 regulatory accountability from the US Department of Agriculture to the Environmental Protection Agency (EPA) was to lessen the influence of farmers and pesticide producers.

But this shift of liability naturally increased the persuade of consumers and environmentalists. Indeed, Cropper *et al.* (1992) showed that both grower and environmental groups' participation played a key role in explaining the EPA decisions to cancel a pesticide in the1970s and 1980s. Risk assessment practices also play a role in pesticides regulation. The zero_risk or“ de-minimise risk” target has long been the sophisticated objective of regulators. But this objective is overly ambitious and often not implemented as a result. Some of the evidence for instance that a significant fraction of food samples still exceeds the maximum residue limits set by regulators both in the US and in Europe. Finally, risk perceptions may also persuade pesticide regulation. Slovic (2000)reported the grass root of these challenges, there is the gigantic difficulty of producing more food with the minimum use of pesticide, and the vaguenessa bout health sound effects of pesticides. Given the mounting health concerns over the population, some extreme actions to curb the employ of pesticides have been decided in some countries.

Denmark decided in 1986 to diminish the pesticide treatment rate of recurrence in agriculture. Recently, France also announced in 2008 a lessening by two of pesticide use by 2018 in its “Ecophyto 2018” plan (MAP, 2009). A key problem with such ruthless policy targets is that they need not replicate an appropriate balance of benefits and costs induced by pesticides used in our societies. Also, these policy targets may be difficult, if not impossible, to implement in practice, in part because of the opposition of farmers. However, only a few types of research are available in relation to benefit_cost analysis (BCA) concerning pesticides have been produced so far (Pimentel, 2005).

Aquatic toxicology

Aquatic toxicology is the study of the effects of environmental contaminants on aquatic organisms, such as the effect of pesticides on the health of fish or other aquatic organisms’ Figure -2. A

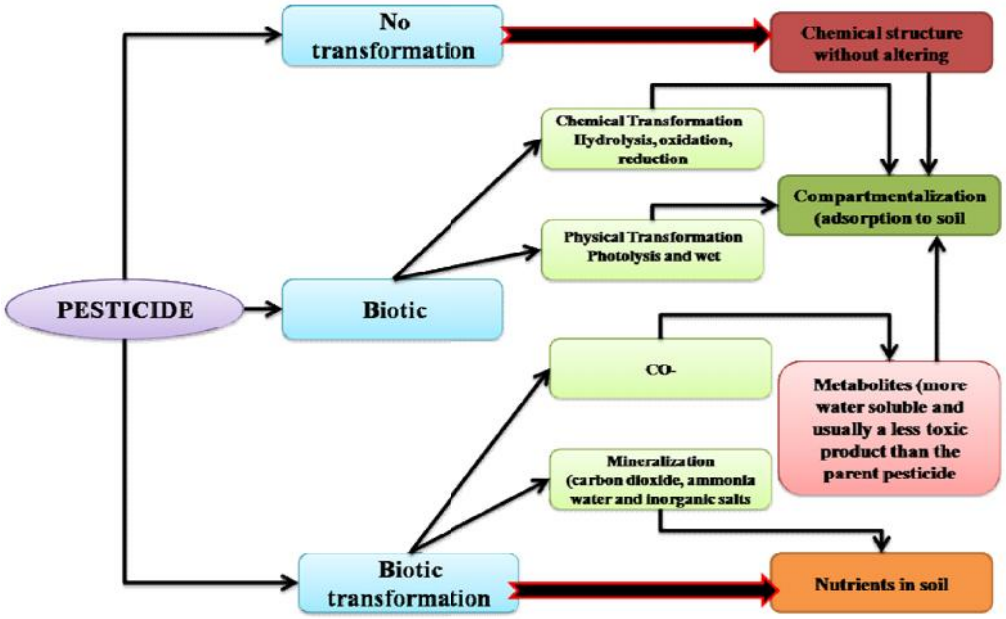

Figure-2:*Different route of exposure of pesticides in aquatic system*

pesticide's capacity to accelerate the harmful effect of fish and aquatic animals are large. It toxicity always depend upon exposure time, dose rate, persistence time in the environment. Toxicity of the pesticide refers to how poisonous it is. Brief exposure to some chemicals may have little effect on fish, whereas longer exposure may cause harm (Arbuekal and Server, 1998; Barone *et al*., 2000). Bio-concentration is the accumulation of pesticides in animal tissue at stages more than the ones in the water or soil to which they have been carried out. The poisonous substance inters into the aquatic animal body and effected on the idea of attention of toxicant. The sediment and soil are ecologically important for aquatic habitat, which plays a significant role in nutrients hooding capacity. Highly polluted sediments or accumulation of nutrients are adversely affecting the ecological functioning of rivers due to persistence in the environment and longrange transport. Repeated exposure to certain insecticides can result in decreased fish egg production and hatching, nest and brood abandonment, decrease resistance to disease, reduced body weight, hormonal modifications, and reduced avoidance of predators. The general effects of sub-lethal doses of insecticides can be decreased adult survival and reduced population abundance (Hoppin *et al*., 2002; Kamel and Hoppin, 2004; Gupta, 2004).

Different aquatic animals exposed to a pesticide, its survival relies upon on its biological availability (bioavailability), bioconcentration, biomagnification, and persistence inside the surroundings. Bioavailability refers to the amount of pesticide within the environment to be had to fish and flora and fauna. Some insecticides swiftly breakdown after utility. Some bind tightly to soil debris suspended in the water column or to stream bottoms, thereby reducing their availability.

Challenges of the global pesticide market

Fast increase in globalization are affecting pest management practices on and off the farm. The decline in the trade barriers also increases the competitive pressures and provides extra incentives for farmers to reduce costs and increase crop yields. Former participation and input markets, often branded as successful marketplace reform, can lead to incompetent pesticide use and high external costs (FAO, 2009). Other types of forms of trade barriers create a disincentive for adopting new technology such as the unwillingness of the EU to accept (GMO) genetically modified organisms. It may be imperative to indicate that it is not only the big multinational that are an important group of parties in pesticide policy but also the many new based companies in the developing countries who manufacture generics. An increases trend in the agrichemical industries is the big movement of many chemical pesticides off patent. As a result of these chemicals become generic pesticides, manufacturers lose their monopolies on them. Overall, generic type companies make up about 30 % of total sales. Mounting sales of generic pesticides, especially in some countries not only in Africa and Latin America but also in some of the Asian countries, is often facilitated by weak authoritarian control and the lack of an IPM oriented national policy framework (FAO, 2009). Around 30 to 35% of pesticides marketed in the developing countries with an estimated market value of USD 900 million manually do not get together internationally accepted quality standards. They preteens a serious threat to human health and also on their associated environment. Such types of pesticides often put into the accumulation of outdated pesticide stocks in developing countries (FAO, 2009).

Crop losses to pests

Crop productivity may be greater than before in many regions in various parts by high-yielding varieties, enhanced water quality and soil supervision, fertilization and other cultivation modern techniques. As a result of increased in the yield potential of crops, still, it is often linked with high insusceptibility to pest attack leading to increasing absolute losses and loss

rates (Oerke *et al*., 1994). An average ofabout35to 35 % of potential crop yield is lost to pre-harvest pests worldwide (Oerke, 2005).In adding together to the pre-harvest losses transport, pre-processing, storage space, dispensation, packaging, promotion, and plate waste losses along with the whole food chain account foranother30 to 35 %. In adding together to lessen crop losses due to pests, avoiding squander along with the whole distance end to end of the foodstuff chain is also a key (Popp, 2011). Evolutionary communications between pests and farmers predate predictable pesticides by thousands of years. Various levels of loss may be differentiated, e.g. direct and indirect level of losses or in the ways of primary and secondary losses, indicating that pests not only imperil crop yield and reduce the farmer's net income but may also affect the contribution of food and feed as well as the economy of different rural areas and even countries (Zadoks and Schein, 1979). Weeds affect crop efficiency particularly due to the antagonism for inorganic nutrients (Boote *et al*., 1983). Crop fortification has been residential for the prevention and control of yield losses due to pests in the field (pre-harvest losses) and during storage space (post-harvest losses). This paper concentrates on pre-harvest losses, i.e. the effect of pests on crop production in the field and the effect of control measures applied by farmers in order to minimize losses to an acceptable(Oerke,2005).

Costs and benefits of pesticide use

The profitable analyses of pesticide remuneration are hindered by the lack of pesticide use data and fiscal models for minor and crops as well as non-agricultural pesticides. Cost–benefit analysis of pesticides use is increasingly used to measure resource supervision and environmental policies. This approach monetizes all costs as well as benefits so that they are deliberate in currencies and its full functioning might be constrained by data limitations factor and difficulties in monetizing human and environmental health risks. Further economic impacts are complicated by the various government programmes that support pesticide users, such as price and cost supports system and deficit payments.

The most usually economic incentives are based on the "polluter pays" principle, including the use of licensing fees, user fees or taxes. Denmark, Sweden, and Norway are some of the countries which experience the introduced taxes in such a way of reducing pesticide use. However, the price elasticity of this chemical is estimated very low and can suggest comparatively very little effect in terms of quantity reductions, unless they may set very high rates relative to price. Some suggestions in regard to pesticides are to revenue

and recycling may have been more effectual, with revenues redirected to research and information. Using further research or to encourage various changes in farming activities would appear to make more sense (Pearce and Koundouri, 2003).

Pesticides may vary in their toxicity by design, by concentration and also according to the conditions in which they are receiving environment. The main theoretical solution is to articulate the tax as an absolute sum per unit of toxicity-weighted ingredient. The overall stipulate for pesticides and insecticides are not reduced drastically by a tax, a toxicity-differentiated tax may be more effective if the exchange between pesticides will occur in a way that the all over the toxic force of pesticides will be abridged. This means that the pesticide and its use, as well as toxicity, could be "decoupled" by a pesticide tax. The various problems with pesticide tax studies are few of them simulate the "cross-price effects" of such a policy, i.e. they do not look directly at the changeover between different types of pesticides (or between pesticides and other inputs such as fertilizers and land). Simulations of such type of toxicity-weighted taxes for the UK show that overall cost price elasticity is demand for pesticides was consistently low and may never greater than −0.39. Nevertheless, cross-price elasticities in between the “banded” pesticides (banded according to toxicity) were greater than the “own” price elasticity, telltale that farmers might be switch between various types of pesticide (Pearce and Koundouri, 2003). Nonetheless, the "polluter pays" principle (i.e. adding the environmental and public health costs to the price paid by consumers) can be an efficient loom toward internalizing the social costs of pesticide use. The fees, as well as taxes generated, can be used to enhance (sustainable) pest management system. In instruct to place the right level of levies and taxes, it may be obligatory to estimate the positive and negative impacts of pesticides. Various attempts have been made to establish the costs price related to public health (risks to farm workers and consumers and drift risk) and spoil to favourable species, and also to the ecosystem (Pimentel *et al*., 1992; Pimentel and Greiner, 1997; Pimentel, 2005). However, the result of the use of the pesticides can in a range of benefits including wider public outcomes with benefits being manifested in increased income and reduced risk, plus the aptitude to hire manual labour and provide the employment opportunities and other services. Some other outcomes were also the evolution of more multipart hamlet facilities, such as educational institutes, schools, and shops in such a way to improved health structure (Bennett *et al*., 2010). Some of the sub-lethal effects include:

- Loss of attention.
- Low diseases resistance.
- Low predator avoidance.
- Reduced egg production.
- Sterility.
- Weight loss.

Exposure of pesticides to aquatic animals

Both in fish species, as well as aquatic flora and fauna, are exposed to a variety of pesticides in three common ways as dermal, direct absorption all the way through integument by swimming in contaminated surface water with pesticide as well as subordinate surfaces of waters in form of lentic and lotic water bodies, direct or indirect uptake of pesticides through inhalation by the way of gills during respiration, and directly throughout, drinking pesticides contaminated water or feed pesticide contaminated prey as in Figure -3. The sources of pesticides in the aquatic system through the agricultural runoff and industrial effluents, the entire foreign toxic compound mixed in the aquatic ecosystem and disturbed all aquatic life.

There are also some minor causes that affect the attention of fish species and aquatic flora and fauna to pesticides and resulted in toxicity. By the utilization of pesticide contaminated animal and their by-products also transfer toxicity to consumer's i.e. various carnivorous fish species feed upon the variety of aquatic insects already killed due to the toxicity of pesticide may transfer effect to next tropic level. Mainly surface water of the riverine ecosystem generally comes first with pesticides contact, and various organic substances like algae, mosses, vascular hydrophytes, leaf litter, and branches, etc. may also behave as secondary causes of toxicity. The revelation of any fish species and other aquatic community to pesticide may be widespread problem realized by the people. Most of the case related to the pesticide toxicity in fish species goes unreported and also in some known cases, the quantity of fish species mortality is often underestimating. The scientific knowledge regarding possible pesticides affect fish species and other aquatic living organism depend mainly upon seven factors i.e. category of pesticide and its by-product, concentration rates, climate conditions, type of aquatic species concerned, degree of the dilemma (number of fish mortality), place and dimension of water body affected. Acute effect of toxicity with different types of pesticides

mainly depends upon the fish species and duration of exposure as in Tables 9.1-9.3.

Various steps to reduce the effect of pesticides: Before using any pesticide, think about the following:

- Only use the pesticide whenever necessary.
- Use another ways of treating the predicament. Landowners should think about the expenses and consequences of pesticide cure relative to the problem.
- Use pesticides having less toxicity.

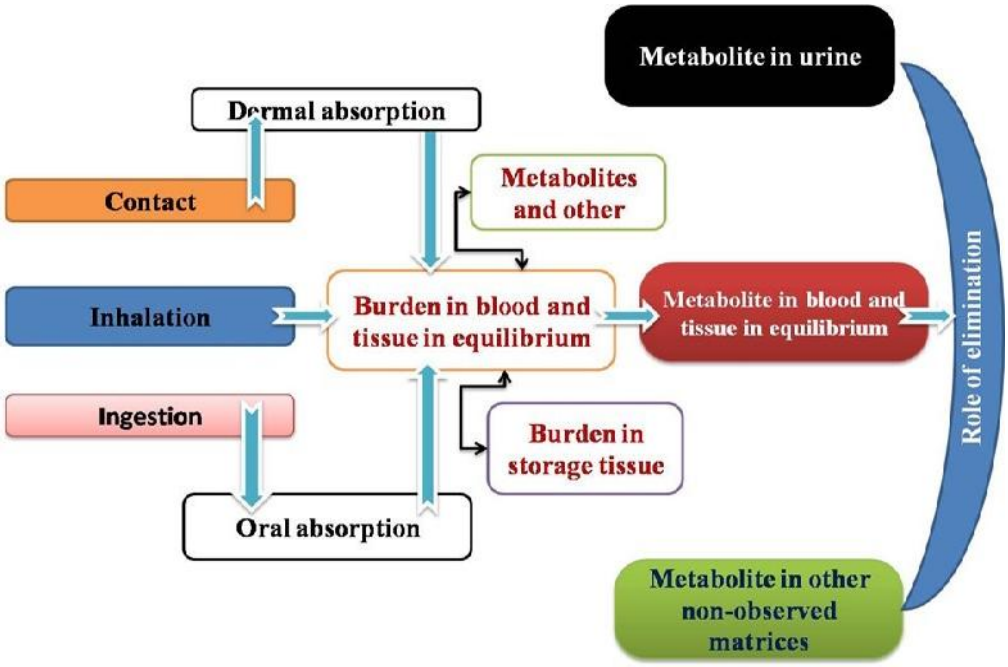

Figure -3. *Distribution toxicant by route of exposure in the animal body and representation of the toxic kinetic model*

- To reduce the sound effects of pesticides on aquatic ecosystems, use only those least toxic pesticides to the aquatic organism. Some relative toxicity lists of pesticides used in various agricultural activities are presented in tables at the end of this booklet.

- Application methods must be safe and sensible
- The initial tenet of accountable in the use of pesticide is to understand and then go through the pesticide label and follow the guidelines precisely. Label information sometimes can be mystifying. Contact extension agent, supplier in a case if don't recognize the directions or the company of pesticide for more information.
- Give meticulous awareness to the word of warning about ecological hazards on the sticky label. Look the label to confirm that: "These manufactured goods are toxic to fish species." think about supplementary pesticide or any other alternative control technique.
- Certify that equipment is working in fine proviso. Check for any leakage, reinstate worn out parts, and vigilantly standardize your equipment.
- While preparing the pesticides for relevance, subsist that you are assimilation them accurately.
- Never rinse spray tools in lakes, ponds, or rivers. If you use water directly from the natural ponds, lakes, or streams, use an anti-siphon device to avoid backflow.
- In some case applying pesticides near surface water, ensure the sticky label to locate the suggested buffer zone. Buffer strip widths varied between the water and the treatment areas.

Depart a broad buffer zone to shun contaminating fish species and aquatic flora and fauna.

- Store up and dispose of unused pesticides and their containers according to the label directions.
- Avoid the use of pesticide waft into no target areas, or applications for the period of wet, turbulent weather that may endorse runoff to non-target streams, ponds, or lakes. Mist on cool days or in the early hours or evening when it is less windy.
- Pesticide applicators are legally responsible for downstream fish mortality and pesticide contamination.

Table -1.*The toxicity of pesticides on the basis of concentration.*

Hazard rating	Dose (mg/L)
Toxicity	LC50
Minimal	>100
Slight	10-100
Moderate	1-10
High	0.01-0.1
Extreme	0.01-0.1
Super	<0.01

Table-2. *The acute toxicity (LC50) of some pesticides against certain fish species.*

Name of pesticide	Fish species	Duration of exposure
DDT	*Rainbow trout*	96 hrs-8.7 µg/l
Akton	Channel catfish	96 hrs-400 µg/l
Acephate	Feathed M.	96hrs>1000 µg/l
Alachlor	*Rainbow trout*	96hrs 2.4 µg/l
Endosulfan	*Channel catfish*	96hrs 1.5 µg/l
Malathion	*Labeorohita*	96hrs 15 µg/l
Malathion	*Heteropneustesfossilis*	96hrs 0.98 ppm
Methyl parathion	*Catlacatla*	96hrs 4.8 ppm
Roger	*Pontius stigma*	96hrs 7.1 and 7.8 ppm

Table-3. *Acute toxicity of some insecticides against certain fish species (Source: Hanazato, 2011).*

Insecticides	Fish species	96hLC50
Azodrin	Rainbow trout(RT), bluegill (BG), Channel catfish, Feathered minnows (FM)	4.9-50 ppm
Aldrin	FM, Chinook Salmon, RT, blue head, bluegill	2.5-53 ppm
Carbaryl	Coho salmon, Chinook salmon, RT, green sunfish, largemouth bass, yellow perch, and black crappie	0.9-39 ppm

Carbofuran	Walked catfish, Chubs	0.22-23 ppm
Chlordane	Coho salmon, cutthroat, RT, FM, Channel catfish	0.72-11.9 ppm
Chlorpyrifos	Nile tilapia (NT), Bluegill , FM, RT, Goldfish	0.72-11.9 ppm
DDT	Coho salmon, cutthroat, RT, FM, Channel catfish	1.5-21.5 ppb
Diazinon	Guppies, Channapunctatus	0.9-2.6 ppm
Dieldrin	Coho salmon, Chinook salmon, RT, green sunfish, largemouth bass, yellow perch and black crappie, Cutthroat	1.2-19 ppb
Diflubenzuron	FM, Brook trout, Yellow perch, RT and Cutthroat	25-240 ppm
Dinitroceresol	RT and bluegill	66-360 ppb
Dioxathion	Cutthroat, Largemouth bass	22-110 ppb
Disulfoton	Coho salmon, Chinook salmon, RT, green sunfish, largemouth bass, yellow perch, and black crappie, Cutthroat	60-4700 ppb
Fenthion	Coho salmon, Chinook salmon, RT, green sunfish, largemouth bass, yellow perch and black crappie, Cutthroat	1.1-3.4 ppm
Trichlorfon	Eel, RT, Cutthroat, Brown trout, bluegill, Largemouth bass	1.1-3.4 ppm

Modification in habitat

Increase in pesticides concentration can diminish the accessibility of aquatic plants and insects that in order to serve as food for fish species and another aquatic organism. Use of pesticides in various agricultural practices can affect the food chain of insect eating birds and also for fish species. An unexpected, insufficient availability of insect's food can force fish species to migrate in search of food, where they might found the availability of greater revelation to predation. Similar to pesticides, herbicides can also trim down the reproductive success of fish species and other aquatic flora and fauna (Malik *et al*., 2015; Maurya *et al*., 2016c; Maurya *et al*., 2019).

The deep, weedy nursery areas for various fish species supply rich food and protection for fry and fingerlings. Spraying pesticides along weedy

nurseries can diminish the quantity of cover and protection that fry and fingerlings need in order to hide from predators and to feed. Most fry and fingerlings depend on aquatic plants as a refuge in their nursery areas (Schreinemachers *et al*., 1999). Aquatic flora contributed about 80% of the total dissolved oxygen essential for aquatic organism present in different ponds and lakes. Pesticides kill all aquatic organisms due to the low oxygen levels and the suffocation mainly in fish species. Future use of herbicides to utterly "clean up" a pond will drastically reduce fish habit and habitat, food supply, dissolved oxygen, and fish yield.

Control of pests

Chemical control

The remedial technique for pest control with noxious chemicals has been proved the major prevailing pest control approach about an average of 50 years. Security exertion and environmental disruptions go on to ensure (Wright, 1996) and renewed appeals for efficient, safe, and cost-effectively adequate alternatives (Benbrook, 1996).

Pesticides carry synthetic chemical are the most extensively used scheme of pest management. Mainly four problems are encountered with toxic pesticides are its residues, pest resistance, pests as secondary form, and pest resurrection (Lewis, 1997). Many pesticides, as well as organophosphates that are eco-friendly, must be preferred and synthetic form pesticides should only be preferred as the last option as to use only when required.

Biological control

From time to time, the word ‘‘biological control’’ has been used in a broad perspective to include a full scale of biological organisms and products based biologically including some i.e. phero‗110 Weed and Pest Control - Conventional and New Challenges mones, resistant plant varieties, and autocidal techniques such as sterile insects. IPM is mostly intended at developing systems based on the use of various biological and non-chemical methods as much as possible.

Mechanical control

By the help of machinery and other modern tools as well as advanced technique are used now a day to control pests in any agricultural practices. It involves some farming practices like tillage, slash and burn, and also by manual hand weeding. The pruning of infected parts of various fruits, forest

trees and defoliation in certain standing crops help to reduce the population of the pest.

Chaffing of sorghum/maize part of stalks and blazing of stubbles to kills maize borer is also used.

Sanitary control

Sanitary control comprises cleaning field equipment (tillage equipment, haying equipment, etc.), certified seeds should be planting and quarantine of infected crops from farmlands. These are some methods which help to prevent the introduction of a pest into the agricultural field.

Natural control

Certain techniques which only involve the improvement of naturally occurring pest management methods to conflict with pests like using valuable insects. Here only insecticides are applied to efficiently realistic and it is obvious that natural predators will help to control the pests.

Resistance in the host plant

This method involves various breeding strategies with enviable financial traits, but a smaller amount of attractive for pests, egg laying and consequent progress of insect, disease as well as a nematode. It also involves the infestation/infection or the lessening of pests to some level that they are not in huge figures during the growth period of an aquatic plant (Sharma, 2007).

Cultural measures

The developments of cultural control are the oldest methods that have been used to manage pest populations. However, with the development of synthetic pesticides, these controls were rapidly de-emphasized and research on them was largely discontinued. The involves practices that suppress pest problems by minimizing the conditions that favour their existence of life (water, shelter, food). The selection of an appropriate site for the cultivation of field crops and fruit trees can reduce future infestation from insect pests. The culture should be selected in such a manner that it should be suitable for growing in the area and tolerant of important pests diseases of the area.

Integrated pest management (IPM)

IPM is a science based on scientific thought and decision-making process that identifies and reduces the risk of pest management related strategies. IPM coordinates the pest biology of the environmental information and available different technology to prevent unacceptable levels of pest

damage by the most economical means while minimizing risk to people, property, resources, and the environment. The key to pest control strategies is to determine the extent of the problem**.** IPM takes benefit of these natural controls and their programs come to mind in numerous places all over the country. They may be applying in several situations from small home gardens to trade water weed administration. IPM involves an array of methods, including pesticides in order to reduce the pest contaminated populations to adequate levels. Due to the overdependence on pesticides, IPM was developed. Many factors i.e. contamination in groundwater, the ever-increasing cost of agricultural pesticides, concerns of the customer regarding pesticide contaminated foods, and also concern about the environment persuade the use of IPM. IPM provides an effective improvement, all encompassing, low risk approach to protect resources and people from pests" (USDA NIFA, 2013). IPM integrates multiple management tactics mostly allow the production system to move away from traditional, chemical-based management in ways that usually allow production systems to move away from traditional management to ecologically sound strategies. IPM practices are typically crop and region-specific and are intended to result in effective, timely and affordable pest control while also reducing the use of pesticides to health and the environment (Biddinger and Rajotte, 2015). IPM can readily evolve to meet new challenges such as food safety. IPM protocols, or collections of practices for specific crops and regions, often include related practices such as irrigation and nutrient management, at least to the extent that they influence pest management. The carefully timing management for irrigation cycles so plant foliage will dry quickly limits the potential for plant disease growth and spread (Waage, 1997). On the other hand, bio-pesticides may be safer comparing to that of conventional pesticides, the manufacturing groups of these bio-pesticides composed mostly of small to average sized enterprises, and it is very difficult for such companies to fulfil and comprehensively subsidize investigate and expansion, marketing and promotion services of such companies required to make a successful way to aware the use and benefits of bio-pesticide. Yet it is a major challenge for anyone to initiate this process due to the lack of innovative bio-pesticide goods impending to the open market and also for their registration (Popp, 2011; Farm Chemical Internationals, 2010). Types of strategies under IPM include:

- Cultural control in the form of crop rotation and planting season to avoid pests.
- Host resistance plants are used and select livestock that is resistant to pests.

- Mechanical control by uprooting, weed harvesting, cultivation, and use of various types of traps to the captured insect)
- Biological control as stocking some carp fish species that feed on water weeds.
- Control of pesticides with chemical
- Proper sanitation

Efficient supervision practices for the protective quality of water

- Preferred only IPM practices in order to avoid the chemical controls methods or will be applied only whenever necessary. Preventive measures should be taken before using any pesticide and can be applied safely and in an effective manner.
- Estimate the concentrations of chemical control in agricultural practices. Separate out the major option that is the slightest adverse impact on water quality. Select those products which reduce waste and applicator exposure.
- Proper care should while incorporation and loading pesticides. Check equipment working correctly and is properly calibrated in advance. Prepare only the required amount of pesticide needed for the urgent application.
- Apply pesticides in short and precise time period. Think about climate as well as the life cycle of pest before planning applications.
- Store pesticides products safely in a ventilated away from sunlight, and protected area free from flooding.
- Disposal of empty containers of pesticides should not rinse in water.
- Keep records about the concentration and timing of all pesticide used in the area. This will help in assessment of pest control efforts and also help to plan future treatments.

Conclusion

Exposure of aquatic as well as terrestrial organisms to pesticides for the long term means an incessant health risk for the inhabitants. So, directly and indirectly, human populace is at elevated risk by consuming the toxicities fish species. This clearly reveals that the individual should take the required preventative measure in the application of pesticides to guard the fish population and also to other aquatic fauna. Thus it is probable that many

approaches using according to molecular biology techniques will modernize toxicological applications that are cheaper and do not entail the animals to identify ecological stressors. Different effect of pesticide toxicity in fish species has been premeditated by a number of researchers, who have revealed that at chronic level, may cause different effects i.e. oxidative damage, the reticence of AchE movement, changes in histopathological, embryonic and developmental changes, carcinogenicity and mutagenesis. Usage of pesticide and its undesirable effects on non-target aquatic organisms including fish species, it has befallen crucial to plan rigid rules and regulations against the arbitrary use of this pesticide.

Since pesticide in the environment have some other toxicant compound i.e. compounds of organophosphate, additive responses to organophosphate compounds may bring on poisonous or lethal effects in fish species. Therefore it is an issue of enormous public healthiness consequence to habitually supervise the concentration of pesticide residues in foods material and also supervise the humans in a way to measure the resident's exposure to the pesticide. More experimental effort should be performed to establish the concentration and exposure time of these pesticides and also induce significant lethal and sub-lethal effects on the organism.

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Over view – Honey Bee

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Abstract

Our Survival is Depends upon the Biodiversity, Bees plays a major role in it. They gives us a natural medicines such as Honey, Royal jelly, Pollen, Beewax, Propolis and Honey bee Venom. Honey from the bees is used to treat many diseases such as tuberculosis, throat infection, eye infection, bronchial asthma, hepatitis, and worm infestation, etc,.. Honey bees also worked as a worker for the Society by pollination in cross pollinated crops.

Key words: Honey bee, Bee wax, Royal jelly

Introduction

Kingdom:	Animalia
Phylum:	Arthropoda
Class:	Insecta
Order:	Hymenoptera
Family:	Apidae
Clade:	Corbiculata
Tribe:	Apini

Scientific Classification

The bee clade includes the eusocial honey bee (also written honeybee), all of which are indigenous to mainland Afro-Eurasia.Several subspecies of honey bees were introduced by humans into South America (early 16th century), North America (early 17th century), and Australia (early 19th century) after bees expanded naturally throughout Africa and Eurasia. (Whitfield, Charles W.; Behura, Susanta K.; Berlocher, Stewart H.; et al. 2006).

Honey bees are renowned for building long-lasting colonial nests out of wax, for the size of their colonies, and for the abundance of honey they produce and store. These traits make honey bee hives a valued foraging target for many animals, including honey badgers, bears, and human hunter-gatherers. Although traditionally 7 to 11 species have been recognized, there are only eight recognised species of honey bees that are still alive today, with a total of 43 subspecies. Only a tiny portion of the 20,000 or so species of bees that are known as being alive today are honey bees.

The western honey bee (Apis mellifera), which was domesticated for honey production and agricultural pollination, is the most well-known type of honey bee. The eastern honey bee (Apiscerana), which is found in South, Southeast, and East Asia, is the only other tamed bee. Only individuals belonging to the genus Apis are considered genuine honey bees, but other species of bees, such as the Indian stingless or dammar bee Tetragonulairidipennis and stingless bees from the genus Melipona, also produce and store honey. Beeswax is also used by contemporary people to create candles, soap, lip balms, and other products, as a lubricant, and in the lost wax mould-making process.(Buchmann, Stephen L. et al. 2010).

Origin and Distribution

All of the extant species of honey bees, with the exception of Apis mellifera, are native to South and Southeast Asia (including the Philippines), suggesting that this area is where honey bees originated. It is noteworthy that there is the origin of the surviving representatives of the earliest diverging lineages (Apisflorea and Apisandreniformis).

At the Eocene-Oligocene border, in European sediments, the earliest Apis bees are first documented in the fossil record. The fact that these ancient honey bees were prevalent in Europe at the time does not inherently mean that the genus' origins were in Europe. South Asia is thought to be the area of origin for honey bees, but very few fossil layers there are known, and even fewer have been fully investigated.(Han, Fan; Wallberg, Andreas; Webster, Matthew T. et al. August 2012)

Before Europeans brought A. mellifera to the New World, there were no Apis species there during the period of early humans. Apisnearctica, the only fossil species known from the New World, is only known from a solitary individual that dates to 14 million years ago and was discovered in Nevada.

Bumblebees and stingless bees, which are near relatives of contemporary honey bees, are also social to some extent, and social behaviour is thought to be a characteristic that precedes the beginning of the genus.(Han, Fan; Wallberg, Andreas; Webster, Matthew T. et al. 2012) The more recently developed species of Apis nest in cavities and have numerous combs, which has greatly aided their domestication, while the more basal species create solitary, exposed combs.

Types of Castes:

Drone:

Drones are usually haploid, meaning they have just one pair of chromosomes, and their main function is reproduction.If the monarch decides not to fertilise an egg, she will make them, or an unfertilized laying worker will. Drone embryos that are haploid do occur occasionally. When there have been more than two generations of brother-sister coupling, this occurrence typically occurs. In honey bees, a singular locus known as the complementary sex determiner (csd) gene is originally responsible for determining sex. If a growing bee has the csd gene heterozygosity, the individual will eventually turn into a female. The person will turn into a boy if the circumstances are such that they are either hemizygous or homozygous for the csd gene. When a person has this trait homozygosity, it usually occurs in diploid men.Up to 500 drones can be created per hive between summer and fall, and they can take 24 days to mature.During the winter, when the hive's main priorities are warming and food preservation, they are ejected from the colony. During courtship trips, drones use their large eyes to find females. They lack a stinger and neither protect the colony nor kill trespassers.

Worker:

There are two genetic groups in workers.They come from an egg that the queen has carefully fertilised using sperm that has been kept in storage. Worker development usually takes 21 days. There could be as many as 60,000 worker bees in a normal hive.More behaviours are displayed by workers than by monarchs or drones. Feeding brood, obtaining nectar, cleaning the colony, performing watch duty, and foraging are the sequence in which their responsibilities shift as they get older (starting with clearing out their own cell after chewing through their capped brood cell).Some employees also participate in more specialised activities like "undertaking." (removing corpses of their nestmates from inside the hive).

The pollen receptacle (corbicula), abdominal glands that make beeswax, brood-feeding glands, and barbs on the lash are just a few of the physical specialisations of workers. A labourer may grow ovaries under specific circumstances (for instance, if the population goes without a queen).

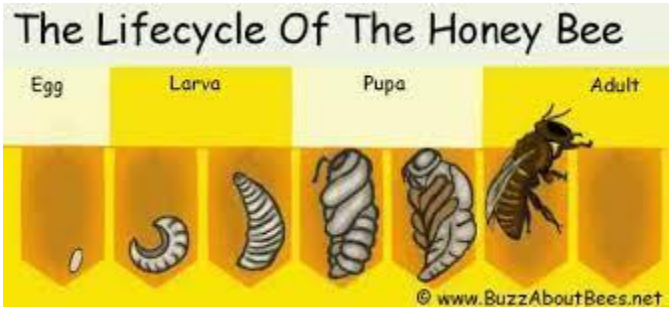
Honey bee workers engage in a variety of behavioural activities that subject them to various regional settings. The gut microbial makeup of employees changes with various colony duties, such as parenting or food

preparation, and with the environment and plant species they graze, such as variations in rapeseed crops

Queen:

When worker bees exclusively nurse a single female pup a substance known as "royal jelly," queen honey bees are produced.In contrast to worker bees, queens have a different metabolism, appearance, and behaviour. They are born in oversized cells and mature in just 16 days. A working pair of ovaries and a spermatheca, which stores and keeps sperm after mating, are two additional features of the queen in addition to her larger size. Apis queens engage in polyandry, whereby a single female mates with a number of males. The Apisnigrocincta species has the greatest recorded number of matings per queen, with reported numbers of different matings varying from 42 to 69 drones per queen. Queens in this species mate with a very high number of males. Queens lack the organs that make honey, and their stings are not barbed like a worker bee's. Queens can produce up to 2,000 embryos per day after mating. They create a variety of pheromones that control worker behaviour and aid swarms in locating the monarch while swarming.

Life Cycle:



1. Worker bees make and shape the wax honeycomb in which the eggs are deposited singly in each cell. The queen can choose to fertilise the egg she is depositing with her spermatheca, typically based on which cell she is putting it into. Females (queens and worker bees) grow from fertilised eggs and are diploid, whereas drones (which are formed from unfertilized eggs) are haploid. Royal jelly made by worker bees serves as the larvae's primary food source. Honey and pollen are then added afterward. The one exception is a caterpillar that only consumes royal jelly and grows into a queen bee. Before making a web inside the cell and pupating, the larva goes through several moults.

2. Young worker bees, also known as "nurse bees," take care of the hive's cleaning and provide food for the offspring. They start constructing comb cells when the glands that make royal jelly start to diminish. As they mature, they move on to other within-colony duties like nest protecting and collecting nectar and pollen from scavengers. A worker eventually departs the colony after taking her first orientation flights and usually spends the rest of her life foraging.
3. 3. While the bee dance or waggle dance differs from species to species, all extant species of Apis show some variation of the behaviour. Worker bees cooperate to locate food and use a pattern of "dancing" (also referred to as the bee dance or waggle dance) to share information regarding resources with one another. A less specific movement known as the "round dance" might also be seen if the resources are very near to the colony.
4. Honey bees also engage in tremble dances, which entice recipient bees to gather honey from foraging foragers who have returned.
5. Before returning to their home colony, virgin queens fly to a drone gathering location on mating missions and mate with a variety of drones. The drones perish while coupling. The drones from their own group are not allowed to reproduce with queen honey bees.
6. As opposed to the majority of bee species, which have isolated queens, "swarms" are made up of a paired queen and a sizable number of worker bees. This group travels collectively to a nest site that was previously surveyed by worker bees and whose position is signalled by a particular kind of dance. As soon as the colony appears, they build a fresh wax comb and start raising fresh worker brood. No other extant bee species exhibits this form of nest founding, though several swarming vespid wasp groups have also established new nests. (sometimes including multiple queens). (James L. Gould; Carol Grant Gould et al. 1995)

Nutrition:

Honey bees receive all of their dietary needs from a variety of pollen and juice sources. For honey bees, pollen is their only natural supply of energy. To satisfy a daily dry matter requirement of 66-74% protein, adult worker honey bees eat 3.4–4.3 milligrammes of pollen. For one larva to grow properly, 125–187.5 milligrammes of pollen or 25–37.5 mg of protein are needed. Ten of the twenty-one amino acids that make up dietary proteins—methionine, tryptophan, arginine, lysine, histidine, phenylalanine, isoleucine, threonine, leucine, and valine—are thought to be necessary for honey bees.(Brodschneider, Robert; Crailsheim, Karl et al . 2010). Leucine, isoleucine, and valine are the amino acids that honey bees need in the greatest

quantities; however, brood rearing also calls for high concentrations of arginine and lysine. In addition to these amino acids, raising larvae also requires the B vitamins biotin, folic acid, nicotinamide, riboflavin, thiamine, pantothenate, and—most crucially—pyridoxine.

The B vitamin pyridoxine is the most common one to be found in royal jelly, and its amounts change throughout the hunting season, peaking in July and August and being lowest in May. Without nutritional pyridoxine, honey bees were unable to raise offspring. Honey bees can get lipids from pollen in amounts varying from 0.8% to 18.9%.During the brood stage, lipids are metabolised to produce the components needed for upcoming biosynthesis. Although not deemed necessary, the fat-soluble vitamins A, D, E, and K have been shown to greatly increase the number of brood produced.Honey bees cannot directly synthesise cholesterol from phytosterols; instead, they consume phytosterols from food to make 24-methylenecholesterol and other sterols. Through the use of brood food, nurse bees can specifically transmit sterols to larvae.(Karasov, William H.; Martinez del Rio, Carlos et al. 2008).

Foraging worker bees gather nectar as a supply of hydration and sucrose-based carbohydrates. Fructose and glucose are the two main monosaccharides in honey bee meals, but trehalose, a disaccharide made of two glucose molecules, is the most frequently moving sugar in hemolymph. For normal growth, larvae need about 59.4 mg of carbohydrates per day and adult worker honey bees need 4 mg of utilisable sugars daily.

Honey bees need water to keep their osmotic balance in check, make liquid sustenance for the larvae, and cool the colony through evaporation. Foraging for honey, which has a high water level, can typically satisfy a colony's water requirements. (Kuhnholz, Susanne et al. 1997).On sweltering days or when nectar is scarce, foragers will occasionally fetch water from pools or waterways.

Honey Bee Products

Bees make a variety of products that they use as food, for production of honey, in construction and repair of the hive and as sealants to prevent spoilage.

Beewax

Beeswax (*Cera alba*) is the natural wax produced in the abdominal segments of worker bees which is secreted and deposited in scales and then collected and used to build the honey comb for storage of honey and protection of larvae in the hive. Beeswax consists largely of fatty acid esters of long-chain

alcohols. Beeswax has been used by humans for centuries as a lubricant, glaze or polishing solution or waterproofing gel. Beeswax is edible, but is usually combined with other ingredients or used as a covering for products such as cheese for preservation and prevention of mold or fungal contamination.

Pollen

Bees use bee pollen, a combination of plant and floral pollen, nectar, and secretions, to produce honey. By setting up traps in the bee colony that strike some of the pollen the bees gather off, the pollen is collected. Although its makeup varies greatly, it contains vitamins, minerals, and carbs. Bee pollen is marketed as a nutritional additive with antibacterial and anti-inflammatory properties. Bee pollen is supposedly helpful for cancer, arthritis, and improving sports ability, but there is no evidence to support these claims. Patients with asthma, atopic eczema, and pollen sensitivities have all reported having allergic responses to bee pollen.

Propolis

Bees gather propolis, a naturally occurring resinous substance, from a variety of plants and combine it with honey and salivary enzymes. Propolis can be used to cover gaps, seal openings, and construct beehives because it is rigid and breakable at low temps but malleable, flexible, and sticky at higher temperatures. Propolis acts as a barrier, guarding the colony from bacteria, spores, and mould. Humans have used propolis directly to treat cuts, skin ulcers, and rashes, and orally to treat diseases like diabetes, obesity, cancer, and other illnesses. Based on research in cell culture and animal models of illnesses like diabetes, obesity, and cancer, propolis is said to have anti-inflammatory, antioxidant, antidiabetic, and even antineoplastic action. None of these behaviours have been conclusively demonstrated in people with cancer, diabetes, or obesity. Although adverse event rates have not been discussed in the majority of clinical studies, propolis is reportedly well accepted. Similar to bee pollen, propolis is highly varied, with chemical compositions that significantly vary depending on the species of bees and the region. (based upon local plant species). Contaminants, bug pieces, and environmental allergens may be present in propolis. Propolis contact dermatitis, a well-known beekeeping problem, can happen when propolis is applied topically or taken orally. Commercial sources of propolis have been linked to allergic responses like angioedema and anaphylaxis, according to reports. Plant flavonoid aglycones are most likely to blame for the allergy responses.

Royal Jelly

When provided in greater quantities and for longer periods of time, royal jelly, a milk-like secretion from the mandibular glands of worker bees, is used to nourish worker and drone offspring as well as the nutrition and growth of queen bees. (fertile females). As explained in more depth in a different chapter, royal jelly is obtained from the individual cells of queen bees and is frequently used in complementary and conventional medicine.

Defence

Apiscerana japonica forming a ball around two hornets: The body heat trapped by the ball will overheat and kill the hornets.

All honey bees reside in hives where employees defend themselves by stinging invaders, and alarmed bees emit a pheromone that prompts other bees to attack. The presence of tiny barbs on the bite distinguishes the various types of honey bees from all other bee species, but these barbs are only present in worker bees.

The fact that the barbs typically do not work (and the sting apparatus does not detach) unless the sting is lodged in fleshy tissue suggests that the sting apparatus, including the barbs, may have developed particularly in reaction to predation by animals. In the case of Apisceranajaponica, defence against larger insects like predatory wasps (e.g. Asian giant hornet) is typically performed by surrounding the intruder with a mass of defending worker bees, which surround the intruder and vigorously vibrate their muscles to raise the temperature of the intruder to a lethal level. While the sting can also penetrate the membranes between joints in the exoskeleton of other insects (and is used in fights ("balling"). Invading wasps were previously believed to be killed by heat alone, but new tests have shown that the lethal impact is actually produced by a combination of higher temperature and increased carbon dioxide levels within the ball. This occurrence is additionally utilised to eliminate a monarch deemed intrusive or unfit, an action known to beekeepers as 'balling the queen', named for the ball of bees formed.

Depending on the bee's environment, defence may change. Would-be predators are given a warning signal in the form of a "wave" that ripples across a layer of bees tightly packed on the surface of the comb in the case of honey bee species with open combs (such as A. dorsata), consisting of bees briefly arching their bodies and flicking their wings when a threat is perceived. The openings to these holes are watched and scrutinised for intruders in inbound traffic in species that live in cavities such as Apiscerana, Apis mellifera, and

Apisnigrocincta. Worker bees also execute "body shaking," a violent, pendulum-like sway of the abdomen, as a form of defence against colony intruders, especially wasps.

Although the collection and use of faeces in nest construction is well-known in stingless bees, a 2020 study of Apiscerana in Vietnam found that they use faeces and even human urine to defend their hives against raids by hornets (Vespa soror), a strategy not replicated by their European and North American counterparts.

Venom:

Honey bee stings are barbed, which helps them implant in the impact site. The sting gear also has its own musculature and ganglion, which continue to release poison even after it has detached. The gland responsible for the warning scent is also connected to the stinging device. Other defensive workers are drawn to the bite site as a result of the embedded stinger continuing to release warning pheromone after it has ripped free. After the venom becomes embedded and is later torn free from the bee's abdomen, the worker perishes. The poison of the honey bee, known as apitoxin, contains a number of active substances. Melittin is the most prevalent of these substances, and enzymes, especially phospholipase A2, are the most biologically active.

For its possible characteristics and applications in lowering the risks of adverse events from bee venom therapy, rheumatoid arthritis, and use as an immunotherapy for protection against allergies to bug bites, honey bee venom is being studied in the lab and in clinical settings. goods made from bee venom are sold internationally, but as of 2018, there are no clinical applications for these goods, which come with a variety of cautions about possible allergic responses.

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Cerebellar Ataxia

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Abstract

Ataxic symptoms are caused by a variety of illnesses affecting cerebellar function, known as cerebellar ataxias. The fundamental reasons of ataxia are likely to be discovered through a step-by-step diagnostic process that includes genetic research.New hereditary causes for ataxia have been discovered as a result of recent genetic discoveries, and the molecular pathways essential for healthy cerebellar function. This review article discusses the symptoms, diagnosis and treatment of the cerebellar ataxia.

Keyword: Cerebellar Ataxia, DNA, Neurological Disorder, Inherited

Introduction

Cerebellar ataxia is a lesion in cerebellum, may sudden onset or progressive brain degeneration. It may cause in-coordination muscles of limbs, trunk.It leads to imbalance, co-ordination loss, involuntary difficulties of swallowing (disphagia) difficulties of speech (dysarthia). commonly classical features ataxic gait - drunken walk. Algorithms for diagnosing Cerebellar ataxia based on clinical characteristics, imaging, and neurophysiologic and biochemical markers can be used to guide genetic testing for hereditary ataxias, with the development of next-generation DNA-sequencing technologies anticipated to improve diagnosis significantly[1].

Ataxia causes

Genetic disorders, Multiple disorders, Tumour, Stroke, Certain medications, Alchol, Stress/ fatigue, Head trauma, Some type of chemotherapy, Toxins- heavy metals (mercury, lead), Auto-immune disorders,Severe COVID-19, Cerebral palsy, Transient ischemic attack and (B12) Vit deficient[2].

Types of ataxias

- Acquired
- Inherited
- Sporadic
- Cerebellar ataxia- Disrupt the part of the brain
- Inherited
- Vestibular ataxia - Disrupt the sense of balance
- Sensory ataxia -Disrupt the self positioning[3]

Symptoms

Several neurological disorders, Incoordination movements of fine movements, Imbalance walking -ataxia gait,[4]Involuntary movement of eyeball, Bladder bowl incontinence, Dysphagia- difficulties of swallowing and dysarthia- blurring speech.

Diagnoses

Besides conducting physical exam, neurological examination,checking vision,checking balance including blood test (DNA gene Mutation). Genetic mutation ataxia Friedreich's Ataxia, Telangiectasia and Most Common Spinocerebellar Ataxia.

Bacterial infections[5], viral infections especially chicken pox, parasites infections and fungi infections lead to brain and spinal cord inflammations.Nerve end paining tickling. Depression, Most widely used for brain images, MRI scan -(magnetic resonance imaging), CT scan-(computerised tomography)[6]

Other tests

- Lumbar puncture
- Nerve conducting studies
- Electrocardiogram
- Echocardiogram
- Ultrasound scan of the heart
- Vitamins dificiency[7]

Treatment

Depending for adaptive devices, such as walker'scanes, physical therapy, occupational therapy was given to patient. To help in the daily living tasks and enhance mobility of the body[8].Speech therapy is improving speech and swallowing.Patient diagnosed with vitamin B12 deficient to treat with vitamin B12.

Genetic testing involves taking a sample of blood for analysis of DNA Mutation. Most common of genetic ataxia is spinocerebellar ataxia[9].Supportive treatments to control the symptoms including speech and swallowing problem. Episodic Ataxia iscontrolled by Acetazolamide. Maximum to avoid stress, caffeine and Alcohol. The breathing exercise strengthening the abdominal and chest muscles.

The Strengthening exercise of limbs - upper limb / lower limb.Oscillopsia - incoordination movement of eye ball leads to double vision, visual distribution, reading difficulties. The ocular exercise to be taught in these cases. Extreme tiredness leads to sleeping disturbance. Muscles problem of spasm painful, stiffness to be treated by muscle relaxant such as Baclofen, Trizanidine. (Botox) injection blocking relieve the brain and affected muscles.Urinary incontinence leads urgency of urine and frequent emptying the bladder.To teach the patient many self-care techniques and Animus Carnic (relaxant of urinary bladder)

Episodic Ataxia controlled by medication Acetazolamide and avoid trigger, stress, alcohol and caffeine. Damage of nerve ending neuro pathic pain starts burning sensation, shooting pain and tinkling.Ibuprofen and Paracetamol not effective for neurological pain, so Doctors prescribed Amitriptyline, Gabapentin, Pregabalin. Friedreich Ataxia, shortening life expecting is the most common cause of death.

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Diabetes mellitus and Infectious diseases

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Abstract

Individual with Diabetes mellitus is more prominent to infectious diseases than non diabetic. Immunity is lowered in patients with diabetes especially their humoral immunity and neutrophil content. All vital organs have been damaged by the attack of hyperglycemia. Neuropathy, retino pathy and angiopathy are some of the examples. Bacteria can grow in favor of hyperglycemic medium in body. Hospitalization of diabetic patients has been increased as compared to non diabetic individuals. It has proved that metformin has good impact on diabetes.It reduces blood glucose level to normal. Lack of exercise, imitating of western type diet are the main causes of diabetes. Older people are at high risk category for infection along with diabetes.

Key words: Diabetes Mellitus, infectious diseases, immunity, Non-communicable diseases.

Introduction

Diabetes is a complicated as well as economic burden disease to our whole Universe. It has estimated US spending around 612$ billion for diabetic care every year. It comes 11% for old age health care [(1)].One of the Canadian study showed that half of the hospital admission is due to diabetes associated

infection. Hypoglycemia and ketoacidosis are the other major complications of DM [2].

Pathophysiology of diabetes mellitus and infections

Role of Humoral Immunity

Bacteria and virus that enter through the respiratory tract and intestinal tract are defended by humoral immunity. Humoral immunity is mediated by antibodies. Plasma cells produceantibodies which are in turn produced by the B lymphocyte. In DM, mainly lymphocytes are reduced. And in this way primary and secondary immune response is lowered.

Cytokines

Immune response is regulated by small protein structures which act like hormones to regulate immune response. IL-1, IL-6 are the important cytokines participating in pathogenesis of DM[3].One of the recent studies showed in diabetic rats urinary excretion of IL6 is more prominent than non diabetic rat. And wet weight of renal of diabetic rat that is hyper trophy kidney can be seen in DM rats. Studies showed renal injury is directly proportional to excretion of IL6 cytokine. Diabetic glomerulopathy and diabetic nephropathy also correlated with IL6 [4].

TNF-α

TNF-α is a cytokine which produce inflammation, which is produced from endothelial cells, glomerular cells of kidney. TNF-α is present inside the cell as inactive form and TNF-α converting enzyme can convert into active form [5].

Most common respiratory diseases associated with diabetes mellitus

Diabetes Mellituspatients are more vulnerable to respiratory disease. The most common respiratory diseases are Influenza, tuberculosis, COVID-19. Pulmonary fibrosis can develop in individual with DM because of high glycation End products (AGEs), and high level of Reactive Oxygen Species (ROS)([6].Experimental evidence showing survival rate is less and viral load is more in diabetic mice. And studies also mentioned diabetic rats have increasedpulmonary cytokines [7].Epithelial junction complex in lungs can be damaged by pro inflammatory response. Severe hyperglycemic individual have glycemic variability, that is it glucose level can fluctuate very much after meals. In influenza, glycemic variability can lead to cell death and severe weight loss [8].It causes cardiovascular diseases in diabetic people. But when they are getting influenza vaccine their risk can be greatly reduced [9].

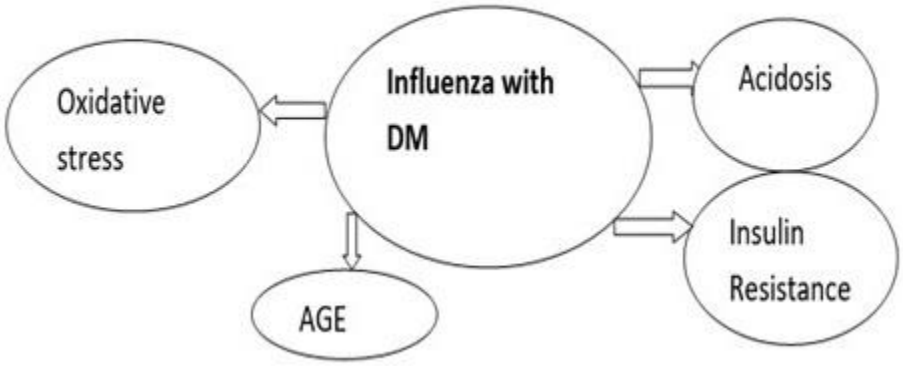

Fig 1: Influenza and Diabetic Mellitus

COVID 19 and diabetes mellitus

When SARS-CoV-2 enters in DM individual's body, virus can multiply in hyperglycemic medium. Cascading effect of virus action increases mortality rate. Thrombosis and endothelial dysfunction are the main effects of COVID - 19 in DM. Oxidative stress, pulmonary microvasular thrombosis and early endothelial dysfunction in DM individuals accelerate multiple organ failure in DM. Inflammatory markers such as D dimer, ferritin, procalcitonin are present in high amount in DM patients as compared to non DM patients[(10)]. Studies shows that hyperglycemia and hyperinsulinemia assist ACE2 formation different type of tissues, it acts as receptor for corona virus [(11)].

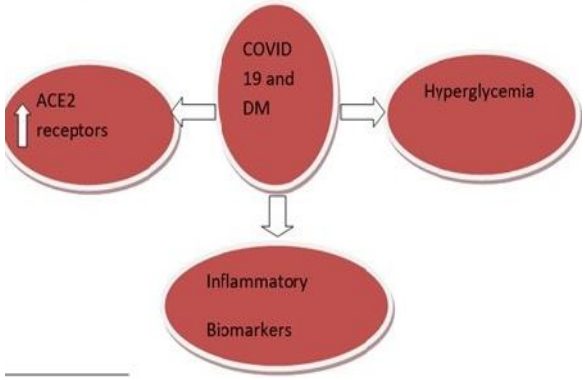

Fig 2: Covid 19 and Diabetes Mellitus

Conclusion

DM is a chronic complicated disease with hyperinsulenimia and hyperglycemia. When beta cells of islets of Langerhans do not produce orinsulin does not enter into cells, glucose level rise in blood. This in turn activates entry of microbes into host through respiratory tract, urinogenital tract. Controlled HbA1c and improved lifestyle with nutritive food can improve the life of diabetic patients with fewer recurrences of infections.

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Pediatric ECMO

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Introduction

Extracorporeal membrane oxygenation (ECMO) is a term used to describe short or long term cardiac and/ or pulmonary support in neonates, children & adults.

Its use is increasing worldwide due to favorable result and the continuous reduction of absolute contraindications.

Indicators in children are different from those in adults. The ECMO circuit, and intubation strategy are also individualized.

ECMO – Definiton

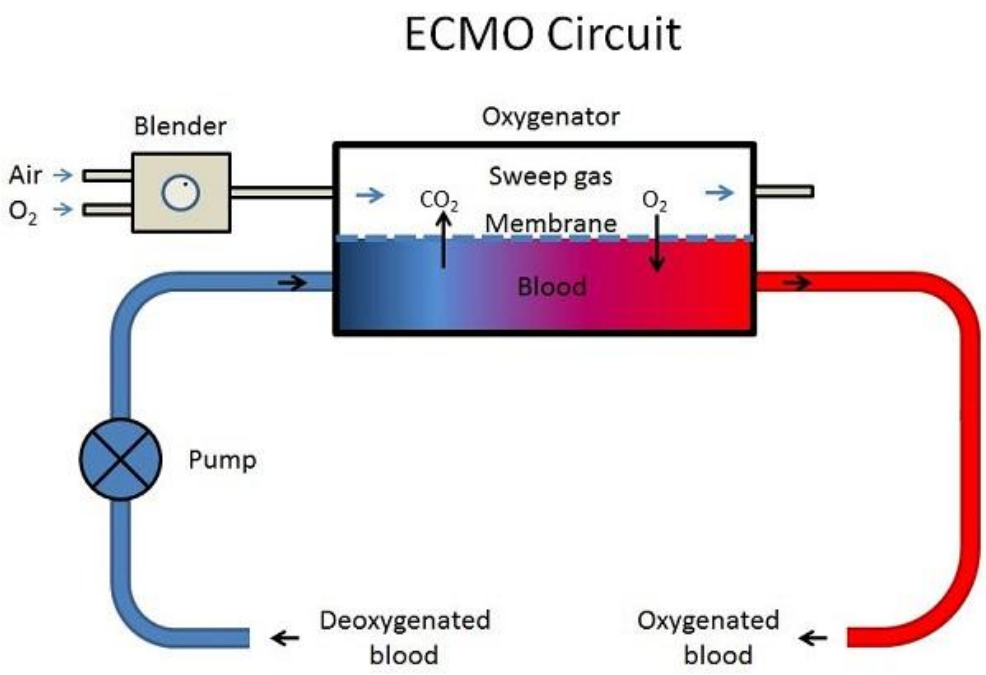
Is a form of extracorporeal life support where an external artificial circuit carries venous blood from the patient to a gas exchange device (oxygenator) where the blood becomes enriched with oxygen and has carbon dioxide removed.

ECMO – Modes

ECMO mode is determined by the placement of access and return cannulas, there are three types of ECMO;

1. VENO-VENOUS ECMO: venous blood is aspirated and pumped through the vena cava. It returns to the venous system near the right atrium. Support for severe respiratory failure in which blood circulation is completely controlled by the heart's natural function.
2. VENO-ARTERIAL ECMO: venous blood is accessed from the large central veins and pumped through the oxygenator and is returned to the systemic arterial system. Support for severe cardiac failure.
3. VENO- pulmonary ECMO: Venous blood is pumped from the vena cava through oxygenator and returned to pulmonary arterial system. Support for ventricular and respiratory support.

ECMO Circuit:



Points to be remembered to compose an ecmo circuit:

- Circuit should simple and portable
- Consider the proper size and length of tubing and oxygenator required.
- Minimize the diameters, connectors, 3way stop clocks, inline probe.
- Secure all the non- sealed connections.
- Sufficient access ports (priming, blood sampling, hemofilter, pressure monitoring)

Common indications for pediatric ECMO:

Indication	Neonate	Pediatric
Cardiac	Congenital Defect i. Hypoplastic left heart syndrome ii. Left ventricle outflow obstruction iii. Right ventricular outflow obstruction iv. Septal defects Cardiomyopathy (bridge to recovery, transplant or long term MCS) Myocarditis	Congenital Defect i. Left ventricular outflow obstruction ii. Right ventricular outflow obstruction iii. Septal defect Cardiomyopathy (bridge to recovery, transplant or long term MCS) Myocarditis
Respiratory	i. Meconium aspiration syndrome ii. Persistent pulmonary hypertension of newborn/ persistent fetal circulation iii. Respiratory distress syndrome iv. Congenital diaphragmatic hernia v. Pneumonia(viral/bacteria/aspiration) vi. Sepsis	Pneumonia(viral/bacterial/aspiration) Acute respiratory distress syndrome

Contraindications of pediatric ECMO:

As the number of absolute contraindications to ECMO decrease, more and more patients are being evaluated for candidacy on a case by case basis. Nevertheless, the most current contraindications are generally futile cases with high rates morbidity and mortality.

Absolute	Relative
⁾ Lethal chromosomal abnormalities(eg;trisomy13,18) ⁾ Severe neurologic compromises(eg;irreversible brain damage, ischemic encephalopathy) ⁾ Uncontrollable bleeding ⁾ Incurable malignancy ⁾ Prematurity<30 weeks gestation ⁾ Low birth weight <1kg	⁾ Duration > 2 weeks of mechanical ventilation before ECMO ⁾ Recent neurosurgical procedures <7days

Cannulation:

Access to cannulas of various size is essential in the case of pediatric. Cannula design should maximize blood flow for a given diameter without compromising cannula strength and function due to cannula walls that are too thin or too weak. Wire reinforcement is beneficial and may reduce the risk of cannula collapse and/or kinking. It is important to recognize Poiseuille's law, which states that the flow rate of a fluid through a pipe is proportional to the fourth power of the pressure divided by the length, but it is important to remember that the reduction is often small.

Choosing the right cannula is critical to ECMO success and must be chosen carefully for each patient. There must be sufficient blood flow, and returns is also important. Cannula selection is dictated not only by the level of support expected, but also by vessel size and condition, patient size, possible placement, type of insertion procedure, and desired site of return.

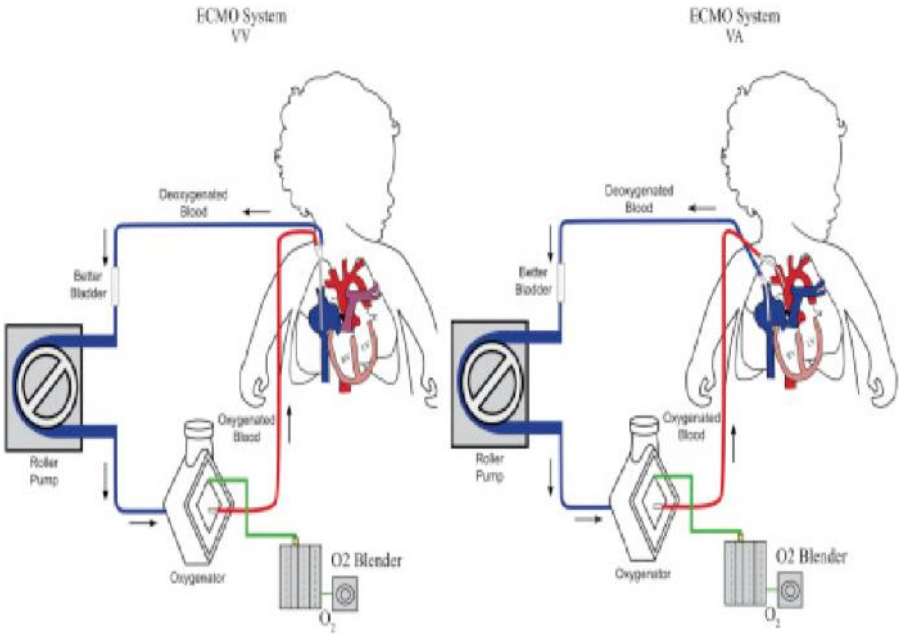
When you simply insert the largest possible cannula into the vessel. Larger cannulas tend to damage vessels or cause venous occlusion, and if the cannula is not extended to a large blood reservoir such as the right atrium, the proximity of the venous wall may block the side drain hole of the cannula; obstruction of the lateral port can lead to intermittent drainage with associated pressure fluctuations and increases the risk of hemolytic complications.

A guide to the required cannula size is provided below;

Patient size (KG)	Arterial cannula(FR)	Venous cannula (FR)
2	8	8-10
3-6	10	10-12
6-8	12	14
8-16	14	17
16-30	17	19
30-40	17	21
>40	21	25

Sites for cannulation:

For most neonates, common site for cannulation is central access.Alternatives; right jugular access, abdominal IVC, peripheral access in certain conditions.



Tubing:

Size: for patients weighing less than 10-15kg use ¼ inch tubing. Patients over 15kg use 3/8 inch tubing's.

Surface coating: add pre coating or surface modification

Adsorption of plasma proteins on biomaterial surfaces leads to platelet adhesion/ activation and thrombin activation, leading to clot formation. Other coatings exist because the perfect biocompatible surfaces have yet to be discovered.

25% albumin may be added and administered. Crystalloid priming circuits with heparin coatings and additions.

Membrane oxygenator:

ECMO oxygenators, in most models are designed to deliver oxygen, remove carbon dioxide and warm the blood. The most commonly used membranes are made up of POLYMETHYLPENTENE (PMP). Modern oxygenators are characterized by low resistance to blood flow, low fill volume, easy ventilation and rarely plasma leakage. Typical volume range from 80ml for small neonatal pediatric oxygenators.Duration of use: 15-21 days approx.

Blood pump for ECMO:

Blood pumps regulate the blood flow needed by the patient. Different models are available. There are roller pumps and centrifugal pumps, of which centrifugal pumps are currently the most widely used.

ROLLER PUMP; to prevent excessive suction from the drainage catheter, suction directly from the pump inlet where the reservoir may be restricted by the pump control. The tubing's may be worn out or broken at the pump head.

CENTRIFUGAL PUMP; these are electro magnetically driven pump with shaft control that generates negative suction which drains the blood. All the centrifugal pumps have a dedicated control panel to control pump operation, and each pump has specific monitoring and safety features.

Management of pediatric ECMO:

1. ECMO Flows;

Flow between 100-150 ml/kg/min. The arterial line pressure of less than 200 mmHg is of accepted value.

2.Ventilator management;

- Fractional inspired oxygen of 40%
- Tidal volume of 6-8 ml/kg
- Respiratory rate of 20 bpm.
- Positive and expiratory pressure of 6-8 cm H2O

3. Coagulation management;

- Activate clotting time : 180-200 sec.
- Activated partial thromboplastintime : 50-70 sec.
- Prothrombin time of 18-24 sec.
- An INR OF 1.5-2.0
- Platelet count more than 50000/ microliter.

4. Inotrope support;

- Dopamine
- Dobutamine
- Millirinone
- Adrenaline
- Noradranaline

5. Ivestigations;

- Echocardiogram
- Chest x-ray
- Daily blood investigations.

6. Other monitoring;

- Heart rate
- Mean arterial pressure
- Oxygen saturation
- Urine output
- Temperature
- Arterial blood gas
- NIRS
- Abdominal girth
- Peripheral pulse
- Amount of hemofilteration.

Weaning from ECMO:

The following checklist for successful weaning;

- Stable heart rate and rhythm
- Hemodynamically stable optimal.
- No active bleeding
- Arterial blood gases within acceptable limits
- Lactate less than 4.0 mmol/L
- Chest X-ray normal
- Normal breath sounds with minimal added sounds and no evidence of lower respiratory tract infection.
- Hematocrit between 30-35%
- No end organ dysfunction.

Complications of ECMO:

1. The most common complication is bleeding, this is often due to heparin anticoagulation therapy, most severe site of bleeding is the brain. Cerebral hemorrhage can cause brain damage. Surgical procedures to insert cannula into the neck or groin require anchoring a vein or an artery.
2. The risk of infection increases whenever a cannula is inserted.
3. Clots or thrombus formed can travel from ECMO circuit into the blood stream.

4. Heparin induced thrombocytopenia.
5. Neurological complications like seizures,

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Antidiabetic potential of Indian medicinal plants- A review

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Abstract

Diabetes mellitus is one of the greatest health problems in the world and is associated with higher prevalence and mortality.Plants have long been revered as excellent sources of medicine. The use of plants to heal various illnesses was documented in Ayurveda and other Indian literature. Nowadays Herbal sources are focused for the treatment and management of diabetes mellitus due its active phytoconstituents which leads to discovery new antidiabetic agent.

Keywords: Diabetes mellitus, medicinal plants, antidiabetic, hypoglycemic.

Introduction

Diabetes mellitus (DM) is a severe, persistent and complex metabolic condition with severe short- and long-term consequences[1]. It is a major threat to human health, according to estimates from the World Health Organization (WHO), there are around 70 million individuals suffering from diabetes mellitus in developing nations, where the prevalence of diabetes is rising[2].In

India, it is reported that 25 million are prediabetics (with an increased risk of developing the disease in the near future)[3]. Diabetes is typically categorized into four categories: type 1 diabetes (T1DM), type 2 diabetes (T2DM), gestational diabetes mellitus (GDM), and specific types of diabetes[4].

Type 1 diabetes is characterized by autoimmune destruction of beta cells. People with type1 diabetes are prone to ketoacidosis and they require daily insulin to control the blood glucose[5]. Type 2 diabetes mellitus, one of the most common metabolic diseases, is caused by a combination of two main factors, such as impaired insulin secretion by pancreatic β cells and the inability of insulin-sensitive tissues to respond adequately to insulin[6]. Gestational diabetes mellitus is defined as the condition of hyperglycemia that was first recognized during pregnancy and is the most common clinical complication in pregnancy. It affects about 15% of pregnancies worldwide and accounts for about 18million livebirths annually[7].

Management of diabetes is complex and multidisciplinary. However, the early diagnosis is paramount to achieve all goals set in diabetes management. Nutritional management and exercise are key pillars of care and are essential in the management of type 2 diabetes, and both may be appropriate for achieving and maintaining normolipidemic and normoglycemic treatment goals[8].There are several classes of oral hypoglycemic drugs that can cause anti-diabetic effects through various mechanisms such as sulfonylureas, biguanides, thiazolidinediones, α-glucosidase inhibitors, and non-sulfonylureas secretagogues[9,10].Although synthetic oral hypoglycemic agents along with insulin are the primary way to control diabetes, they cannot completely reverse the course of complications and worsen the disease due to severe side effects. This forms the main force for finding alternative sources of antidiabetic agents[11].

Medicinal plants have great potential in treating various conditions due to the presence of important phytochemicals[12]. Traditional herbs have a significant anti-diabetic property without any harmful side effects. They are rich sources of active phytoconstituents such as flavonoids, alkaloids, phenolic and tannins that helps to improve the efficiency of pancreatic tissues by raising the insulin secretion or decreasing the intestinal glucose absorption[13].Easy availability, low cost and low side effects make plant-based products a key player in all available treatments, especially in rural areas[14].

Medicinal Plants with Antidiabetic Activity

Several plant species with hypoglycemic activity are available in the literature. Most of these plants contain bioactive compounds such as glycosides, alkaloids, terpenoids, flavonoids and carotenoids that have a history of being linked to antidiabetic effects.

Psidium gujava

Psidium guajava L. is a small pantropical tree, the leaves and bark of this species are also widely used in traditional medicine. The ethanolic leaf extract of *Psidium gujava* (300 mg/kg of b.wt) for 30 days were evaluated in Streptozotocin-induced diabetic albino rats. The results of this study showed that the administration of *Psidium gujava* leaf extract restored the levels of glucose, insulin, glycosylated hemoglobin, and hemoglobin to near normal levels. It also improved the activity of key enzymes involved in the metabolism of glucose and glycogen[15].

In another study the antidiabetic effect of aqueous extract of *Psidium gujava* (400 mg/kg body weight)were evaluated in Streptozotocin induced diabetic Sprague-Dawley rats. The result of the study showed significant reduction of blood glucose, glycogen Phosphorylase expression and also increased the activity glycogen synthase enzyme in diabetic animals[16].

Scrophularia striata

Scrophularia striata is an important traditional herbal medicine. It has various medicinal property including antitumor, hepatic protective and anti-inflammatory, analgesic and antimicrobial activity. The effect of ethanolic leaf extract of *Scrophularia striata* (100, 200 and 400 mg/kg of b.wt) was investigated in STZ -induced diabetic rats for 4 weeks. The treatment significantly decreased the blood glucose, glycosylated hemoglobin and increased blood insulin level. The histopathological result of pancreas also indicates the effectiveness of plant extract[17].Moreover, the ethanolic extract of *Scrophularia striata* (100 and 200 mg/kg of b.wt) attenuates oxidative stressmarkersandfasting blood glucose (FBG), lipid profile, creatinine, urea in streptozotocin induced diabetic rats[18].

Mimosa pudica

The ethanolic leaf extract of *Mimosa pudica* demonstrated dose-dependent antidiabetic efficacy in high-fat diet- and STZ-induced diabetic rats.The treatment (100,200,300and 400 mg/kg of b. wt) significantly altered the level of glucose, glycosylated hemoglobin, lipid profile and insulin. The

extract was effective at the dosage of 300mg against the streptozotocin induced type 2 diabetes[19].Oral administration of methanolic extract of *Mimosa pudica (*125, 250 and 500 mg/kg body weight) was evaluated on streptozotocin-induced diabetes mellitus in Sprague-Dawley rats. The results of this study showed the significant decrease in the levels of glucose, Triglycerides,LDL, and VLDL[20].

Achyranthes rubrofusca

The hypoglycemic effect of aqueous and ethanolic extracts of *Achyranthes rubrofusca* leaves (200 mg/kg of b.wt) was investigated in alloxan-induced diabetes. The decreased blood glucose level and increased pancreatic antioxidant enzymeswere reported in aqueous and ethanolic extract treated groups[21].

Stevia rebaudiana

The preliminary phytochemical and antidiabetic activity of crude extract of *Stevia rebaudiana* was evaluated. In that study, different solvent used for the extraction of plant leaves such as ethanol, methanol and aqueous solution. The result of the study showed that the presence of the phytoconstituents like alkaloids, phenolic compound, flavonoids and saponins. The stevia leaves extract reduced the blood glucose level in diabetic rats[22]. Same result reported by Chang et al[23].

Piper longum

The aqueous root extracts of *Piper longum* was tested in in STZ induced diabetic rats. The oral administration of root extract 200 mg/kg in albino rats showed a significant reduction of blood glucose and it restored the lipid parameters to near normal. Since there is a significant decrease in the activity of liver and kidney function markers in treated diabetic mice compared to untreated diabetic rats, the extract has a protective effect against the liver and kidney damage.Therefore, the plant extract is beneficial in the management of diabetes mellitus[24].

Table:1. Plant Extract with antidiabetic activity

Species	Extract	Part of the Plant	Dosage mg/Kg	Induction of Diabetes	Result	References
Anacardium occidentali	Ethanol	Leaves	100	Streptozotocin (STZ)	Decreased blood glucose level and decreased fasting Insulin resistance (FIRI).	[25]
Sesbania sesban(L) Merr	Distilled Water	Leaves	250 and 500	STZ	Reduced blood glucose and glycosylated hemoglobin. Increased serum Insulin level and liver glycogen	[26]
Solanum torvum	Ethanol	Fruit	120,160, 200	STZ	Blood Glucose, Cholesterol, Triglycerides, LDL, SGOT, SGPT were significantly decreased and HDL were increased in treated (200 mg/kg)animals.	[27]
Choloroxylon Swietenia	Methanol	Bark	250	STZ	Moderate reduction in blood glucose and glycosylated hemoglobin levels, plasma insulin and hemoglobin levels were elevated.	[28]
Cestrum nocturnum	Hydroalcoholic Extract	Leaves	200 and 400	STZ	Blood glucose levels in diabetic rats was decreased.	[29]
Merremiaem aginata Burm .F	Methanol	Whole Plant	100 200 400	STZ	A significant reduction in blood glucose, serum urea and creatinine and significant increase in body weight, insulin and protein level.	[30]

Spondiasmombin (MESM)	Methanol	Leaves	125,250, 500	STZ	significantly altered the elevated levels of glucose, reduced aspartate Transaminase (AST), alanine transaminase (ALT), alkaline phosphatase, total bilirubin, urea, creatinine, total cholesterol (TC), serum triglyceride (TG), low-density lipoprotein (LDL), Very low-density lipoprotein (VLDL), and increased plasma insulin, total protein,	[31]
Choloroxyon swietnia	Aqueous Ethanol	Leaves	200 and 400	STZ	Significant decrease in glucose, AST, ALTand ALP	[32]
Aloe megalacantha Baker (Aloaceae)	Methanol	Leaf Latex	100,200, 400	STZ	The extract significantly reduced the level of glucose, Total Cholesterol, and Triglycerides and increased HDL.	[33]
Zizyphusmauritiana	Petroleum Ether, Ethanol, Chloroform, Acetone Water	Fruit	400, 200	Alloxan	Petroleum ether extract and aqueous extract restored the level of glucose, urea, creatinine, serum cholesterol and serum triglyceride to near normal level.	[34]

Melia azedarach *Zanthoxylum alatum* *Tanacetum nubigenum*	Ethanol	Twings Leaves Leaves	60 100 60 60	STZ	The ethanolic extract of *Melia azedarach* and *Tanacetum nubigenum* significantly reduced the blood glucose level.	[35]
Punica granatum	Methanol	Leaves	100,200, 400,600	Nicotinami-de/STZ	The leaf extracts significantly alter the glucose, insulin, antioxidant markers and liver marker enzymes.	[36]
Piper longum	Hexane, Ethyl Acetate, Methanol And Aqueous Extracts	Root	200	STZ	Significantly decreases the blood glucose level and liver and renal functional markers.	[37]
P.macrocarpa	Ethanol	Fruit	50,100, 200	STZ	Administration of *P.macrocarpa* at concentration of 100 and 200 gm/kg showed hypoglycemic effect.	[38]
Becium grandiflorum Lam	Hydro-ethanol	Leaves	200,400, 600	STZ	Reduced blood glucose and improved the glucose tolerance in treated animals.	[39]

Conclusion

Medicinal plants have vast potential in treating various diseases due to the presence of important bioactive compounds. Herbs may serve as more efficient, safer and cheaper adjunctive therapies in the management of diabetes. The actions of these herbs can delay the development of diabetes complications and correct metabolic abnormalities. WHO notes that prevention of diabetes and its complications is not only a major challenge for the future, but is essential to achieving good health for all.

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Mycoremediation – A step towards sustainability

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Introduction

Safeguarding environment is a major concern of this era. The rising population, rapid rate of industrialization and urbanization are exacerbating the pollution- related problems. Soil and water pollution affect human health and environment. Understanding of ecological problems influenced by waste of industries has forced many countries to frontier the expulsion of noxious outcomes.

The overall environment is undergoing through vast trauma due to the development of many industries and urbanization as well as increase in population with limited natural resources. The ecological troubles are miscellaneous and occasionally precise with indication to space and time. Environmental problems can be describe as following (waste coming from industries, sewage drainage, effluents, agricultural waste, waste matter from kitchen and wastage of peels of food) and utilize some chemicals for different purpose in the variety of chemical fertilizers, pesticides, insecticides, noxious stuff from industries. Noxious chemicals from environment like halogens, polychlorinated biphenyls (PCBs) and some other inorganic & organic contaminants which may get to the soil, air and water and have an effect on the environment in many conduct and is eventually aggressive (Sen*et al.*, 2009) (Prasad *et al.*, 2010) (Davies *et al.*, 2006).

The underground water is increasingly becoming contaminated due to water contaminants coming from industries. Some substances may get contact with surroundings in a low proportion and get conducted to food chain, biomagnification or bioaccumulation have freshly detect contaminants, dichlorodiphenyltrichloroethane (DDTs), polychlorinated biphenyls (PCBs), and their byproducts, metabolites and some other contaminants. The nature of environmental problems give new challenges and approach to every technique applied to overcome the problems. Microbiology and Biotechnology gives hope for the care of environmental protection (Azadi., 2010) (Hatti-Kaul *et al.*,

2007). Several techniques like bioremediation are one of the fine applications of biotechnology there are numerous that are in a round about way helpful for pollution avoidance, waste treatment and ecological remediation (Sen*et al.,* 2009).

Environmental preservation is one of the key strategies addressing sustainable development. An awareness of environmental problems and potential hazards caused by industrial waste waters has prompted many countries to limit the discharge of toxic effluents. There are three ways through which contaminated sites can be dealt; first the trouble should be recognized than the character of contaminant and finally the choice for finest techniques according to the contaminant. The desire to remediate sites of contamination leading anew technologies, efficiently degradation of the contaminants (Busca *et al.,* 2008) (Whiteley *et al.,* 2006).

Fungi can easily colonize and degrade large varieties of waste e.g. waste paper, saw dust, wood chips, bagasse, black liquor of pulp and paper industrial effluents etc.. Fungi utilize some of these hazardous compounds as nutrients source and degrade or fragmenting the pollutants into non-toxic simpler forms. The aim of the chapter is to address or develop a suitable low cost biologically or environmental friendly method for bioremediation of industrial effluent has capacity of efficient biodegradation of organic and inorganic pollutants. Mycoremediation play an important role in the treatment of effluents containing numerous toxic substances like hydrocarbons, polychlorinated compounds, heavy metals, phenolic derivaties and high concentration of lignin and cellulosic materials.

This chapter is committed to the most noticeable concern of the contemporary world, that is, the severely escalating contamination of the land and water with a special emphasis on the emerging and novel approach of using the fungi for the remediation and rejuvenation of the land and water resources. The use of biological agents in the remediation of the contaminants is very recent in scientific world and has attained a pace of promising strategy. The emerging bioremediation technique using fungi is commonly introduced as the mycoremediation in the scientific literature. Mycoremediation plays an important part in dealing of these hazardous possessing many different noxious material like hydrocarbons, phenolic derivatives etc. Fungus consumes various noxious compounds as their source of nutrition and converts complex matter into simpler ones. In order to eliminate toxic heavy metals and other toxic compounds from soil, this technique used as an addition to treat industrial

waste, the technique mycoremediation, is promising as possible approach for less expensive technique to remove contaminants from soil.

Bioremediation and its characteristics

The term Bioremediation indicates the technique used to degrade and manage wastes, it involves a use of cultivated microorganisms chosen for their capability to metabolite the particular pollutant. The technique of bioremediation has been broadly used for decontamination of surface soil, marine systems as well as fresh water and ground water and contaminated land ecosystems. The techniques of remediation were developed to treat contamination caused by petroleum hydrocarbons that alter these hydrocarbons to chemical substances that are not hazardous for environment and bioremediation of soil may be enhanced by fertilizing or seeding with suitable microbes. This process is known as improved bioremediation. Intrinsic bioremediation, which utilizes already accessible microbes at the working site is more costly method for decontamination of land.

Even in the most contaminated soil, naturally present microbes are enough to do activity to clean the soil. Once the soil has been seeded with some factors like oxygen content, controlled temperature and water. They can be used to speed up the process of removing contamination. Generally, process of treatment relies from 2 to 48 months. Three primary ingredients for bioremediation are 1) presence of a contaminant, 2) an electron acceptor and 3) presence of microorganisms that are capable of degrading the specific contaminant. Two different strategies of bioremediation are utilized to remediate toxic pollutants, in-situ, where the process of decontamination occurred at the contaminated place itself by bringing the biological agent to the site of contamination or promoting the indigenous organisms to deal with contaminants by facilitating the suitable condition for their propagation. The second one is ex – situ, by which the contaminated place is transferred away to another site to be processes (Kumar *et al.*, 2011; Raghunandan *et al*., 2014, 2018).

There are many mechanisms by which the organisms can manipulate the detoxification process, however the utilization of toxic metal by the microorganism as a source of nutrition is the main concept (Sun *et al.,* 2020). So, microbial bioremediationis considered a multidisciplinary field that gained more research andinvestigations. Most microorganisms follow two common mechanisms in the bioremediation process; metal sequestering or immobilization and enhancement of solubility properties of the metals and reduce the heavy metals to a less toxic form (Donald 2013).

Methods of bioremediation

Bioremediation can be followed by these three methods such asMycoremediation, Phytoremediation and Bacterial bioremediation.

Mycoremediation

The use of fungi for the removal of organic contaminants from the land and water. To make the contaminants less toxic and non-hazardous, the fungus exploit the certain enzymes and acids in this method as this is one of the current method for the removal and decomposition of contaminants**(**Barry *et al.*,1994).

Mycoremediation is a form of bioremediation in which fungi based remediation methods are used to decontaminate the environment (Kulshreshtha*et al.*, 2010). Fungi have proven to be a cheap, effective and environmentally sound way for removing a wide array of contaminants from damaged environments or wastewater. This technique also helps in removal of heavy compounds from the land and surroundings by fruiting bodies of fungi (Leitao., 2009).

Fungi have all the naturally active components for the breakdown of contaminant material and they are an essential part of the soil food chain. Forest floor is expanded with the litter of leaves by the action of season which are not useful for the plants and do not let the other plants to grow on that litter filled floor. These leaf litters are difficult to break or to be digest, any diet they consume are sheltered in them. An important agent for converting this leaf litter is fungi. Mycelium which is a vegetative part of fungus have white threads that decay dead woods etc (Rhodes., 2012).

Certainly fungi are the single creature by God that decay wood. Certain acids and enzymes excreted by mycelium that have ability to degrade cellulose and lignin. A material known as humus is released by the breakdown of wood and leaves (Rhodes., 2013). There are many studies in the world of science demonstrated that various species of fungus are capable to help in detoxifying various pollutants present in the environment including heavy metals, pesticides, effluents. To attain a victorious mycoremediation the right species of fungi must be selected to remove particular pollutant, from which an easy process of screening has been assessed. Laboratory studies show that fungal mycelial networks of all fungi may modify the molecular composition and structures of soil pollutants and other nutrient sources. During their metabolic breakdown they excrete certain toxins, providing a suitable output to facilitate

their withdrawal from the affected areas at sensible levels of natural economy and with the smallest amount of effects on the surrounding.

Phytoremediation

The removal of pollution from soil, water and air the plants has been used for this process. The contaminants such as complex organic and inorganic compounds such as metals, sewage, leachates, sludge, salts and xenobiotic has been removed through this process.

Bacterial bioremediation

Environment contamination such as oil spills, mine waste and human waste can be clean up by natural metabolic processes of bacterial activity and bacteria is make in use for this particular methods.

Categories of fungal remediation

Remediation by fungi is categorized into several types. They are lignolytic fungal degradation, soil fungal biosorption. Lignolytic fungal degradation is the most broadly affected fungi in degradation and decoolorization of dye. Lignolytic fungi belongs to basidiomycetes class. White rot fungi such as *Phanerochaete chrysosporium* produces manganese peroxidise (MnP), lignin peroxidise (LiP) and laccases which are the primary agents in degradation of many aromatic compounds.

Soil fungal biosorption is carried out by filamentous fungi such as *Penicillium, Aspergillus, Trichoderma, Rhizopus, Mucor* and *Fusarium.* These fungi can absorb heavy metals from aqueous solutions. The sorption of heavy metals C, Zn, Cd, Pb, Fe, Ni, Ag, Th, Ra and U by fungal biomass has been observed to varying extents.

Mycorrhizal fungal biomerediation is carried out by Arbuscular mycorrhizal fungi (AMF). AMF may be beneficial for PAH rhizodegradation because they affect root exudation and root associated microbial populations and because, in some ways, they act as an extension of the roots outside the rhizosphere.

Role of mushrooms in mycoremediation

Fungi and mushroom has been used for the elimination of waste from the environment. Mushrooms and other fungi release enzymes which decompose large quantity of waste. Mushrooms have fruiting body or mycelium as a way of protein. The mushrooms and other fungi possess enzymatic machinery for the degradation of pollutants and can be applied for a

wide variety of pollutants (Purnomo*et al.,* 2013; Kulshreshtha*et al.*,2013). However mushrooms, fungi belonging to basidiomycetes are becoming more famous nowadays for remediation purposes because it is not only a bioremediation tool but also provide mycelium or fruiting bodies as a source of protein. Fungi break down most contaminants into non-toxic by-products but just act like dynamic accumulators with heavy metals. Oyster mushrooms are also great absorbers of mercury and cadmium. Their mycelium channels mercury from the ground up into the mushroom itself.

Enzymes from fungal mycelia are able to cleave certain atoms like chloride of large molecules, and then break the bond between hydrogen and carbon. Recently, it is reported that mushroom species are able to degrade polymers such as plastic (da Luz *et al.,* 2013).The biodegradation mechanism is very complex. The reason is the influence of other biochemical systems and interactions of lignolytic enzymes with cytochrome P450 monooxygenase system, hydroxyl radicals and the level of H_2O_2 which are produced by the mushroom. Other than mushrooms, certain fungi have also proven useful in remediation of heavy metals, such as lead and cadmium. These metals are aleady at their simplest state and not degraded further; fungi can extract them from soil or water and accumulate them in their tissues. Mushroomfruit bodies attracted innumerable flies and insect and the previously contaminated soil become its own life sustaining habitat.

Pros of mycoremediation

Safe in use

Mycoremediation is safer than other techniques of remediation since it does not require the process of digging and disposing.No machinery is requiredtherefore it is an easy method and safer than othertechnologies. Results are not harmful therefore humans and animals are not affected. Moreover this technique does not produce secondary waste streams therefore no extra cleanup required.

Cost effective

This is an obvious advantage of Mycoremediation. It is a low cost technique as compare to other bioremediation techniques. As fungi will expand within the soil with its own reproducing ability in a short time. No other expenses are needed to start the process of mycoremediation. A small portion of fungus or fungal spores only can be helpful to remediate the entire contaminated surface.

Reusable products

Mycoremediation technique converts thetoxic compounds to non-toxic one therefore theseproducts are not harmful to humans and animalsif reuses them. It is an eco friendly process of treating wastes/pollutants.

Quick results

Mycormediationprocess give faster results than other process of bioremediation. The results are observed by mitigation of odour and focusing on improvement at the site of performance.

Cons of mycoremediation

Not approved

Organization that presently wants to use the skills are finding it a tough because this technology is still unproven and most often people wants to use authentic technologies.

Relevancy

There are multiple approaches for the removal or recycling; and certain are appropriate in specificconditions e.g. multiple approaches are there for residue remediation that describe for building of factories that twist the impure sediments and incineration plants or into helpful things such as tiles, gas etc.

Efficiency

Bio systems are in no way 100 percent capablethat is hard for user to recognize and to decidethe method according to their requirement**.**

Surrounding environment

The utilization of ordinary scheme can rush into troubles with the aggressive atmosphere in various areas or among often efficiency in intense habitat.

Conclusion

Mycoremediation has develop into a centre of attraction, green and hopeful remediation of pollted sites as it is able to degrade specific contaminants without damaging the habitat of that environment. Conversely, the techniqw of bioremediation have several restricted applications and the less potential of biodegradation. The aim of this chapter is just to approach the advance technology to reduce the pollution. To summarize, mycoremediation techniques are in ongoing to expand the production and scientific work that

gives the basis to assess the framework of technology and at the same time in explanation and mitigating the valid reasons by which scientists use these techniques for the well-being and beneficiary of a community.

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Current update on stem cell research – A new era life saving therapy

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Abstract

In recent years, stem cell therapy has become a very auspicious and advanced scientific research topic. It only established therapy using stem cells. It plays a vital role in regenerative medicine. The ability to directionally differentiate into somatic cells allows stem cells to play an essential role in disease modelsdrug screeningcell developmentand cell Patient tissue-derived iPSCs which are then differentiated into cardiac, neural, endothelial, and other cells, are widely used in disease modelling. Using patient-derived iPSCs, many genetic diseases, such as long QT syndrome Bragada syndrome hypertrophic cardiomyopathy However, some diseases are not genetically inherited and such diseases-derived iPSCs are likely to be non-phenotype observed. In this review we focused on various clinical applications of Stem cell therapy.

Keywords: Stem Cells, Type of Stem Cells, Stem Cell Therapy Differentiation Between Totipotent, Pluripotent, Multipotent and Oligopotent

Introduction

In multicellular organisms, stem cells are undifferentiated or partially differentiated cells that can differentiate into various types of cells and proliferate indefinitely to produce more of the same stem cell. The ability to directionally differentiate into somatic cells allows stem cells to play an essential role in disease modelsdrug screeningcell developmentand cell Patient tissue-derived iPSCs which are then differentiated into cardiac, neural, endothelial, and other cells, are widely used in disease modelling. Using patient-derived iPSCs, many genetic diseases, such as long QT syndrome Bragada syndrome hypertrophic cardiomyopathy However, some diseases are not genetically inherited and such diseases-derived iPSCs are likely to be non-phenotype observed, in future stem cell therapy will open a new era for treatment of various diseases[1].

Human pluripotent stem cells (hPSCs), including human embryonic stem cells (hESCs) and the closely related human induced pluripotent stem cells (iPSCs), are characterized by self-renewal and can differentiate into a huge number of different functional cell types via directed differentiation[2].

Embryonic Stem Cells (ESCs)

During days 3-5 following fertilization and before implantation, the embryo (at this stage, called a blastocyst), contains an inner cell mass that can generate all the specialized tissues that make up the human body. ESCs are derived from the inner cell mass of an embryo that has been fertilized in vitro conduction[3].Embryonic stem cells (ESCs) have a unique property of capable of self-renewal and multi-directional differentiation. The factors regulating self-renewal of ESCs includes signalling pathway proteins, transcription factors, epigenetic regulators, cytokines, and small molecular compounds, and non-coding RNAs, small RNAs, and microRNAs (miRNAs) also play the vital role in the process. The set of core transcription factors, primarily Sox2, Oct4, and Nanog regulates the pluripotency and differentiation states of embryonic stem cells (ESCs)[4].

Induced Pluripotent Stem Cells (iPSCs)

Induced pluripotent stem cells are stem cells that are created in the laboratory, a happy medium between adult stem cells and embryonic stem cells. iPSCs are created through the introduction of embryonic genes into a somatic cell that causes it to revert to a “stem cell-like” state. These cells, like ESCs, are considered pluripotent Discovered in 2007, this method of genetic reprogramming to create embryonic cells[5].

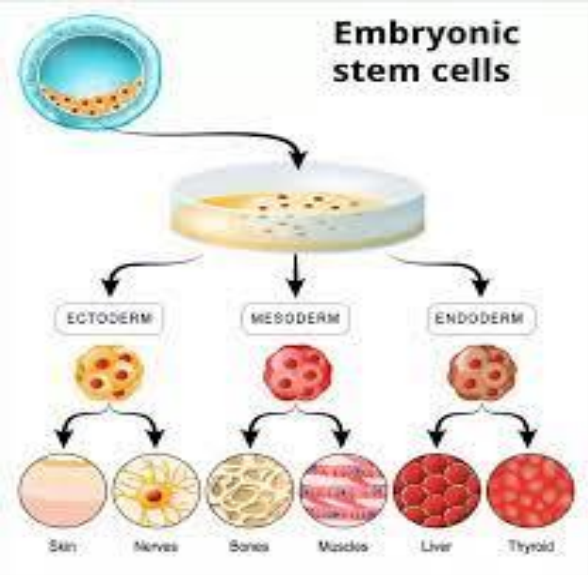

Figure: 1 Embryonic Stem Cells

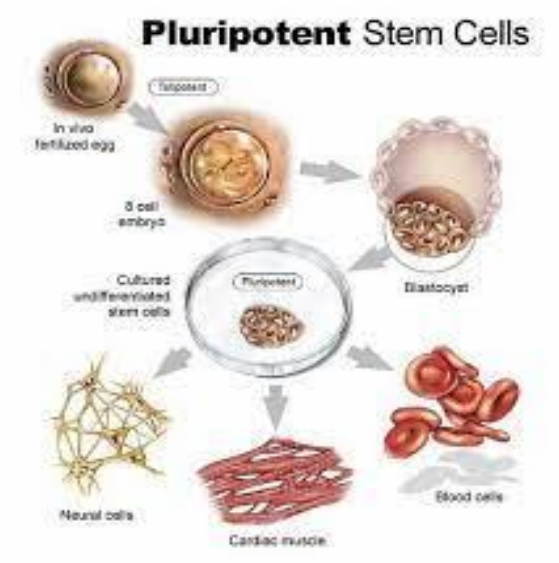

Figure: 2 Pluripotent Stem Cells

Adult Stem Cells (ASCs)

ASCs are undifferentiated cells found living within specific differentiated tissues in our bodies that can renew themselves or generate new cells that can replenish dead or damaged tissue. The term “somatic stem cell” used to refer to adult stem cells. The term “somatic” refers to non-reproductive cells in the body (eggs or sperm). Resident in most tissues of the human body, discrete populations of ASCs generate cells to replace those that are lost through normal repair, disease, or injury. ASCs are found throughout one's lifetime in tissues such as the umbilical cord, placenta, bone marrow, muscle, brain, fat tissue, skin, gut, etc[6].

Adult stem cells (ASCs), are a type of cells which has a regenerative property to regenerate the damaged tissues and repair the damage. Due to their homing ability toward tumour foci, it is emerged as the leading therapeutic candidates in cancer therapy. Stem cells can precisely target malicious tumours;therefore,it minimizes the cytotoxicity of normal cells and reduces unfavourable side effects. Adult stem cells such as mesenchymal stem cells (MSCs), neural stem cells (NSCs), and hematopoietic stem cells (HSCs), are powerful tools for delivering therapeutic agents to various primary and metastatic cancers[7].

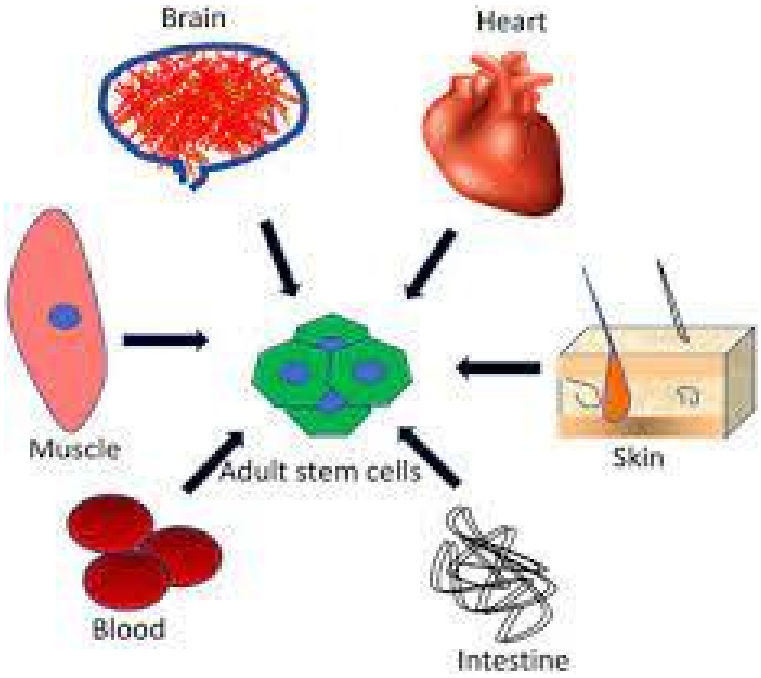

Figure: 3 Adult Stem Cells

Types of stem cells

- Hematopoietic Stem Cells (Blood Stem Cells) (HSCs)
- Mesenchymal Stem Cells (MSC_S)
- Neural Stem Cells
- Epithelial Stem Cells
- Skin Stem Cells

Stem cell therapy

Cardiovascular Stem Cells

Cardiovascular disease is a major cause of morbidity and mortality throughout the world. Most cardiovascular diseases, such as ischemic heart disease and cardiomyopathy, are associated with the loss of functional cardiomyocytes. There are still several major hurdles to be taken. Stem cell-derived cardiac cells should resemble original cardiac cell types and be able to integrate with the damaged heart. Integration requires the administration of stem cell-derived cardiac cells at the right time using the right mode of delivery. Once delivered, transplanted cells need vascularization, electrophysiological coupling with the injured heart, and prevention of the heart[8].

Table 1 Cardiovascular stem cell therapy

Stem cell	Origin	Stem cell type	Research stage	Primary intended effect	Immunological status cells	Remarks
Embryonic stem cell	Inner cell mass of the blastocyst	Pluripotent	Pre-clinical	Structural Integration	Allogenic/ matched	Ethical and safety issues
Induced pluripotent stem cell	Somatic cell	Pluripotent	Pre-clinical	Structural Integration	Autologous/ matched	Safety issues
Cardiac stem cell	(Adult) Heart	Multipotent	Pre-clinical	Structural Integration	Auto- and allogenic/ matched	Limited availability

Mesenchymal stem cell	Bone marrow, fat, and cord blood	Multipotent	Clinical	Paracrine	Tolerated/autologous	No structural effects
Bone marrow cell	Bone marrow	Multipotent	Clinical	Paracrine	Tolerated/autologous	Hetero-genous cell population, no structural effects
Directly reprogrammed cell	Somatic cell	No stem cells involved	Pre-clinical	Structural Integration	Autologous	Safety issues limited and efficacy of differential on cells

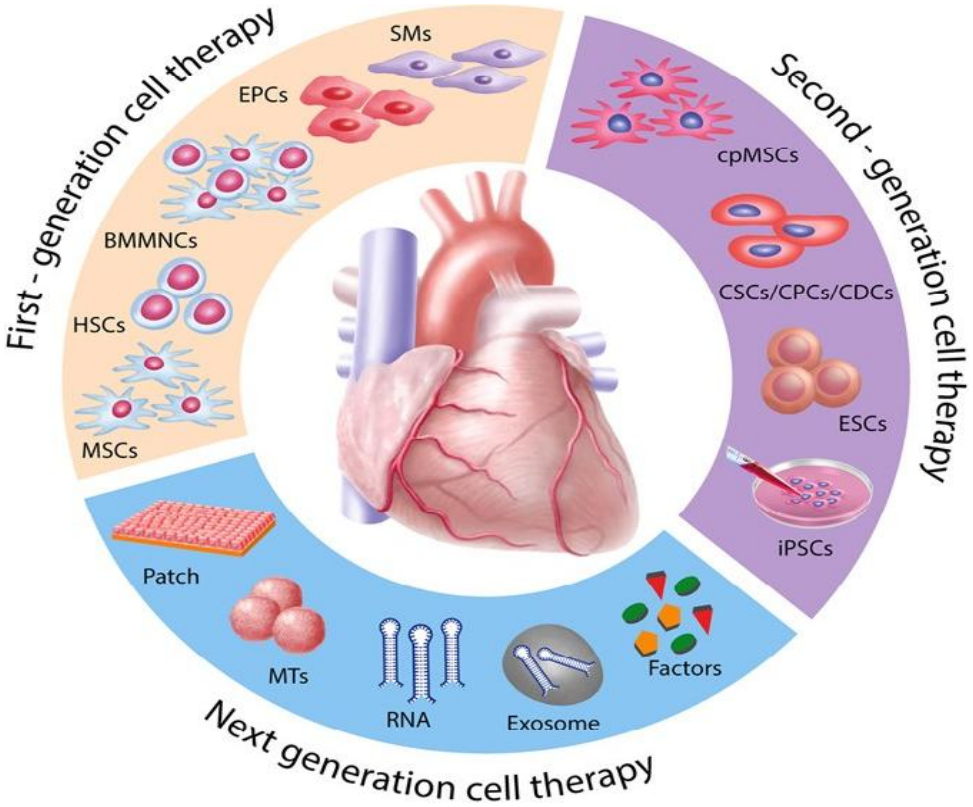

Figure: 4 Cardiovascular stem cell therapy

Table 2 Difference between Totipotent, Pluripotent, Multipotent and Oligopotent.

Types	Totipotent	Pluripotent	Multipotent	Oligopotent
Relative potency	High	Medium	Low	Medium
Cell types capable of generating	Differentiate into any cell type	Differentiate into cells from any of the three germ layers	Differentiate into a limited range of cell types	differentiate into only a few cells and include the myeloblast stem cells that produce 3 types of white blood cells – eosinophils, neutrophils, and basophils.
Terminology	Toti = Whole	Pluri = Many	Multi = Several	Oligo= few
Examples	Zygote, early morula	Embryonic stem cells, Induced pluripotent stem cells	Hematopoietic stem cells, neural stem cells, mesenchymal stem cells	hematopoietic stem cells (HSC). HSCs are cells derived from mesoderm that can differentiate into other blood cells. Specifically, HSCs are oligopotent
Found	Early cells of the fertilized egg	Inner mass cells of the blastocyst	In many tissues	lymphoid or myeloid stem cells
Expression of pluripotency genes	+++	++	+	++
Expression of lineage-specific genes	+	++	+++	++
Pros of use in research	Easy to isolate and grow	Easy to isolate and grow	Less ethical issues, and less chance of immune rejection if taken from the same patient	PROS AND CONS of Using Various Stem CELLS
Cons of use in research	Ethical issues	Ethical issues, teratoma formation	Hard to isolate, limited differentiation, scarce	Cannot be grown for long periods in culture

Stem cell injection

Stem cell skin therapy;

Stem cells can be classified based on their source and differentiating capacity. In the skin, they are present in the inter-follicular epidermis, hair follicle, dermis, and adipose tissue, which help in maintaining normal skin homeostasis and repair and regeneration during injury. Because of their unique properties, they have been employed in the treatment of several dermatoses including systemic sclerosis, systemic lupus erythematosus, scleromyxedema, alopecia, Merkel cell carcinoma, pemphigus vulgaris, psoriasis, wound healing, epidermolysis bullosa and even aesthetic[9].

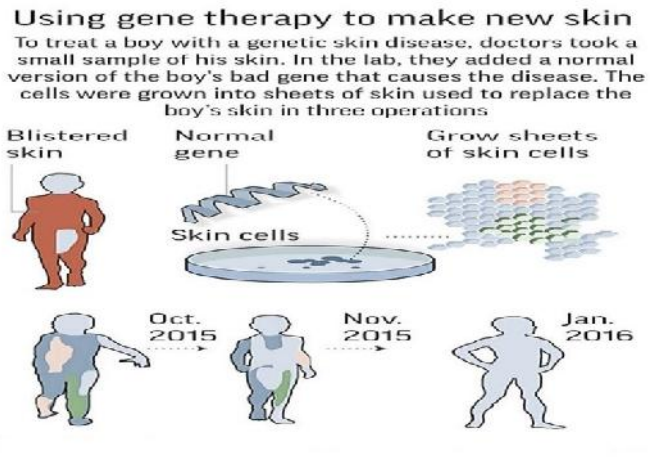

Figure: 5 Stem cell therapy in skin

The advent of stem cell therapy has undoubtedly brought us closer to the curative treatment of disorders previously considered untreatable.Skin stem cells make all this possible. They are responsible for the constant renewal (regeneration) of your skin and for healing wounds.Epidermal stem cells are responsible for the everyday regeneration of the different layers of the epidermis[10].

Stem cell for joint pain

To analyse the outcomes of the treatment of temporomandibular joint (TMJ) articular pain (AP) and restricted maximum mouth opening (MMO) with intra-articular administration of mesenchymal stem cells (MSCs)[11].

The temporomandibular joint (TMJ) consists of two separate functional joints due to the existence of an articular disc The joint between the temporal bone and the articular disc is the upper cavity of the TMJ. Similarly, the lower TMJ cavity has articular surfaces on the disc and head of the mandible. Originally, the articular disc is a dense fibrous tissue, which changes to fibrocartilage with age Also, the above-mentioned surfaces of the bones are covered with cartilage. These structures are covered with a joint capsule and are immersed in the synovial fluid. The synovial fluid consists largely of hyaluronan, and its role is to lubricate the surfaces that are rubbing against each other. For various morphological and physiological reasons, the function of this complex system can be disturbed. The characteristics of TMJs disorders (TMDs) include inflammation and degeneration TMDs are caused by multiple reasons, such as malocclusion, malformations of the structure of the temporomandibular joint, degeneration of the joint surfaces and/or articular disc, and muscle and ligamentous apparatus disorders. These may result in restricted movement of the mandible and articular pain The pain itself, along with inflammatory processes, further limits the opening of the mouth[12].

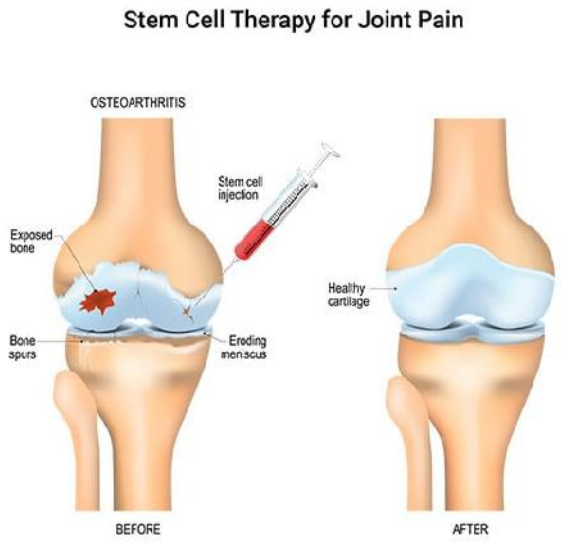

Figure 6: Stem cell therapy for joint pain

Stem cell therapy for Hair loss:

Stem cell therapy treating hair loss methods stem cell sources allogeneic and autologous cell-based treatment in injection intra-surgical cell treatment is patient own cells obtained through centrifugation filtration and isolation without cell expansion[13].

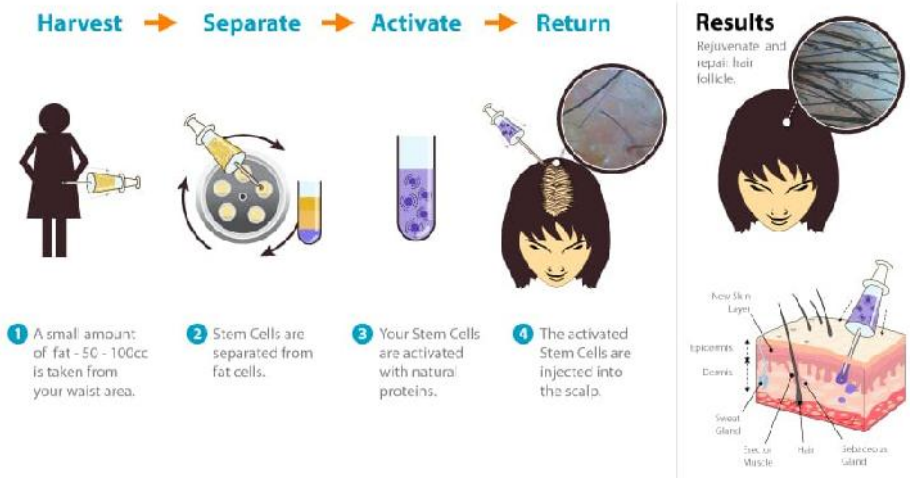

Figure: 7 Stem cell therapy for hair loss

Stem cell therapy is a new approach to treating hair loss which is also called as alopecia. The incorporated stem cells obtained from allogeneic and autologous sources, especially intra-surgical cell treatments which incorporates with autologous cell-based treatments with a one-step approach (cell harvesting, minimal manipulation, and immediate injection) into a single technique offer tremendous potential clinical applications. Intra-surgical cell treatment benefits from the availability and safety of using the patient's own cells, which do not trigger an adverse reaction, as well as from the numerous important cell types that can be harvested using minimally invasive strategies[14].

Stem Cell Breast Augmentation:

In stem cell breast augmentation, stem cells are taken from another part of the patient's body and injected into the breasts to stimulate the growth of new breast tissue. In breast augmentation with implants, breast implants are inserted into the breasts through incisions made in the skin[15].

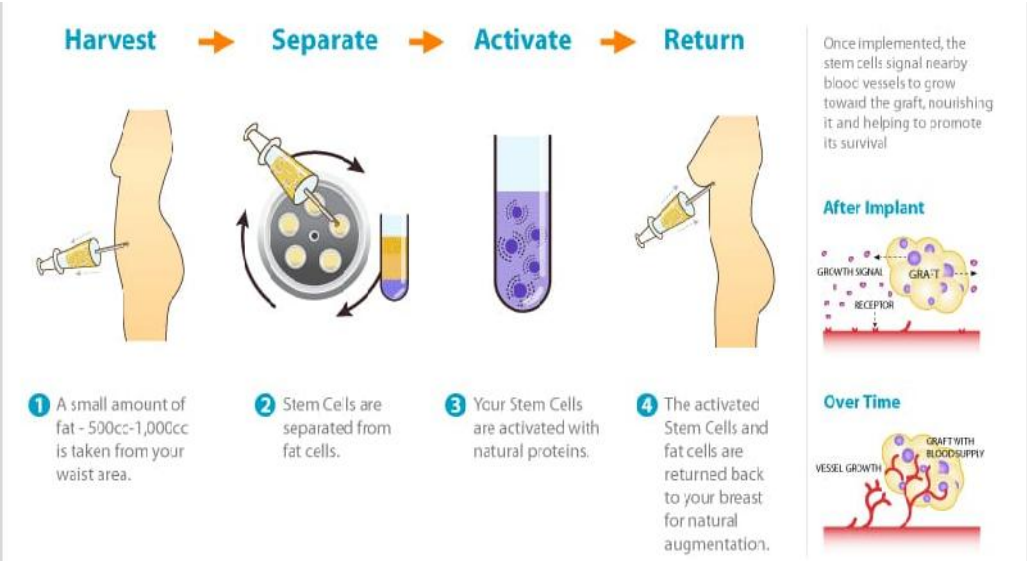

Figure: 8 Stem cell therapy for Breast Augmentation.

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Endophytic Fungi in Bioremediation

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Introduction

Endophytic fungi live inside the internal tissue of their host plant symbiotically and do not show any disease symptoms. They have gone through years of evolution and have the ability to adapt to different environmental conditions by producing enzymes and secondary metabolites. The biotransformation properties of fungal endophytes are being widely studied for their application in pharmaceutical industries, sustainable agriculture, medicine, and restoration of the environment. Endophytic fungi produce a lot of extracellular enzymes like protease, lipase, amylase, cellulase, tyrosinase, and phosphatase, which are useful for nutrient assimilation, fermentation, and biomass degradation in the soil. The biotransformation mediated by endophytic fungi is eco-friendly and does not produce any harmful bi-products, for which it has been included under "green biocatalysis" (Choudhary *et al*., 2021). The rapid rise of industries and factories increases the production of environmental pollutants such as petroleum hydrocarbons, polycyclic aromatic hydrocarbons, heavy metals, fertilizers, pesticides, insecticides, polyethylene, etc., which cause environmental deterioration. The release of carcinogenic substances has a great impact on animals, fish, and especially humans and leads to ecological imbalance. Bioremediation is an eco-friendly approach to cleaning the environment from toxic pollutants such as biochemical waste, heavy metals, industrial waste, synthetic compounds, plastic waste, chemical fertilizers, pesticides, insecticides, etc. It may be used for, extraction (removal of heavy metals or toxic compounds from soil or water), stabilization (immobilization of metal and reduction of bioavailability of contaminants in different trophic levels), accumulation (accumulation or absorption of organic and inorganic contaminants), filtration (water filtration via root system to remove contaminants from the aqueous ecosystem), and evapo-transpiration of volatile compounds.

Heavy metal contamination refers to the excessive accumulation of heavy metals like lead (Pb), mercury (Hg), chromium (Cr), platinum (Pt), cadmium (Cd), arsenic (As), zinc (Zn), copper (Cu), cadmium (Cd), and silver (Ag) whose concentrations are enhanced through the food chain. Heavy metals are deposited on the surface of vegetables and fruits and readily absorbed inside the tissue. They are non-biodegradable and stay in the environment for a long time as contaminants. The presence of heavy metals in soil restricts the growth and development of plants by damaging cell membranes, chlorosis, necrosis, deforming enzymes and proteins, producing oxidative free radicals, etc. Several studies have reported that endophytic fungi with xenobiotic properties can enhance the growth of the host plant and combat biotic and abiotic stresses. The natural ecosystems are largely threatened by synthetic polymers. Many fungi isolated from soil, such as *Mucor circinilloides*, *Aspergillus flavus*, *Fusarium* spp., *Phanerochaete chrysosporium*, *Trichoderma viride*, *Aspergillus nomius*, etc., have been reported to degrade plastic pollutants (Skariyachan*et al*., 2022). The concern for environmental pollution and health hazards posed by heavy metals and synthetic compounds has been increasing, and newer methods are being sought. Bioremediation using endophytic fungi is low-cost, less time-consuming, and highly effective. Microbial bioremediation mainly depends on the concentration of contaminants, edaphic factors, the presence of microorganisms, mobility, and the degradability of contaminants. Many endophytic fungi have metal sequestration properties, which are very useful in bioremediation and also increase soil nutrients. Endophytic fungi have grabbed the attention of microbiologists and biotechnologists due to their role in plant protection, plant growth promotion, and the production of numerous bioactive secondary metabolites showing antimicrobial, antioxidant, anticancer, antiparasitic, etc. properties that have potential applications in the pharmaceutical, agriculture, and food industries. This book chapter summarizes the importance and role played by endophytic fungi in the bioremediation of the environment.

Sources of heavy metals:

Environmental pollutants exist in two categories: (i) elemental pollutants and (ii) organic pollutants (Nwoko, 2010). Elemental pollutants include isotopes of uranium (U), cerium (Ce), and tellurium (Te); heavy metals and metalloids, including mercury (Hg), lead (Pb), cadmium (Cd), chromium (Cr), copper (Cu), cobalt (Co), cesium (Cs), strontium (Sr), arsenic (As), zinc (Zn), manganese (Mn), and many more. Since there are a few exceptions, tissue-specific translocation, and accumulation are the most feasible approaches for immutable elemental contaminants. However, organic

pollutants encompass things like polychlorinated biphenyls (PCBs), halogenated hydrocarbons, and polycyclic aromatic hydrocarbons (PAHs). Numerous factors, such as atmospheric deposition, sewage irrigation, improper stacking of industrial solid waste, mining operations, and the use of pesticides and fertilizers, contribute to the presence of excessive levels of heavy metals in the soil. The irrigation of crop fields allows heavy metals to enter the soil. This results in an ongoing annual buildup of heavy metals (Hg, Cd, Pb, Cr, etc.) in the soil. Pesticides, fertilizers, and other agricultural inputs are crucial for agricultural production. A small number of pesticides are made of pure minerals or organic-inorganic complexes, and some pesticides contain heavy metals such as Hg, As, Cu, and Zn. One of the most significant heavy metal contaminants in the soil is cadmium. The application of phosphoric fertilizers introduces cadmium to soils. Numerous studies revealed that the availability of Cd in soils continuously rises with the application of large amounts of phosphate fertilizers and compound fertilizers, and the amount of Cd absorbed by plants rises in direct proportion. Fluorescent lighting, hospital waste (broken thermometers, barometers, and sphygmomanometers), thermal power plants, chlor-alkali plants, electrical appliances, and other sources all produce mercury (Hg). Smelting activities, thermal power plants, fuel, and geogenic or natural processes all emit arsenic (As). Smelting, electroplating, and mining processes all emit copper (Cu). The spent catalyst from the sulphuric acid plant releases vanadium (Va). From the used catalyst, molybdenum (Mo) is liberated. Smelting and electroplating processes emit zinc (Zn). Waste batteries, e-waste, sludge from painting operations, incinerations, and fuel combustion all release cadmium (Cd). Thermal power plants, battery manufacturing, and smelting activities all release nickel (Ni). Lead (Pb) is released by lead-acid batteries, paints, electronic trash, smelting processes, coal-based thermal power plants, ceramics, and the bangle industry.

Impact of heavy metals on living organisms:

Photosynthesis, water uptake, and nutrient uptake are all reduced in plants exposed to high levels of cadmium. Chlorosis, growth inhibition, browning of the root tips, and eventually death are all evident signs of harm in plants cultivated in soil with high levels of cadmium. High soil zinc concentrations impair a variety of plant metabolic processes, slow development, and hasten senescence. Zinc poisoning in plants inhibits root and shoot growth. When exposed for an extended period of time to high soil zinc levels results in chlorosis in the younger leaves, which can spread to the older leaves (Hafeez *et al.*, 2013). An increased level of copper in the soil has a cytotoxic effect that stresses plants and harms them. Plant growth is slowed

down as a result, and leaf chlorosis results. Oxidative stress and reactive oxygen species (ROS) are produced when plants are exposed to too much copper. Damage to macromolecules and disruption of metabolic pathways are both results of oxidative stress. Strong phytotoxicity occurs when Hg^{2+} levels are higher in plant cells. Mercury ions at toxic levels can cause physical harm and physiological disruptions in plants. For instance, Hg^{2+} can bind to water channel proteins, causing the physical closure of water channels and the closing of leaf stomata. By triggering the production of ROS, high levels of Hg^{2+} interfere with mitochondrial function and cause oxidative stress (Zhou *et al*., 2008). In plants, this results in the disruption of biomembrane lipids and cellular metabolism. Changes in the germination process as well as in the growth of roots, stems, and leaves are among the toxic effects of Cr on plant growth and development. As a result, exposure to high levels of Cr had an impact on plant yield and overall dry matter output. Chromium also has a negative effect on physiological processes such as photosynthesis, water interactions, and mineral feeding. The metabolic changes brought about by Cr exposure in plants have either a direct impact on enzymes and metabolites or their capacity to produce ROS. A higher lead concentration inhibits enzyme activity, disrupts mineral feeding, alters membrane permeability, and promotes a water imbalance (Ashraf *et al*., 2015). By interacting with their sulfhydryl groups, Pb reduces the activity of enzymes at the cellular level. By boosting the formation of ROS in plants, high Pb concentrations also cause oxidative stress. Plants cultivated in elevated Ni^{2+} soil displayed nutritional balance impairment, which led to dysfunctional cell membrane activities. According to studies done on *Oryza sativa* shoots, Ni^{2+} altered the plasma membrane's lipid content and H-ATPase function (Fatemeh *et al*., 2012).

Additionally, heavy metals contaminate food, water, and the atmosphere, which has a negative impact on human health. According to reports, prolonged exposure to air pollutants like volatile organic compounds (VOCs), polychlorinated biphenyls (PCBs), benzene, particulate matter, tobacco smoke particles, etc. can lead to diseases like atopic dermatitis, lung cancer, cardiopulmonary diseases like asthma, hypertension, and chronic obstructive pulmonary disorder (Ferrante *et al*., 2012). Etai-etai, arsenicosis, and minamata disease are three hazardous conditions that are connected to Pb, As, and Hg poisoning, respectively. Cadmium may interfere with the metabolism of calcium, which could result in calcium deficiency and other issues like bone fractures and cartilage degeneration. Cadmium is ranked as the sixth most dangerous toxin that harms human health by the Agency for Dangerous Substances Management Committee. Lead mostly enters the human

body through the digestive and respiratory tracts before entering the bloodstream as soluble salts, protein complexes, or ions, among other forms. Bones store 95 percent of the insoluble phosphate lead. Numerous bodily organs and systems, including the kidney, liver, reproductive, nervous, urinary, and immune systems, as well as the fundamental physiological functions of cells and gene expression, are affected and harmed by it. Although Cu, Zn, and Ni are necessary trace metals for human health, they can be harmful if the body absorbs too much of them from the environment. Nitrogen and copper are carcinogenic substances that promote tumour growth, raising concerns around the globe. Close exposure to nickel powder increases the risk of lung cancer in workers, and nasopharyngeal cancer is directly connected with the amount of nickel in the environment.

Bioremediation using endophytic fungi:

Through the formation of metal oxalate or chelation on polymers that resemble melanin, fungi immobilize toxic metals and metalloids. Endophytes might carry out internal degradation that would lessen phytotoxicity and the pollutant's overall detrimental impact on any herbivorous species (Griffin, 2013). The genera *Microspaeropsis*, *Mucor*, *Phoma*, *Alternaria*, *Peyronellaea*, *Steganosporium*, and *Aspergillus* are important metal-resistant endophytic fungi. In a study, both *Aspergillus niger* and *Penicillium* sp. were shown to absorb Cr, Ni, and Cd from single and multi-metal solutions, which also emphasized the potential for using filamentous fungi in a metal-polluted environment (Hassan *et al.*, 2020). The endophytic fungus *Microsphaeropsis* sp. was isolated from *Solanumnigrum* L, which can accumulate cadmium (Khan *et al.*, 2017). The two isolates, *Aspergillus flavus* (ASC1) and *Aspergillus niger* (ASB3), are arsenic-tolerant fungal strains (Mukherjee *et al*., 2013). These two strains can remove 50% to 76% of the arsenic from various arsenic-enriched media while also being resistant to several other heavy metals (Cd, Pb, Hg, Zn, and Cr) and will be useful for planning the cleanup of arsenic from areas that have been polluted with it in the near future. The Cd, Pb, and Zn-resistant endophytic fungus *Lasiodiplodia* sp. MXSF31 was first discovered in metal-accumulating *Portulaca oleracea* and then rediscovered in the shoots and roots of inoculated rape (Deng *et al*., 2014). The endophyte demonstrated strong Cd, Pb, and Zn biosorption and bioaccumulation capabilities from the metal-affected solutions and improved rape's ability to take metals from soils that were polluted with several metals. In several wastelands that have been polluted with dangerous substances and heavy metals, a significant diversity of endophytes has been found. The endophytic fungi *Phoma* sp., *Alternaria* sp., and *Peyronellaea* sp., had been obtained from plants grown in soil polluted

with lead (Pb) and zinc (Zn) (Li *et al*., 2012). The unicellular fungi *Rhodotorula* sp., *Cryptococcus* sp., and filamentous fungus *Mucor* sp. have been isolated from *Brassica chinensis* L. from the soil with high metal content. These organisms may increase the bioaccumulation of Pb, Zn, copper (Cu), and cadmium (Cd) (Kumari*et al*., 2023). In a study reported by Xiao *et al*. (2010), an endophytic fungus *Microsphaeropsis* sp. has been isolated from *Solanumnigrum* which can absorb Cd up to 247.5 mg/g.

Zhang *et al*. (2008) reported that the endophytic fungus *Exophiala pisciphila* could absorb Pbupto 20% and Cd upto 5% (Zhang *et al*., 2008). The fungal endophyte *Pestalotiopsis palmarum* has been reported to tolerate high salinity and oil pollutants (Naranjo-Briceno *et al*., 2013). The endophytes, *Pestalotiopsis microspora* obtained from *Dendrobium* sp. and *Phomopsis liquidambari* from *Bischofia polycarpa* were reported for their ability to degrade polyester polyurethane (PUR) and polycyclic aromatic hydrocarbon (PAH) respectively (Rana *et al*., 2019; Fu *et al*., 2018). According to the report, the endophytic fungi upscale rhizodeposition in plants and influence microbial mineralization in the soil without altering the diversity of the microbial community (Nandy *et al*., 2020). In a research conducted by Feng *et al*. (2017), some of the essential characteristics of endophyte-mediated phytotoxicity reversal include the formation of organic acids, iron chelators, siderophores, and degrading enzymes. Radhakrishnan *et al*. (2013) reported that the application of endophyticfungi considerably improved seed germination, which reached 69.8%, and seedling growth. Watermelon seedlings grow much more stems and have longer leaves than controls when the endophytic fungus *Ceratobasidium stevensii* breaks down phenolic acids in treated soil (Mishra &Venkateswara, 2018). Leitão & Enguita (2016) found that a gibberellin-producing endophyte called *Penicillium janthinellum* can reduce the damage to membranes and oxidative stress caused by Cd in host plants. It does this by lowering electrolytes and lipid peroxidation while increasing the content of reduced glutathione and catalase activities.

The endophytic fungi *Nigrospora* sp., *Curvularia* sp., *Aspergillus niger*, *Pestalotiopsis adusta*, *Cladosporium* sp., *Aspergillus* sp., and *Curvularia* sp. that live on mangroves were tested for their ability to break down hydrocarbons (Yadav *et al*., 2022). By analyzing each of them using FT-IR spectroscopy, it was found that *Nigrospora* sp. had the highest hydrocarbon biodegradation capacity. Rape roots growing in Pb and Cd-contaminated soil had a greater capacity for phytoremediation when endophytic *Mucor* sp. was present (Deng *et al*., 2014). Dai *et al*. (2010) found that the endophyte fungal strain *Ceratobasidium stevensii*, isolated from the Euphorbiaceae plant, could

successfully metabolize phenanthrene. The endophytic fungus *Phomopsis liquidambari* isolated from the stem of *Bischofia polycarpa* could also degrade pheanthrene after inoculating on rice plants (Fu *et al*., 2018).In a study conducted by Juhasz & Naidu (2000), an endophytic fungus *Fusarium* sp., which was collected from the leaves of *Pterocarpus macrocarpus* Kurz could break down Benzo(a)pyrene (BAP). BAP is a five-ring polycyclic aromatic hydrocarbon that is made when organic materials are burned incompletely.

Conclusion and future aspects

Heavy metals are persistent in the environment and cannot be broken down into harmless products, so their release into the environment has been steadily rising as a result of industrial activity and technological advancement. This poses a serious threat to the environment, human health, and soil health. The endophytic fungus demonstrated high biosorption and bioaccumulation capabilities of Cd, Pb, Cr, Ni, Hg, and Zn from metal-contaminated soils, which also increased the effectiveness of metal extraction. An endophytic fungus from hyperaccumulating plants was a useful microorganism resource for the bioremediation of soils polluted by various heavy metals because of its wide host range, endophytic nature, and tolerance to multiple metals. There are several uses for fungi, including the absorption of dangerous heavy metals and the breakdown of textile colors, insecticides, and polycyclic aromatic hydrocarbons. Mycoremediation using endophytic fungi, therefore, provides a less expensive and more environmentally beneficial option to decontaminate the contaminated environment. The significant potential afforded by fungal variety in varied ecosystems and their capacity for bioremediation may be further enhanced by the information in this article. Therefore, a deeper understanding of microbial activities, the complexity of heterogeneous environments, and interactions between various organisms aid in the development of new, effective bioremediation techniques. In this study, we have reported on the bioremediation capability of endophytic fungi and spoken about their possible future use in the control of harmful pollutants. Therefore, more research on endophytic fungi with metal resistance and their capacity to aid in bioremediation is needed. More research should be done to comprehend the variety and ecology of endophytes linked to plants growing in soils contaminated with heavy metals. Understanding metabolic pathways and cutting-edge genetic research can help clarify the complex mechanisms behind fungal survival, adaptation, and remediation techniques. The specific mechanisms by which endophytic fungi influence heavy metal tolerance and growth promotion need to be analyzed in further research.

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Reincarnating the Biological Pump – A Brief Review of Cardiac Transplantation

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Introduction

The main function of the heart is to pump oxygenated blood throughout the body and deoxygenated blood to the lungs for re-oxygenation. It moves oxygen-rich blood from the lungs to the left atrium, further on to the left ventricle, pumping it on to the rest of the body as well as to the musculature of the heart. When one or more of the heart's chambers struggle to pump blood – it is termed as heart failure.

Causes of Heart Failure

Heart failure may be congestive, dilated or ischemic based on the cause.

Congestive heart Failure occurs when the blood returning through the veins to the heart backs up due to slowing down of forward flow from the heart, causing congestion of body tissues resulting in edema – either systemic or pulmonary – depending on where backlogging of blood occurs.

Dilated cardiomyopathy causing heart failure occurs when due to inadequate pumping of the heart to empty out the blood entering it, the chambers gradually dilate to accommodate the extra volume. What initially starts as a compensatory mechanism eventually dilates beyond compensation, resulting in grossly enlarged chambers, further reducing force of contractility and emptying of the heart, worsening the condition as a vicious cycle.

Ischemic heart failure typically occurs as a result of ischemia to cardiac muscles, commonly due to coronary artery disease, resulting in a block in the blood vessels supplying the heart, resulting in a myocardial infarction, more commonly known as a heart attack, causing death of the myocardium, resulting in a non-contractile scar tissue formation, that eventually loses its elasticity, causing dilatation of the heart chamber involved, adding to inadequate contractility along with the poor contractility due to the scar tissue.

Types of Heart Failure:

Left-Sidedheart Failure typically affects the left ventricle, causing blood stasis in the left side of the heart, resulting in fluid backup in the lungs, causing pulmonary edema, predominantly presenting as shortness of breath and intractable cough with pinkish frothy sputum in severe cases. Left-sided heart failure can be of 2 types:

1. **Systolic Failure** – wherein the left ventricle loses its ability to contract normally, resulting in the left ventricle being unable to pump enough blood into circulation, resulting in a decreased ejection fraction, to 40% or less, known as **heart failure with reduced ejection fraction (HFrEF)**
2. **Diastolic Failure** – wherein the left ventricle loses its ability to relax normally to fill with blood during the resting phase or diastole, between each beat as the muscle becomes stiff, however contractility is preserved, thus the ejection fraction is preserved, at greater than or equal to 50%, known as **heart failure with preserved ejection fraction (HFpEF)**
3. **Heart failure with mid-range ejection fraction (HFmrEF)** is a newer concept, in which the left ventricle pumps with an ejection fraction between 41 – 49%, placing the patients between HFrEF and HFpEF groups

Right-Sided Heart Failure occurs when the right ventricle is unable to pump blood forward into the lungs for oxygenation, causing back up of blood into the veins, resulting in body edema, presenting as pedal edema, abdominal pain and distension, congestive hepatomegaly, facial puffiness and appetite disturbances. This usually occurs as a result of left-sided failure wherein due to decreased emptying of the left heart; increased fluid pressure is transferred back through the lungs to the right side of the heart, causing damage.

Classes of Heart failure

Class I – No Limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea.

Class II – Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation or dyspnoea.

Class III – Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation or dyspnoea.

Class IV – Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

Introduction to Cardiac Transplant

End-Stage Heart Failure, where the body can no longer compensate for the lack of blood due to poor pumping capacity of the heart and the heart has limited functional recovery, wherein a person may commonly present with NYHA Class IV breathlessness (at rest), has significant morbidity, need for recurrent hospitalization, decreased quality of life and increased mortality. Cardiac transplant acts as an effective therapy for these patients. With widespread achievements in fields of immunosuppression, rejection and infection, cardiac transplant which was once considered an experimental intervention has now achieved the status of a routine treatment worldwide.

Indications and Contraindications of Heart Transplant

Indications:

1. Systolic Heart Failure – as defined by an ejection fraction of less than 35%
   a. Accepted etiology
      i. Ischemic
      ii. Idiopathic
      iii. Valvular
      iv. Hypertensive
      v. Others
   b. Controversial etiology
      i. HIV Infection
      ii. Cardiac Sarcoma
2. Intractable angina
   a. Ineffective maximal tolerated medical therapy
   b. Not a candidate for direct myocardial revascularization, percutaneous revascularization or transmyocardial revascularization procedure
   c. Unsuccessful myocardial revascularization
3. Intractable arrythmia
   a. Uncontrolled with pacing cardioverter defibrillator
      i. Not amenable to electrophysiology-guided single or combination medical therapy
      ii. Not a candidate for ablation therapy
4. Hypertrophic cardiomyopathy
   a. Class IV symptoms persist despite interventional therapies
      i. Alcohol injection of septal artery
      ii. Myotomy and myomectomy
      iii. Mitral valve replacement

iv. Maximal medical therapy
v. Pacemaker therapy

5. Congenital heart disease in which severe fixed pulmonary hypertension is not a complication
6. Cardiac tumor
    a. Confined to the myocardium
    b. No evidence of distant disease revealed by extensive metastatic workup
7. Restrictive Cardiomyopathy
    a. Class IV symptoms persist despite interventional therapies
    b. Amyloid (if concomitant therapy such as chemotherapy/autologous stem cell transplant feasible)

Contraindications

Absolute contraindications:

1. Age more than 65 – 75 years (may vary with centres)
2. Fixed pulmonary hypertension (unresponsive to pharmacologic intervention)
    a. Pulmonary vascular resistance more than 4 – 6 Wood units
    b. Transpulmonary gradient more than 12 – 18 mmHg
3. Systemic illnesses that will limit survival despite transplant
    a. Neoplasm other than skin cancer (less than 2 – 5 years disease-free survival)
    b. HIV/AIDS (CDC definition of CD4 count of less than 200 cells per cu. mm)
    c. Systemic lupus erythematosus or sarcoid that has multisystem involvement and is currently active
    d. Any systemic process with a high probability of recurrence in the transplanted heart
    e. Irreversible organ (renal/Hepatic/Pulmonary) dysfunction

Potential Relative Contraindications:

1. Recent malignancy
2. Chronic obstructive pulmonary disease
3. Recent and unresolved pulmonary infarction and pulmonary embolism
4. Diabetes mellitus with end-organ damage (neuropathy, nephropathy and retinopathy)
5. Peripheral vascular or cerebrovascular disease
6. Active peptic ulcer disease

7. Current or recent diverticulitis
8. Other systemic illness likely to limit survival or rehabilitation
9. Severe obesity or cachexia
10. Severe osteoporosis
11. Active alcohol, nicotine or drug abuse
12. History of noncompliance or psychiatric illness likely to interfere with long-term compliance
13. Absence of psychosocial support

History and Evolution of Cardiac Transplant

The first attempt at cardiac transplant was done by **AlexisCarrel** and **CharlesGuthrie** in 1905 at the University of Chicago where the heart of a small dog was transplanted into the neck of a larger dog, with the jugular vein and the carotid artery of the larger dog were anastomosed to the aorta and the pulmonary vein or the heart harvested from the smaller dog.

Figure 1: Alexis Carrel

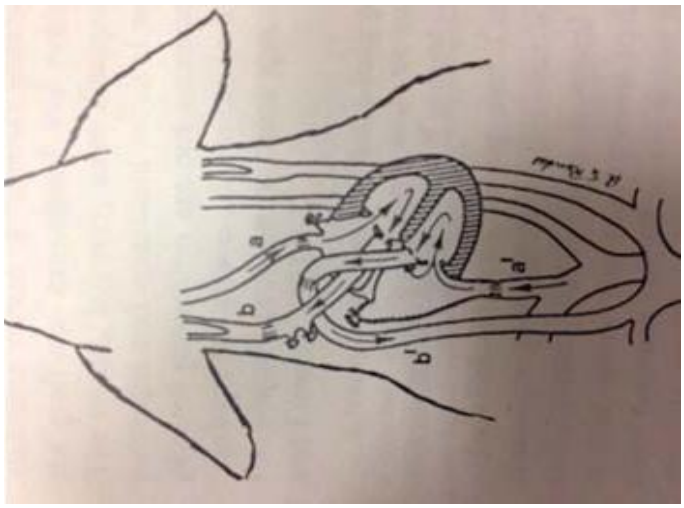


Figure 2: schematic of the probable anastomotic arrangement of the experiment

The animal was not anticoagulated, and hence, the experiment ended in about 2 hours after circulation was established because of blood clots in the cavities of the transplanted heart.

Alexis Carrel and Charles Guthrie also revealed that heterotopically transplanted hearts resume spontaneous contraction for several hours through their varied experiments with animal hearts – predominantly those of dogs – the basis of their transplant anastomoses in 1905.

Another pioneer whose surgical experiments were mainly concerned with cardiac transplants was **VladimirDemikhov** in Russia, who in 1950 described more than 20 techniques for heart transplantation theoretically and experimentally. He proceeded to do an orthotopic heart transplant on a dog, where the donor heart was placed above the dog's heart and blood rerouted from one heart to the other – the first documented heterotopic heart transplant ever. He was the creator of the famous *two headed dog* – a bizarre medical experiment in February 1954 where the torso of one dog, a smaller one, was connected to another larger dog at the back of the neck.

The heads of both dogs and the body of the larger dog remained fully functional and responsive, with both dogs obeying commands and even interacting with each other. One of his dogs climbed the steps of the Kremlin on the 6th postoperative day but dies shortly afterward of graft rejection.

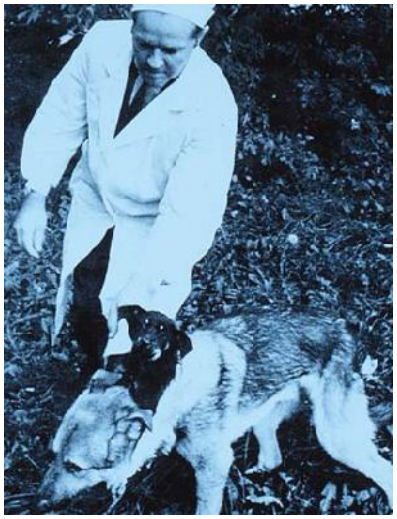


Figure 3: Demikhov with the two-headed dog

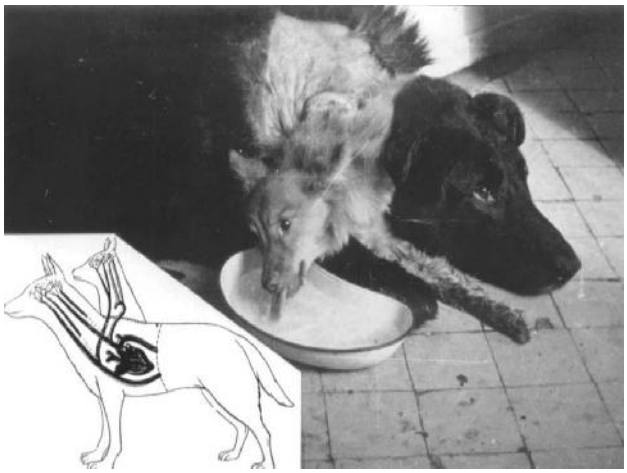


Figure 4: Demikhov's two-headed dog with the puppy's head lapping up milk when the host dog felt hungry - an example of full functionality of both heads independently to responses from the body

Though widely criticized as unethical all through the Soviet, Demikhov continued with his head and heart transplant experiments and had been performing these procedures for five years before the news of his experiments spread outside of the Soviet. He went on to coin the term “transplantology” to refer to organ transplant in his monograph “Experimental Transplantation of Vital Organs” in 1960, that received wide critical acclaim and became a hugely influential publication for emerging transplant surgeons of the period.

The first attempt at human heart transplant was made by **JamesHardy** in 1964, at the University of Mississippi Medical Centre. It was on 68-year-old Boyd Rush who was found comatose 2 days before admission with lower limb gangrene and a faint pulse in sepsis and cardiac failure. He underwent amputation of the lower limb, however went into cardiogenic shock the very next day – putting him on the list to consider for cardiac transplant – though being the first of its kind in humans.

Figure 5: James hardy

The patient was planned for cardiac transplant and there was a trauma victim who was declared brain the in the hospital, the next day after his amputation whose family had consented for transplant. However due to the legal definition of death at the time being that the heartbeat had to completely stop to declare the patient dead – and trauma victim’s heart was still beating, it couldn’t be harvested without ending up in a myriad of legal issues. With Boyd Rush going into shock and his pulse rapidly dropping – he was rushed to the OT and connected on cardiopulmonary bypass just as his heart stopped beating on his own; but with no heart, a collective decision by the surgeons, after oral consent from the patient’s only relative – his step sister, to use the heart of the largest of 4 chimpanzees brought in for research purposes was made.

The *chimpanzee heart was transplanted into the patient* in a surgery lasting at least 3 hours. The chimp heart after suturing and a shock of defibrillation for sinus rhythm beat smoothly for half hour, required pace

maker assistance for the next half hour then couldn't be restarted even with cardiac massage. The patient dies of a hyperacute rejection, without ever regaining consciousness even once.

The first human-to-human heart transplant was performed on 3rd December 1967 in Cape Town, South Africa at Groote Schuur Hospital by **ChristiaanBarnard** on 55-year-old Louis Washkansky with the heart from 25-year-old brain dead patient Denise Darvall in a surgery that lasted 6 hours.

Figure 6: The donor denise darvall

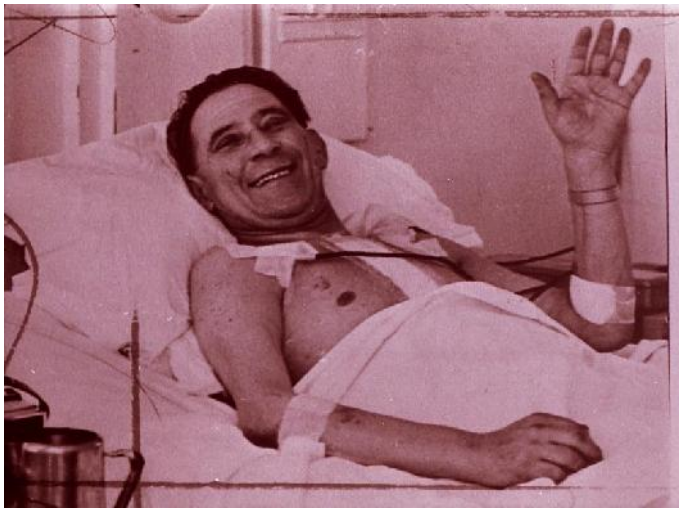


Figure 7: Louis washkansky after being told of a potential donor for heart transplant

Denise Darvall sustained a head injury after being struck by a drunk driver while crossing a busy road with her mother, who died on the spot. Her father gave consent for the surgery after there was no electrical activity in her brain. Her heart was kept pumping with the help of blood transfusions and a respirator. To avoid legalities, Dr. Barnard brought in a forensic pathologist, shifted the body of Denise to the OR on life support and disconnected ventilation after having prepared the patient for chest surgery. As her pulse and blood pressure steadily fell with withdrawal of supports, her heart arrested and she was declared dead by experts following which Dr. Barnard's assistants rapidly opened her chest, connected her to a cardiopulmonary bypass machine and cooled her heart sufficiently for myocardial protection before harvesting it. The recipient had been pre-prepared in the adjacent OR with an empty pericardial cavity ready to receive the recipient heart and the procedure went well.

The procedure was a success as the heart began and continued to beat on its own without external electrical stimulation. The patient regained consciousness and made a progressive recovery, the daily details of which were documented in detail by the media. However, Washkansky died 18 days later of bilateral pneumonia due to a weak immune system, exaggerated by extra immunosuppressants that were stepped up under the suspicion of pulmonary edema due to heart failure caused by graft rejection, when in reality the radiological evidence of lung patches was due to pneumonia.

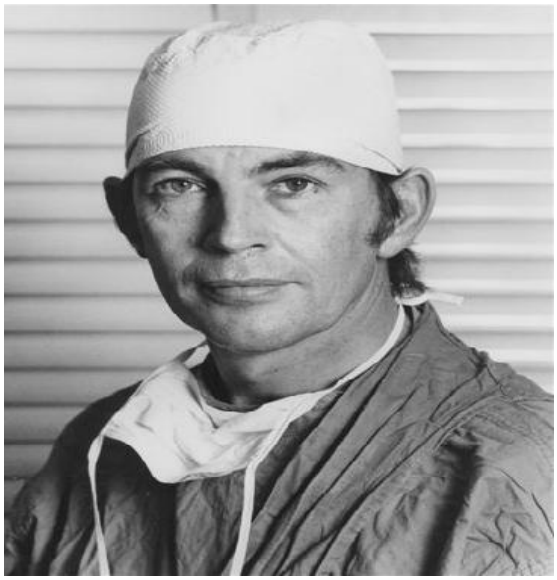
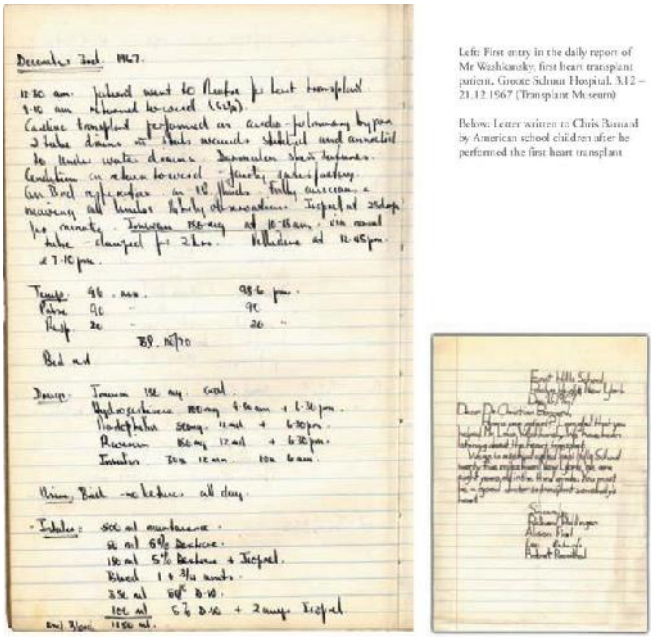


Figure 8: Christiaan Barnard



Left: First entry in the daily report of Mr Washkansky, first heart transplant patient, Groote Schuur Hospital, 3.12 – 21.12.1967 (Transplant Museum)

Below: Letter written to Chris Barnard by American school children after he performed the first heart transplant

Figure 9: Progress notes and letters received

The second human-to-human heart transplant was performed by **AdrianKantrowitz** on December 6th, 1967, 3 days after Christiaan Barnard, on an 18-day-old baby from a 2-day-old anencephalic male in Brooklyn, New York, having the patient in deep hypothermic arrest. Though the surgery was technically successful, the patient died within the 1st 24 hours from bleeding complications and severe respiratory and metabolic acidosis.

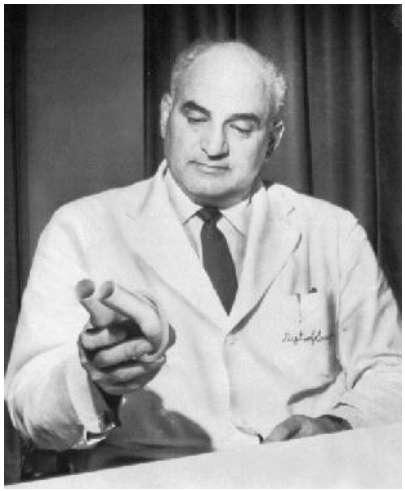


Figure 10: Adrian Kantrowitz

On January 2nd, 1968, **Christiaan Barnard** performed a 2nd human-to-human heart transplant – on a dentist, Phillip Blaiberg, suffering from heart failure. He discharged from the hospital and lived for many months – surviving 593 days after the surgery. He became the 1st transplant patient to be discharged and go home. He showed complete recovery in 3 months, his immunosuppressant doseswere reduced and he was even able to drive his car by himself. However, in June 1968, Blaiberg was found to have contracted hepatitis on routine tests and though emergency treatment kept him alive, he had suffered long-term complications with respect to the transplant. He succumbed on 17th August 1969 at the age of sixty to chronic organ rejection with his autopsy showing severe and widespread coronary artery disease.

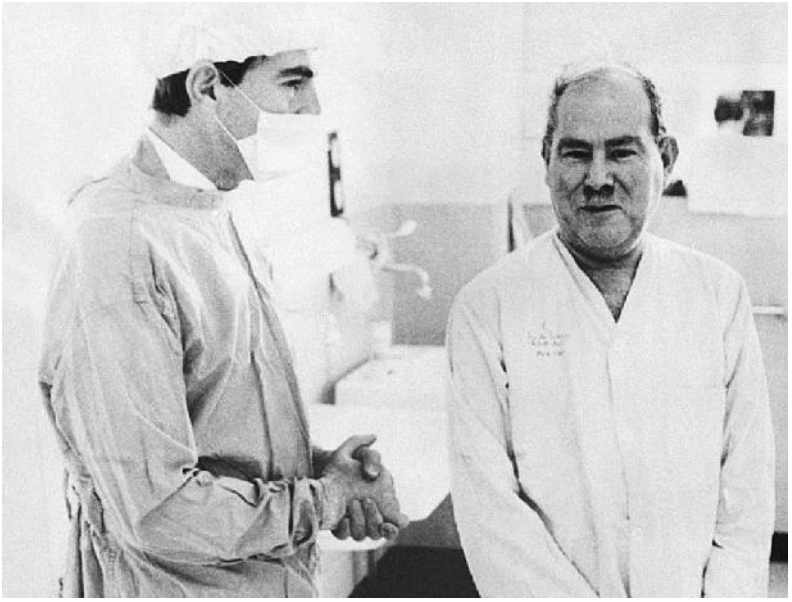


Figure 11: Blaiberg with his surgeon 6 weeks after the surgery, who was discharged 1 month after this photo was taken

Richard Lower and **Norman Shumway** established the technique for heart transplantation as it is performed today. Preservation of the cuff of recipient left and right atria with part of the atrial septum was described earlier by Brock in England and Demikhov in Russia, but it became popular only after Shumway and Lower reported it in their 1960 paper.

Within a year of Barnard's first heart transplant, 99 heart transplants had been performed by cardiac surgeons around the world. However, it seemed to be fraught with multiple mortalities and very few survivors. Hence it was abandoned by the end of 1968.

With the development of new drugs for immunosuppression over the next 20 years, to prevent graft rejection, while simultaneously helping the immune system to stay strong, the future of heart transplants seemed brighter as procedures were restarted. **Cyclosporine** discovered by **Jean Borels** and workers at Sandoz Laboratory, Basel, Switzerland in 1972, while searching for novel antifungal agents, it was found that Cyclospirone inhibited both in vitro cell-mediated lysis as well as lymphocyte sensitization by allogenic target cells, exhibiting cell-mediated specificity of cyclosporine. Introduced for cardiac transplants in December 1980, with studies to titrate dosages in view of its highly nephrotoxic potential, did see an improvement in transplant outcomes on the long run.

A clinical trial of heart and lung transplant at Stanford university in 1981 by **Reitz** was done by treatment with combination of azathioprine and cyclosporine as immunosuppression post-transplant. The patients were discharged well and stayed healthy for 5 years after transplant.

The first successful paediatric heart transplant with the use of newer immunosuppressants was done on 9th June 1984 at Columbia Hospital to 4-year-old James Lovette for a congenital single ventricleby **Eric Rose**. Cyclosporine was used for immunosuppression and the body's immune system did not reject the heart. The recipient survived Hodgkin's Lymphoma and then underwent a second heart transplant in 1989 after having outgrown the first heart. He then survived till adulthood before passing away in his sleep during his first week of medical school at the age of 18 years.

Figure 12: Eric Rose

Following the success of homograft heart transplant, venture into xenografting was made. The 1st xenograft surgery survivor who also happened to be the 1st infant to have a xenograft and was the 1st successful infant heart transplant was Baby Fae (Stephanie Fae Beauclair), of 12-days-old, who underwent transplantation of a Baboon heart for hypoplastic left heart syndrome, in 1984, by **LeonardBailey** in Loma Linda, California. Baby Fae survived 20 days post-surgery.

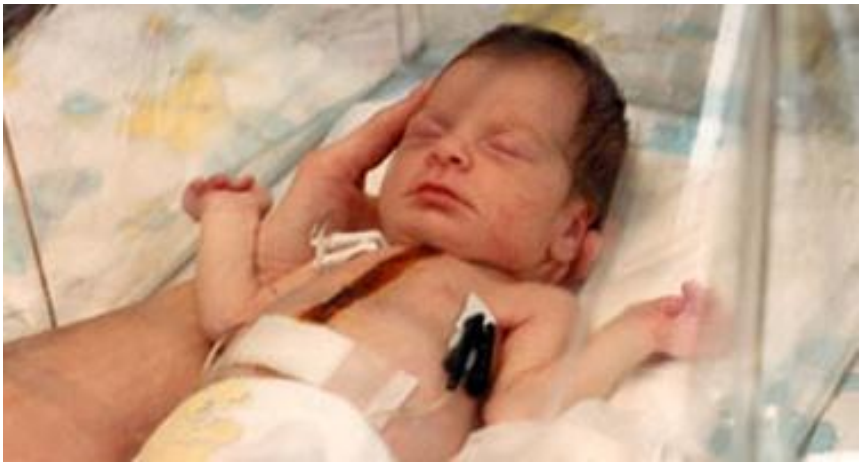


Figure 13: Baby fae post-surgery

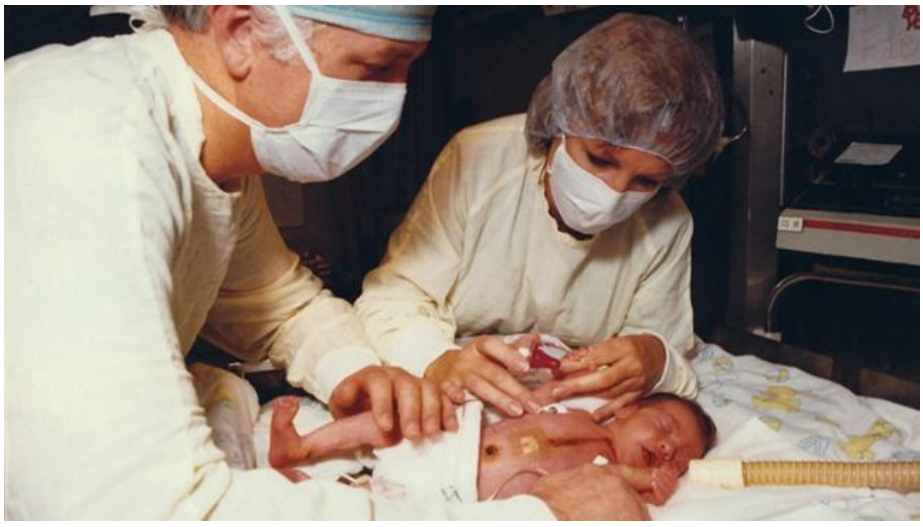


Figure 14: Post-surgery nicu care

Ventures with xenografting continued with **Dhaniram Baruah** in Assam, who, with the help of a Hong Kong based doctor, **Jonathan Ho** transplanted a pig heart into 32 year oldPurnoSaikia, on 1st January 1997, who didn't survive the procedure. The doctors were arrested on counts of manslaughter in view of lack of proper informed consent and clearances from ethical committees.

However, on 7th January 2022, in University of Maryland School of Medicine, a genetically modified pig's heart was transplanted into patient David Bennett Sr. aged 57 years, who survived for 2 months after the surgery; the procedure receiving world-wide recognition.

Figure 15: Photo of the genetically modified pig's heart that was transplanted into David Bennett sr

Figure 16: David Bennett sr with his son, after surgery

Currently, heart transplant has become a widely accepted therapeutic option for end-stage heart failure. In the American scenario, there happens a total of 2400 cardiac transplants/year. In the Indian national scenario with an average of 750 organ donations per year, there has only been reported over 200 heart transplants a year. Overall statistics show about 5000 transplants worldwide per year with at least 3000 people waiting on a heart at any point of time; the main reason for shortfall continuing to be a lack of donors.

Types of Heart Transplant

Heart transplant may be broadly classified into two types:

1. **Orthotopic Heart Transplant** – where the recipient's heart is removed and a donor heart is inserted in anatomical position. Two techniques are described in orthotopic heart transplant:
   a. **Biatrial technique** – which is considered the current standard where the recipient's native atria are left in place. The donor heart is connected by large atrial anastomosis.
   b. **Bicaval technique** – a newer technique which maintains the normal atrial anatomy and a cuff of left atrium containing the entry of the four pulmonary veins are left back in the recipient which is anastomosed to the donor heart along with anastomosis of the great vessels. It results in fewer surgical and post-operative complications like reduced SA node dysfunction.

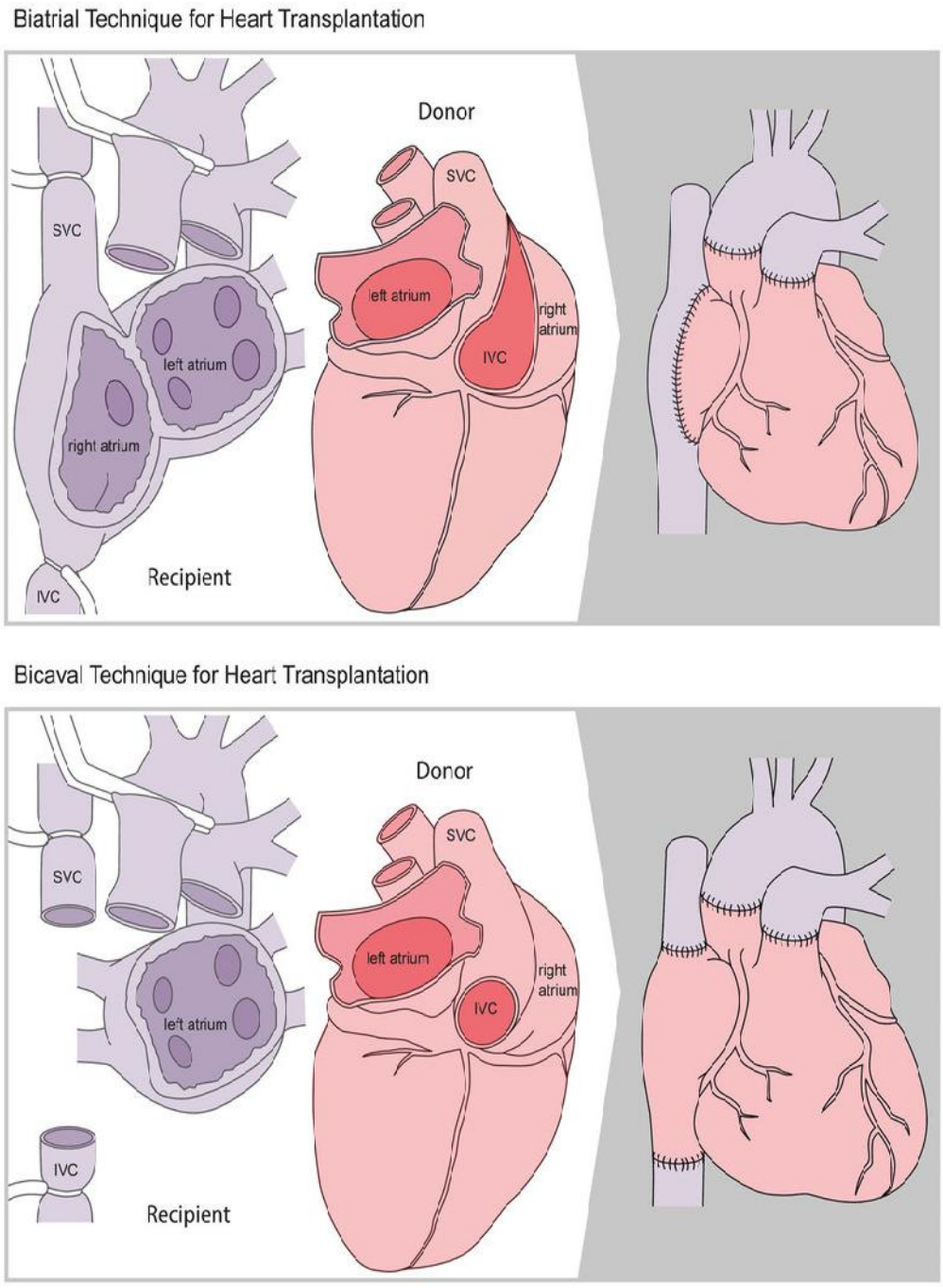


Figure 17: Orthotopic heart transplant - types

2. **Heterotopic Heart Transplant** – also called a "Piggy-back" transplant where the diseased heart is retained in the donor and the recipient heart is transplanted along with it. This is a rarer technique, typically used in patients with pulmonary hypertension. The donor heart is piggy-backed to the recipient heart with anastomoses of the donor SVC and aorta to either the recipient pulmonary trunk and aorta or recipient right atrium and aorta.

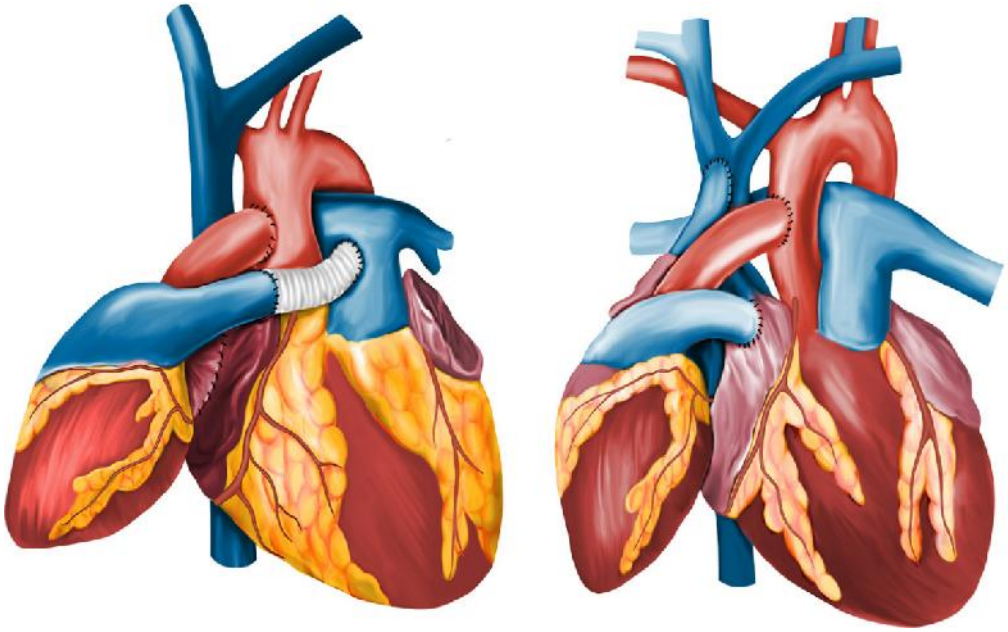


Figure 18: Heterotopic heart transplant - two types of anastomoses

Heterotopic Heart Transplant, initially pioneered by Christiaan Barnard in the late 1970s, was initially used as a means of treatment to combat and treat acute rejection of the donor heart in the recipient in the pre-cyclosporine era, where the recipient heart acts as an assist device, similar to current generation mechanical assist devices, assisting the transplanted heart in episodes of rejection, which can be removed in cases of severe graft rejection, and the patient may still receive and benefit from a subsequent heart transplant. In the setting of an acute rejection, the native heart will support the pumping action while the heterotopic graft recovered. In the pre-cyclosporine era, the heterotopic heart transplant technique offered an extra layer of protection to the transplanted heart, when death within the 1st 24 hours of onset of rejection was common. This technique has also extended the possibility of heart transplant as a viable option for patients with severe pulmonary hypertension and severe

pulmonary vascular resistance who would not qualify for an isolated orthotopic heart transplant without a concurrent lung transplant. It has also been a way to increase the donor heart pool world-over in recent times.

Criteria of Donor and Recipients prior to Heart Transplant

1. Recipient Criteria

Evaluation of a potential candidate is to be done by a multidisciplinary committee and it should ensure equitable, objective and medically justified allocation of donor organs to patients likely to have long-term benefit from transplant. The objective of this evaluation is to identify relatively healthy patients with:

a) End-stage cardiac disease
b) Refractory to appropriate medical and surgical therapies
c) Possessing potential to resume normal active life
d) Maintain compliance with rigorous medications

Criteria for choosing a recipient is multifactorial and needs to be tailored to each recipient assessed but the broad guidelines may be considered as:

a) Age less than 40 years
b) Class III and Class IV heart failure
c) Serum Creatinine less than 1.5mg/dL
d) Serum Bilirubin less than 2.0mg/dL
e) Pulmonary Artery Systolic Pressure less than 60mmHg
f) Transpulmonary gradient less than 15
g) INR less than 1.5
h) Ejection Fraction less than 30%
i) Pulmonary function tests as 50 – 60% of predicted values

Criteria for rejection of a potential recipient may include any of the following reasons:

a) Any active infection (Lungs, tooth, ENT, Urinary tract, Focal abscess, PID)
b) Severe diabetes mellitus with end organ damage
c) Severe peripheral vascular disease and cerebrovascular disease
d) Active neoplasm
e) Obesity (having more than or equal to 140% of the ideal body weight or BMI >30)
f) Acute pulmonary thromboembolism
g) Smoking history in the prior six months

h) History of drug abuse
i) Viral serology positive (HIV/HBsAg/HCV/CMV/EBV/Toxoplasma/Rubella)
j) Epilepsy
k) Mental disorders
l) Pulmonary function tests less than 40% of the predicted values with intrinsic lung disease

Once a potential recipient is evaluated and chosen, the details of the same are to be uploaded in the state and/or national registry to put them on the waiting list for a potential suitable donor. Once a potential donor is identified, after proper and thorough evaluation and assessment, once the donor family has consented for the procedure, probable recipients are picked and matched from the registry pool, based on blood grouping and HLA typing, albeit based initially on priority of sickness and seniority of the registered recipients and a suitable recipient is picked and prepped for surgery.

2. Donor Criteria:

Once a potential brain-dead patient's relatives have consented for the patient to be a donor, the following are evaluated to see if the donor falls into stipulated criteria:

a) Cause of death due to head injury or brain death
b) Blood type and ABO compatibility
c) HLA-DR typing or PRA screening for HLA
d) Age of the donor to be less than 40 years
e) Body size should be a near exact match with that of the recipient in terms of height, weight, BMI, body surface area and chest circumference to match the cardiac function of the donor heart for the recipient
f) Negative viral serologies

A hemodynamically acceptable donor is considered to have clinical parameters of the following:

a) Mean Arterial Pressure more than 60 mmHg
b) Central Venous Pressure 6 – 10 mmHg
c) Left Atrial Pressure (Pulmonary Capillary Wedge Pressure) less than 12 mmHg
d) Normal ECHO findings (exceptions being a small ASD or VSD)

Criteria for donor rejection include:

a) Cause of death involving:
i) Chest injury or cardiac contusion
ii) Cardiac disease
iii) Ventricular tachycardia or Supraventricular tachycardia
iv) Poisoning
v) Electrocution
b) Unbatched blood/ HLA typing
c) Unmatched body surface area
d) Prolonged hypotension more than 3 hours (SBP < 60mmHg/ MAP < 50mmHg)
e) Prolonged high inotropic support (Dopamine or Dobutamine > 20mcg/kg/min)
f) CPR for more than 30 minutes
g) Severe left ventricular hypertrophy (posterior wall and interventricular septal thickness >1.7cm)
h) Prolonged hypoxia

Typically, female donors are not preferred for male recipients.

Assessment of Donor and Recipient prior to Transplant

Recipient Assessment

Assessment of recipients prior to transplant involve a series of blood tests and other investigations to see if a recipient is at the time of procurement of the donor organ fit to undergo transplant.

1. General tests:
a. Complete Blood Count
b. Renal Function Tests
c. Liver Function Tests
d. Serum Electrolytes
e. Blood Sugar Levels
f. Blood grouping and HLA-DR typing
g. PT-INR
h. 24-hour urine collection for creatinine clearance and total protein
i. Panel reactive antibody screening for HLA
2. Tests for Cardiac function:
a. WCG
b. ECHO
c. Right catheter study for pulmonary function
d. Left catheter study/ Coronary Angiogram

e. Peak exercise oxygen consumption or VO2 study
3. General Screening tests:
a. Stool Occult Blood test
b. Mammography
c. PSA levels
d. Pap smear
e. Bone Densitometry
f. Carotid duplex
4. Infectious Diseases Screening:
a. Anti HBsAg Ab
b. HBs Ab
c. HBc Ab
d. Anti-HIV
e. Anti-HCV
f. Human T-cell Leukemia virus I and II
g. CMV – IgM and IgG titres
h. Toxoplasma serology
i. EBV serology
j. Purified protein derivative testing
k. Tuberculin testing
l. VDRL

Recipient Prioritization

Status IA

A. Patients who require mechanical circulatory assistance with one or more of the following devices:
1. Total Artificial Heart
2. Left and/or Right ventricular assist device implanted for 30 days or less
3. Intra-aortic balloon pump
4. Extracorporeal Membrane Oxygenator (ECMO)
B. Mechanical circulatory support for more than 30 days with significant device-related complications
C. Mechanical Ventilation
D. Continuous infusion of high-dose inotrope(s) in addition to continuous hemodynamic monitoring of left ventricular filling pressures
E. Life expectancy without transplant < 7 days

Status IB

A. A patient who has at least one of the following devices or therapies in place:

1. Left and/or Right ventricular assist device implanted for > 30 days
2. Continuous infusion of intravenous inotropes

Status II

All other waiting patients who do not meet Status IA or IB criteria

Donor Selection

1. Criteria for cardiac donor:
   a. Age < 50 – 60 years
   b. Absence of:
      i. Prolonged cardiac arrest
      ii. Prolonged severe hypotension
      iii. Pre-existing cardiac disease
      iv. Intracardiac drug injection
      v. Severe chest trauma with evidence of cardiac injury
      vi. Septicaemia
      vii. Extracerebral malignancy and glioblastoma
      viii. Positive serologies for HIV, Hepatitis B (active) or Hepatitis C
      ix. Hemodynamic stability without high-dose inotropic support (<20 mcg/kg/min of dopamine)
2. Evaluation of Cardiac Donor:
   a. Past medical history and physical examination
   b. Electrocardiogram
   c. Chest x-ray
   d. Arterial blood gas
   e. Lab tests (ABO, HIV, HBV, HCV)
   f. Echocardiogram, pulmonary artery catheter evaluation and coronary angiogram (in selected cases)

Bridge to Heart Transplant

Pharmacological Bridge

This is typically done using drugs – most commonly inotropes to support the heart or lungs like dobutamine, milrinone and dopamine, to improve or sustain and maintain cardiac contractility and rate till availability of a suitable donor heart.

Patients who cannot be weaned off of inotropes will continue to require ICU care until a potential and suitable, matched donor is secured

Mechanical Bridge

These are devices that augment heart function – both contractility and rate to tide over an acute phase of heart failure before it progresses to intractable heart failure. These devices include the following:

1. *IABP – Intra-Aortic Balloon counterpulsation Pump*

Used commonly in heart failure refractory to pharmacological treatment, the IABP inserted via a femoral arterial access into the aorta rests just distal to the left subclavian artery, the balloon inflating at diastole and deflating at systole, augmenting the diastolic blood pressure and in turn improving cardiac blood flow thus improving cardiac contractility, ejection fraction and ultimately systemic blood pressure.

2. *LVADs and Biventricular VADs – Ventricular Assist Devices*

These are devices that renders significant survival and quality-of-life benefits compared with optimal medical management for patients with end-stage heart failure with externally implanted devices that augment blood circulation with a portable external pump implanted on the body with vascular access. Common examples are coronary assist devices and mechanical hearts like the Booster pump devised by Dr.DeBakey

3. *TAH – Total Artificial Heart*

This is a device positioned orthotopically, which replaces both the native cardiac ventricles and all cardiac valves. Use of total artificial hearts have eliminated problems of right heart failure, valvular regurgitation, cardiac arrythmias, ventricular clots, intraventricular communications and low blood flows. The 1st documented artificial heart implantation was done by Dr. Denton in 1969. In 1982, a patient Barney Clark, who was a dentist from Seattle, with congestive heart failure was the first to receive and survive with an artificial heart, living for 112 days with the implant.

4. *AICD – Automatic Implantable Cardioverter Defibrillator*

These are implantable devices with leads implanted onto the ventricular wall, used for life threatening symptomatic ventricular tachyarrhythmias that require cardioversion or defibrillation for reverting.

Figure 19: Jarvik 7 total artificial heart

Figure 20: Abiocor artificial replacement heart

Surgical Procedure

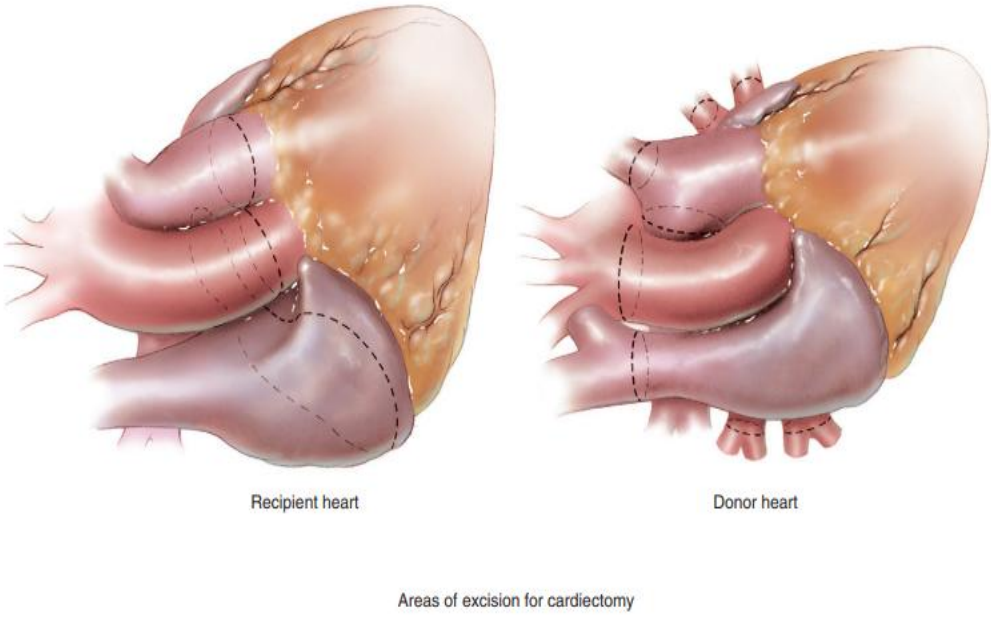


Figure 21: Sites of incision lines in the donor and recipient heart

Donor Heart Procurement

The approach to procure the donor heart is via a median sternotomy. The pericardium is opened longitudinally and the heart is inspected and palpated. The major veins in the chest – SVC, IVC and azygous are mobilized. The aorta is dissected from the pulmonary artery and isolated with umbilical tape for vascular control, other organs are inspected and harvested if suitable, with the heart beating to maintain end-organ circulation as the heart is the last to be harvested. Post harvesting of other organs, 30,000 U of intravenous heparin is given and the azygous and SVC are double ligated after leaving a long segment of the SVC. The IVC is incised, left atrium vented via the appendage or the transected pulmonary vein. Aorta is cross clamped at take-off of the innominate artery. The heart is arrested with a single flush of cardioplegia – custodial solution – at 1000ml or 10 to 20ml/kg, flushed proximal to the cross clamp. Rapid cooling of the heart is ensued with cold saline and cold saline ice shush. Cardiectomy is proceeded with from the apex, elevated cephalad, with division of the pulmonary veins leaving a left atrial cuff.

The donor heart is then preserved after flushing with ice cold custodial solution cardioplegia then stored in a triple layer bag for transport to the recipient OR – the first bag containing ice cold cardioplegia in which the heart is completely immersed and soaked, the second bag containing saline ice slushes and the first bag. This entirely is immersed in the third bag containing ice pieces and the bag tied and stored in an insulated ice box for transport.

Recipient Heart Removal and Implant

The recipient is simultaneously prepared in an adjacent operating room. A median sternotomy is done, pericardium opened and the patient is put on cardiopulmonary bypass to take over the function of the heart and the lungs. Lungs are deflated and the heart emptied. The aorta is isolated from the pulmonary artery with umbilical tape, cross clamped above the root and after adequate cooling of the core, is transected just above the sinotubular junction and the pulmonary artery close to the right ventricular outlet. The SVC and IVC are transected close to the heart, beyond the cannulation sites and the left atrium is opened and excised off leaving a cuff containing the pulmonary veins at its bed.

The donor heart is received with cold chain carefully maintained and the bags are opened once the recipient bed is suitably prepared. The heart is taken out of insulation, examined, extra ends of the great vessels trimmed and anastomosis is initiated. The left atrial cuff is first anastomosed to the left atrial bed containing the entry of the four pulmonary veins, followed by IVC anastomosis, SVC anastomosis, pulmonary artery anastomosis. Aorta anastomosis is done as the end procedure, following which rewarming of the core is initiated and the aortic cross clamp released. It is essential to maintain adequate flows and an FiO2 of 40% throughout pump run to prevent free radical and reactive oxygen species induced injury. Once the heart regains rhythm, with or without defibrillation, core rewarming is completed and the heart is slowly weaned off of cardiopulmonary bypass after adequate support time and venting, with inotropic supports and restarting of ventilation. The sternum is closed after placement of pleuropericardial drain(s) and the chest closed in layers.

Post-Operative Course in a Heart Transplant Patient

Physiology of a Transplanted Heart

In a cardiac transplant, harvesting the donor heart results in transection of sympathetic and parasympathetic ANS fibres of the heart – hence response to catecholamines is lost. This alters the entire normal cardiac physiology and

responses. The SA node fires at a resting rate of 90 to 110 beats per minute causing the grafted heart to respond only to this innate rate. The grafted heart hence relies on non-cardiac sources of catecholamines, thus demonstrating a delayed response to stress.

There also is an absence of the normal tachycardia reflex to venous pooling in the case of orthostatic hypotension due to transection of the ANS fibres, thus resulting in the heart not receiving spinal reflex impulses due to orthostatic hypotension.

Transection of ANS fibres also results in loss of effect of carotid sinus massage, the Valsalva manoeuvre and atropine on the SA node or on AV conduction due to transected fibres.

Post Operative Management

Hemodynamics

Allograft ischemic injury to the donor heart may occur due to donor hemodynamic instability and ischemic insult of preservation of the donor organ during transplant. When such an insulted organ in implanted, it may present to have reduced ventricular compliance and contractility resulting in early failure. Abnormal atrial dynamics may occur due to mid-atrial anastomosis resulting in a reduction in the ventricular diastolic loading,

These may present as an initial altered hemodynamics that can be attempted to be tided over using pharmacological support like inotropes – adrenaline, noradrenaline, dobutamine and milrinone.

Cardiac denervation during explant may cause chronotropic and inotropic super sensitivity to exogenous catecholamines; this will require cautious inotrope weaning within 5 to 7 days.

Long duration of the pump run for cardiopulmonary bypass will result in vasoplegia, requiring the use of vasopressin, noradrenaline or neosynephrine to promote vasoconstriction and warming up of the patient, to promote improvement of the basal metabolic rate, improve renal perfusion and promote urinary excretion of free radicles.

Right ventricular dysfunction, if presents, may be improved with inhaled nitric oxide – which is a local vasodilator, dilating pulmonary capillaries, reducing pulmonary pressures, hence decreasing the work load on the right ventricle, by decreasing its afterload.

Arrythmias

Denervation during donor heart explant results in a loss of ANS fibres, hence resulting in a loss of ANS modulation of the heart's electrophysiology. Parasympathetic denervation causes a loss of SA node automaticity, resulting in an increase in the resting heart rate and a loss of rapid heart rate modulation. Sympathetic denervation causes a decrease and delay in exercise or stress-induced augmentation of SA node automaticity.

Sinus or junctional bradycardia can occur in up to half of the transplant recipients due to risk factors like prolonged organ ischemia, angiographic nodal artery abnormalities, biatrial versus bicaval anastomosis, preoperative use of amiodarone or graft rejection.

Atrial fibrillation, atrial flutter and other supraventricular tachyarrhythmias have been reported in 5 to 30% of patients post heart transplant. Premature ventricular complex runs or PVCs may occur in some patients, though they are not ominous. Sustained ventricular tachycardia or ventricular fibrillation may cause sudden and unexplained deaths post heart transplant.

Systemic Hypertension

Increase in the systemic blood pressure may occur due to pre-existing systemic hypertension or due to altered hemodynamics post-transplant or due to overt use of inotropes. This is to be treated on priority to prevent unnecessary afterload stress on the grafted heart. In the early post-operative period, intravenous nitroprusside or intravenous nitroglycerine may be of use. For a more rapid correction, nicardipine infusion may be instituted. In cases of persistent hypertension, a switch over to oral antihypertensives, carefully titrated to achieve target blood pressure may be preferred.

Respiratory Management

Adequate ventilatory support with gradual weaning and prevention of nosocomial infections and ventilator associated pneumonia as well as barotrauma in the active ventilation period follows the same protocols of routine cardiac surgery.

Renal Function

There remains an increased risk of renal insufficiency due to pre-operative renal insufficiency and the nephrotoxic effects of calcineurin inhibitors. Acute calcineurin inhibitor induced renal insufficiency usually is known to resolve with a reduction in the dose. Concurrent administration of

mannitol with calcineurin inhibitors may reduce their nephrotoxic effects and promote their excretion. A cytolytic agent may be used as well, to delay the initiation of calcineurin inhibitor therapy.

Immunosuppression

Immunosuppression forms a major and important part of post-operative management of heart transplant patients, to ensure safety of the graft and prevent recipient rejection of the donor heart. Immunosuppression has to be initiated prior to seating the donor heart in the thoracic cavity, or at least latest at the time of cross clamp release post anastomosis.

The initial or first course of immunosuppression used is Basuliximab – a calcineurin inhibitor that results in inhibition of IL-2 production, Basuliximab competes with IL-2 receptors on activated T-cells, thus preventing hyperacute rejection of the grafted heart. The standard dose is 20mg given intravenously following completion of cardiopulmonary bypass, prior to seating the donor heart on the recipient bed. The dose is repeated as 20mg IV on POD 4.

The calcineurin inhibitor Tacrolimus is then started, before the onset of rejection by IL-2, hence started in the immediate post-operative period, from POD 1, when the nil per oral period has crossed. It is given at a dose of 0.15mg/kg/day, twice daily, at an exact gap of 12 hours between doses. After a period of the duration of 7 half-lives of the drug – or after three and a half days of starting the drug, Tacrolimus tough levels are measured. TAC Trough levels are typically maintained at 5 – 10 ng/mL through the 1st month post-transplant, reduced to 8 – 12 ng/mL in the 2nd and 3rd month. By the end of the 3rd month, it is maintained within 10 ng/mL. The levels maintained however will also depend on other immunosuppressants used as well as the renal status of the patients, considering the associated nephrotoxicity of the drug.

Mycophenolate Mofetil, an inosine monophosphate dehydrogenase inhibitor, that inhibits T- and B-cell proliferation is started at a dose of 500mg twice daily, on POD 1, to increase it to a maximum dose of 1500 – 1750 mg twice daily to reach a target of 2 – 5 ng/mL.

Steroids paly an important role in post-transplant patients, having both an anti-inflammatory action as well as an immunosuppressant action. Methylprednisolone is typically given intravenously as an induction dose in the OR, at 500mg IV. This is then followed by a maintenance dose of 125 mg IV every 8th hourly on POD 1 and 2. Following this, parenteral steroid is switched over to oral Prednisolone at a dose of 1mg/kg/day from POD 3. This is continued for a week, followed by tapering the dose at the rate of 5mg/day to

reach a dose of 20mg/day, which is maintained as a fixed dose for a duration of 1 month. This is then tapered to 10mg/day and continued during months 1 -to 3. After the 3rd month, till the 5th month, the steroid dose is tapered to 7.5mg/day and continued. This is then tapered and continued as 5mg/day over months 5-7, and then stopped.

Outcomes of Heart Transplantation

There have been no direct comparative trials regarding the survival of post cardiac transplant patients. The reported operative or 30-day mortality of heart transplant patients has been estimated to be 5 – 10%; this being due to primary and non-specific graft failure, multisystem organ failure and infections, most commonly opportunistic, due to immunosuppression.

The overall 1-year survival of heart transplant patients has been estimated to be around 86%. Death at this stage is sue to infection, graft failure and acute rejection of the graft.

After a steep fall in rate of survival in the first six months, the survival decreases by an approximate 3.5% a year, even beyond 15 years post-transplant; the major causes of death in this period being cardiac allograft vasculopathy and malignancy.

Survival, however, following heart transplantation remains favorable, if compared with both the medical and device arms of the REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure) trial. Superiority of heart transplant as a mode of treatment is definitely seen in medium and high-risk end stage heart failure patients, improving their quality of life, chances of and duration of symptom-free survival.

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3D Printing technology in pharmaceutical drug delivery

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Introduction

Over the past 10 years, pharmaceutical 3DP has seen increasing interest and development due to its promise to create highly adaptable therapeutic products that, in turn, enable improved clinical outcomes. In the last ten years, it has drawn a lot of interest due to its capacity to quickly develop customized medications. A patient's therapeutic needs (such as dosage, drug combination, and drug release profiles) and personal preferences (such as shape, size, texture, and flavor) can be provided for in the development of medications using this technology. This overview addresses the fundamentals, challenges and upcoming research in 3D printing drug design.

Fig 1. First 3D printed drug approved by U.S FDA.

https://www.medindia.net/amp/patientinfo/drug-delivery-3d-printing-drug-technology.htm

What is 3D Printing Drug Design?

3D printing, also called additive manufacturing, was first proposed by engineer Charles Hull in the early 1980s. 3D printing is a manufacturing process in which materials are deposited layer by layer to form an entity. Based on a pre-designed 3D digital model, it accumulates the printed layers layer by layer to complete the construction of a 3D object. Pharmaceuticals and clinical pharmacy practice are undergoing a paradigm shift as a result of three-dimensional (3D) printing, moving away from the old mass manufacture of drugs and towards individualized, customized drug products.Due to the tremendous flexibility of 3D printing, material composition and microstructure can be controlled locally. It is more cost-effective and time-saving to use 3D printing to create highly complicated and custom-designed products as opposed to more conventional methods. Fused deposition modelling (FDM), stereo lithography appearance (SLA), and binder extrusion printing are the main 3D printing methods now employed in the pharmaceutical preparation industry.

Principles of 3DP Drug Design:

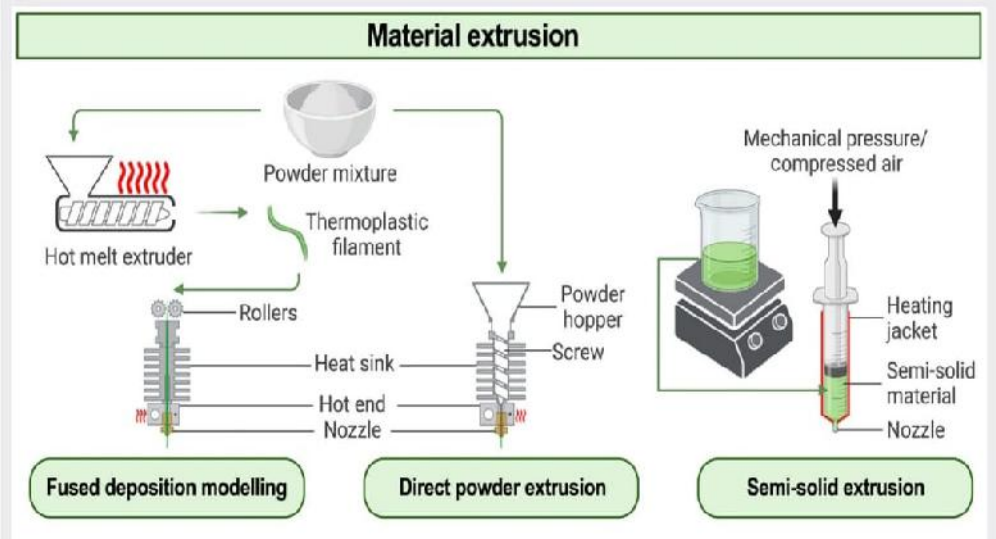
Depending on how the 3D geometry is created, the ASTM divided 3DP (or additive manufacturing) technologies into seven separate groups. These include sheet lamination, directed energy deposition, powder bed fusion, material extrusion, material jetting, binder jetting, and vat photopolymerization. In the field of medicine, sub technologies in the binder

jetting, powder bed fusion, material extrusion, and material jetting categories have made significant progress. As a result, these categories will receive the most of the attention; interested readers can consult the following evaluations for a full description of additional 3DP technologies.

Material extrusion technologies:

To create the necessary 3D geometry, these extrude and deposit a continuous filament through a nozzle. Direct powder extrusion (DPE), semi-solid extrusion (SSE), and fused deposition modelling (FDM) are material extrusion sub technologies that have been investigated in pharmaceutical research. Thermoplastic filaments are heated in the process of FDM through an extrusion head and nozzle, where they melt to create thin strands that are then deposited onto a build plate where they cool and solidify. These thermoplastic filaments are made using a preliminary procedure called hot melt extrusion, which involves blending, melting, and extruding a powder mixture through a nozzle. DPE simplifies this procedure by removing the requirement for filament preparation. A nozzle is used to extrude the powder mixture into thin strands once it has been mixed, melted, and fed directly into the extruder. Gels and pastes, for example, are placed into syringes for SSE and forced under pressure through a nozzle.

Fig 2. Material extrusion technology

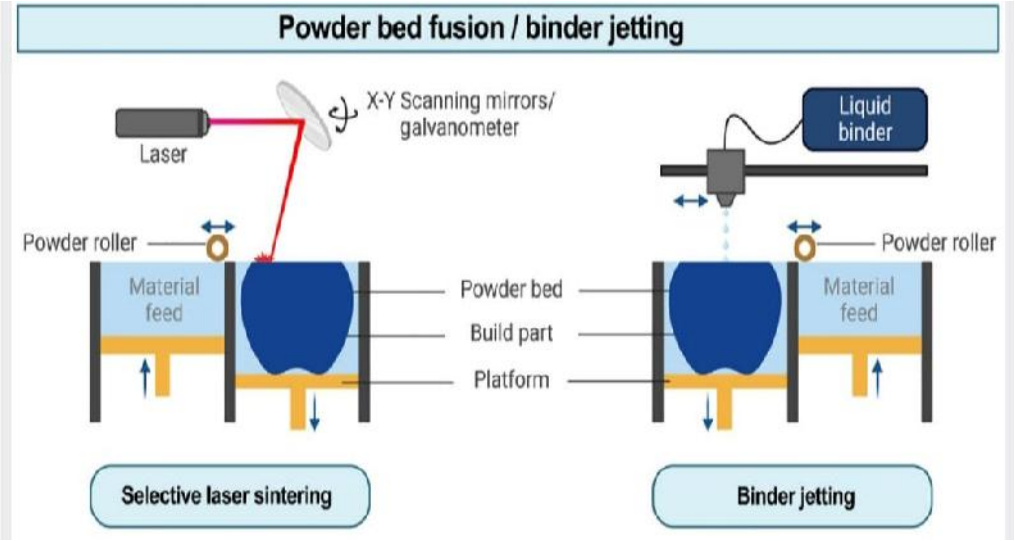


Advancing non-destructive analysis of 3D Printed medicines. Anna Kirstine Jørgensen,1 Jun Jie Ong,1 Maryam Parhizkar,1 Alvaro Goyanes,1,2,3,4,* and Abdul W. Basit 1,3,4*

Powder bed fusion technologies:

These use a laser or an electron beam to melt, sinter, and fuse layers of material powder that have been placed on a powder bed. SLS, or selective laser sintering, is the only powder bed fusion method that has been applied to pharmaceutical applications. Layer by layer, a drug loaded powder bed is sintered using a diode laser. A roller applies a new layer of powder on top of the sintered object after each layer has been sintered.

Fig 3. Powder bed fusion technology



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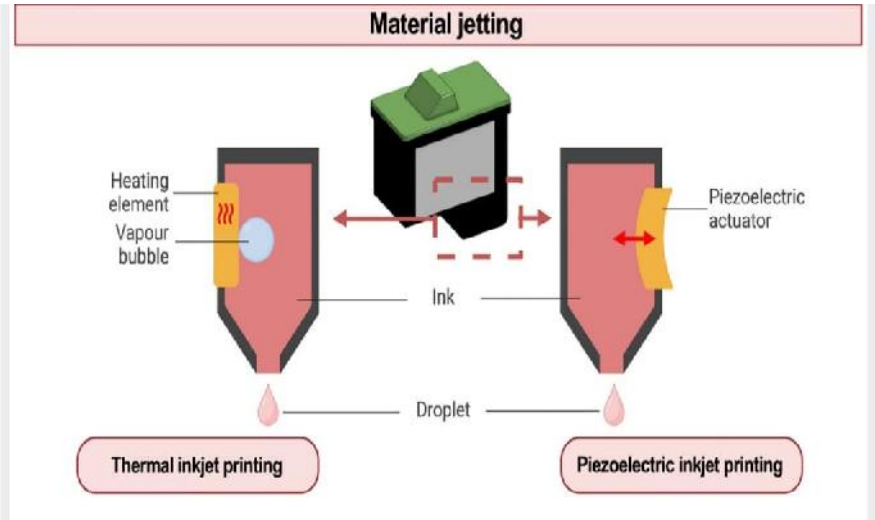
Material jetting technologies:

Droplets are dispensed through a printer in these. Liquid inks serve as the technology's raw material. Inkjet printing (IJP) has been investigated for the fabrication of both drug-loaded films and tablets in the pharmaceutical industry. Either quick heating and vaporization (thermal inkjet) or pressure caused by piezoelectric mechanical deformation (piezoelectric inkjet) are used to dispense ink droplets.

Fig 4. Material jetting technology



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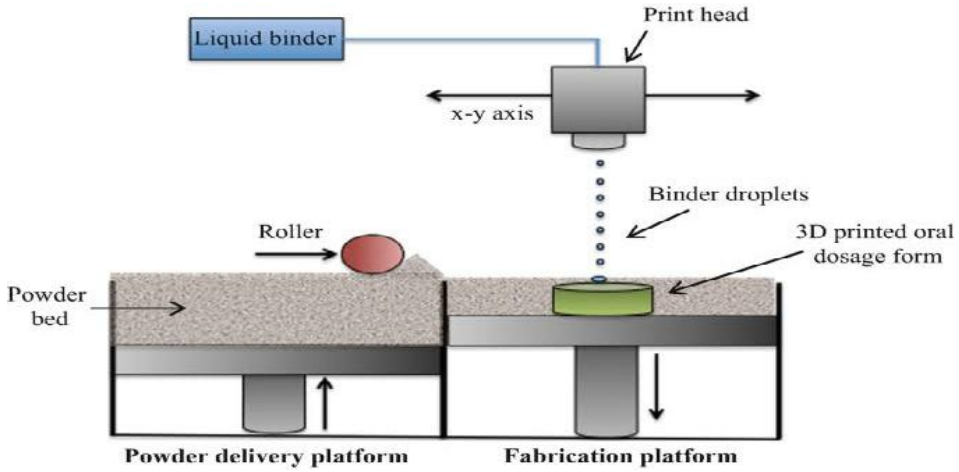
Binder jetting technologies:

These work similarly to SLS and entail adding a liquid binder to a powder bed to 'glue' the particles together. The first 3DP drug to receive FDA approval was made with binder jetting and is called Spritem®.

Fig 5. Binder jetting technology



https://link.springer.com/chapter/10.1007/978-3-319-90755-0_3

Current Uses of 3D printing in medicine

Precise control of drug release:

Tablets make over 70% of all dosage forms produced and are the most often utilized solid oral dose form. Tablet production is more affordable thanks to traditional manufacturing procedures, but preparation development has lagged behind due to their lengthy development timeframes and limited capacity to generate customized preparations on demand.

In contrast to traditional pills, controlled-release preparations enable precise drug release control, reducing side effects and boosting efficacy. However, due to their limitations, conventional manufacturing methods present more difficulties in the design and production of controlled-release preparations. The development and production of complex preparations through the blending of various medications, the creation of intricate models, and the adjusting of printing conditions are ideally suited for three-dimensional printing technology.

Personalized medicines:

Children are in a growth and development stage and have a particular reactivity and sensitivity to medication; the elderly have a reduced capacity for absorption and metabolism; and the coexistence of multiple diseases and combined medication is very common. The health and safety of medication for special populations such as the elderly and children has long been a source of concern. Targeted medications can be printed using three-dimensional printing technology by modifying model parameters such as size, shape, or fill rate. For pediatric patients, 3D printing technology can be used to create low-dose customized medicines that are safe for children. It can also be used to enhance the appearance and flavor of the medications to increase patient compliance. For elderly patients who have difficulty swallowing, 3D printing technology can prepare loose and porous preparations, helping them take medication. For patients who take multiple medications at once, differ rent doctors can be consulted.

Rapid Integration of production:

To meet the demand for traditional drugs on a large scale, conventional pharmaceutical companies typically have very high production capacities. However, because these companies typically use large, largely homogeneous pieces of equipment, they lack the necessary production flexibility to quickly finish cleaning and switch up the types of drugs they produce. On the other hand, three-dimensional printing technology can incorporate rapid

manufacturing, with small equipment, fewer stages in the production process, automated and digital production methods, and the ability to easily change the range of medications produced. For instance, the needs of multiproduct production equipment can be met by the direct replacement of disposable needles holding several medication kinds. Furthermore, due to its lower small-batch production costs and integrated manufacturing process, which can play a significant role in circumstances where there is a shortage of time and resources, 3D printing technology is well suited to small-scale drug production that requires customization and frequent design modifications during the drug development phase. The use of 3D printing technology by Merck to speed up clinical trials and datasupported predictions that in clinical phases I to III, preparation development time will be reduced by 60% and the API required to prepare the medication will be reduced by 50% have significant implications for drug development.

Challenges:

The availability of excipients, the development of printing software and tools, optimizing the mechanical properties of products, and the regulatory environment are the technical challenges and complications that impart 3DP applications despite the implicit benefits of the technology in formulation development. The main obstacle to creating specialized dosage forms is the relatively constrained supply of excipients. Excipients that are non-toxic, biodegradable, biocompatible, and stable are crucial for the widespread use of 3DP in formulation development. Additionally, as dosage form structures get increasingly complicated, modelling and slicing software that is used to plan and guide their manufacture must be updated continuously. To prevent clogging or encourage product uniformity, the mechanical equipment, operating procedures, and control system need to be updated and optimized. The requirements for excipients, the development of printing software and instrumentation, optimizing the mechanical properties of products, and the regulatory environment are the four challenges impacting application, despite the potential of 3D-printed technologies to advance the pharmaceutical industry.

Future Researches:

3D printing could be integrated into various healthcare and resource-constrained settings; The technology can be used to create medicines that are tailored to a patient’s therapeutic requirements (e.g. dosage, drug combination and drug release profiles) and personal preferences (e.g. shape, size, texture and flavor) Conclusion:

The liquid polymeric Nano capsule system and liquid SNEDDS could be successfully converted into solid dosage forms for oral (such as a tablet) and rectal (such as a suppository) administration using 3D printing technology.Additionally, the 3D-printed Nano pharmaceutical items could be utilized to create customized medications and enhance the bioavailability/biopharmaceutical properties of drugs that aren't very soluble in the body. The analysis also emphasized the impact of the 3D printing process parameters on the functionality and results of the created medicinal items.

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Synthetic Seed

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Introduction

Plants are generally propagated through seeds in nature. Seed (zygotic seed) is the vehicle that connects one generation to another in much of the plant kingdom. By means of seed, plants are able to transmit their genetic constitution in generations and therefore seeds are the most appropriate means of propagation, storage and dispersal (Bewley J.D. *et al* 1985). In some crops, propagation through seeds has not achieved success because of seed heterozygosity, minute size, and absence of endosperms and absolute necessity of fungal infection for germination (Saiprasad, 2001). Seed, the functional element of sexual reproduction is the characteristic reproductive body of flowering plants and gymnosperms and mysterious genetic capsule which store the genetic information and carry forward to next progeny but because of recombination and meiotic division among seed-derived plants, the agricultural yield is highly unstable. The alternate way for this issue is synthetic seeds- the functional mimic of botanical seed.

What are synthetic seeds?

Synthetic seed or artificial seed or synseed is one of the most promising tools of plant biotechnology, which could be tailor-made for horti- and agricultural improvement at present as well as upcoming days. An artificial seed is often described as a novel analogue to true seed consisting of a somatic embryo surrounded by an artificial coat which is at most equivalent to an immature zygotic embryo, possibly at post-heart stage or early cotyledonary stage (Bekheet S.A., 2006). In general, synthetic seeds are defined as artificially encapsulated somatic embryos, shoot tips, axillary buds or any other meristematic tissue, used for sowing as a seeds and possess the ability to convert into whole plant under *in vitro* and *in vivo* conditions and keep its potential also after storage (Capuano *et al*., 1998).

Artificial seeds, which are also known by other names such as “synseeds” are firstly described by Murashige. He defined artificial seeds as “an encapsulated single somatic embryo”. An artificial seed was later defined by Gray et al. as “a somatic embryo that is engineered for the practical use in commercial plant production”. The concept of artificial seeds was then limited to those plant species in which the production of their somatic embryos could be demonstrated.

So, synthetic seeds are artificially encapsulated somatic embryos, shoot buds, cell aggregates or any other tissue that can be used for sowing as a seed and that possess the ability to convert into a plant under in vitro or ex vitro conditions and that retain this potential also after storage. In simple words synthetic seed contains an embryo produced by somatic embryogenesis enclosed within an artificial medium that supplies nutrients and is encased in an artificial seed covering.

Discovery of synthetic seed

The origin of the idea of an artificial seed is difficult to determine. Steward et al., 1958 and Reinnert, 1959 was first who produced somatic embryos and procedure of somatic embryogenesis in carrot. The first time the idea of synthetic seed was given by T. Murashige (1977). He conducted research in his laboratory that was focused on the developmental physiology of somatic embryos which he felt to be the limiting factor for large-scale propagation. He presented his ideas on artificial seeds at the Symposium on the Tissue Culture for Horticultural purposes in Ghent, Belgium, Sep 6-9, 1977. He commented in proceedings that *the cloning method must be extremely rapid, capable of generating several million plants daily and competitive economically with the seed method*. During mid 1970’s, Keith Walker identified basic concepts of delivery of cloned, agricultural crops to develop somatic embryo system using a line (Regen S) identified by Bingham *et al.* (1975) in alfalfa. Redenbaugh *et al.* (1984) developed a technique for hydrogel encapsulation of individual somatic embryos of alfalfa. Street (1977) advocated the problem of reliability in embryogenesis according to which morphogenic competence will ensure that the competent cells are involved in callus formation. Sunderland (1977) demonstrated that the production of hundreds of morphologically uniform embryos from *Datura* and *Nicotiana* pollen. Robert Lawrence (1981) started to develop various methods for cloning of forest tress and also focused on delivery of somatic embryos using fluid drilling technology and using polyoxyethylene to form seed tapes or sheets. In one symposium workshop Lawrence and walkers group introduced with each other

and discussed about how low-cost, high-volume propagation system can be developed for vegetables and agronomic crop using somatic embryo and delivered by fluid drilling. Drew (1979) developed methods for commercially propagate crop using somatic embryos. Murashige and Street (1977) suggested that quality and fidelity of somatic embryos are limiting factors for and coworkers prepared first synthetic embryos in carrot. Bapat *et al.* (1987) proposed the encapsulation of shoot tip in *Morus indica.* P.S. Rao's group from BARC, Trombay reported artificial seeds prepared from shoot buds for plant propagation. P.S. Rao and his associates have reported high frequency somatic embryogenesis from *Indica* rice cultivars (Suprasanna *et al*., 1995) and utilized for artificial seed production. Plant species *Brassica campestris* (Kitto and Janick, 1985), *Mangifera indica L. Mango cv. Amrapali* (Ara et al, 1999), *Psidium guajava (Guava)* (Grey and Purohit, 1991), *Solanum melongena (Eggplant)* (Akhtar, 1999) and *Vitis vinifera (Grape)* (Rao et al.1991) in which somatic embryo used for encapsulation technology to produce synthetic seeds. Non zygotic explant tissue can be used in somatic embryogenesis in coffee.

Why synthetic seed?

Primary problem associated with seeds is, on one hand for many crops, such as fruits, nuts, and certain ornamental plants; it is not possible to produce a true-breeding seed from two parents due to genetic barriers to selfing. Other important criteria relate to the type of artificial seeds that can be produced. Seeds of some tropical crops are recalcitrant (unorthodox) in that they have short viability and must be stored at relatively high moisture content to maintain viability (Bewley and Black, 1985).

In some of the horticultural crops seeds propagation is not successful due to

- Heterozygosity of seeds particularly in cross pollinated crops
- Minute seed size eg; orchids
- Presence of reduced endosperm
- Some seeds require mycorrhizal fungi association for germination eg: orchids
- No seeds are formed

After the discovery of somatic embryogenesis in 1950 it was possible to have an alternative of conventional zygotic seeds. Somatic embryo arises from the somatic cells of a single parent. They differ from zygotic embryos since somatic embryos are produced through *in vitro* culture, without nutritive and

protective seed coats and do not typically become quiescent. Somatic embryos are structurally equivalent to zygotic embryos (Dhabhai R. and Prakash A., 2012).

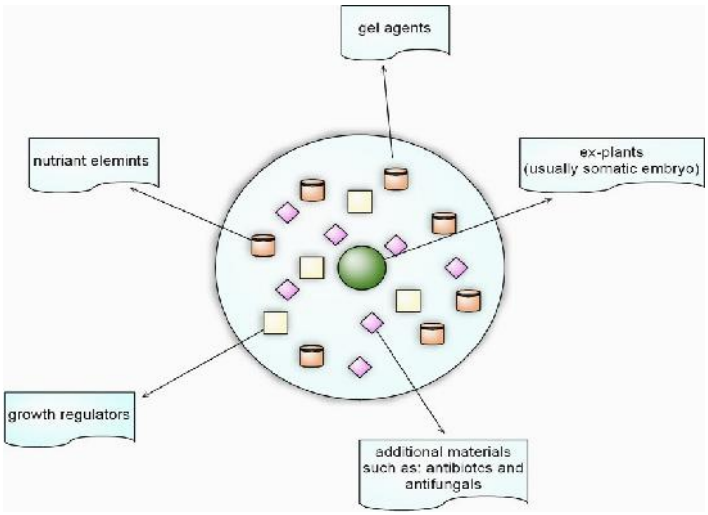
Characteristics of Synthetic Seeds

- Large scale propagation method
- Maintains genetic uniformity of plants
- Direct delivery of propagules to the field, thus eliminating transplants
- Lower cost per plantlet
- Rapid multiplication of plants

Artificial Seed Concept

The artificial seed structure mimics that of the conventional seed. It consists of both explant material, which imitates the zygotic embryo in the conventional seed and the capsule (gel agent and additional materials such as: nutrients, growth regulators, anti-pathogens, bio-controllers, and bio fertilizers), which emulates the endosperm in the conventional seed [Cartes et al., 2009] (Figure 1).

Figure-I



Types of synthetic seed

Two types of synthetic seeds are commonly produced: Desiccated and hydrated (Bapat *et al.,* 2005)

Desiccated artificial seeds:

Desiccated artificial seeds are either naked or encapsulated in polyoxyethylene glycol followed by their desiccation. Desiccation can be applied either rapidly by leaving artificial seeds in unsealed petri dishes on the bench overnight to dry or slowly over a more controlled period of reducing relative humidity. The desiccation tolerance can be induced using a high osmotic potential of the maturation medium and also by applying sub-lethal stresses such as nutrient deprivation or low temperature. The osmotic potential could be increased by using high gel strength or by the addition of permeating osmoticants such as mannitol, sucrose etc. Ex: Carrot, Celery embryos.

Hydrated Artificial seeds

Hydrated artificial seeds can be produced by encapsulating somatic embryos in hydrogel capsules to supply protection and to convert the in vitro micropropagules into 'artificial seeds' or synseeds. They are produced in plant species which are recalcitrant and sensitive to dessication. Ex: Alfafa, Barley, Sandal wood.

Differences between natural and synthetic seeds

S.No.	Natural seeds	Synthetic seeds
1	Produced from the sexual process	Produced from the asexual process
2	Involves the fusion of male and female gametes	Does not involve the fusion of gametes
3	Produced from Germ cells	Produced from vegetative cells
4	Contains genetic constituent from both parents	Contains genetic constituent from single parent
5	Genetic recombination takes place	Genetic recombination does not take place
6	Contains embryo, endosperm and seed coat	Contains only embryo. Endosperm and seed coat are absent

Propagules for the formation of synseeds

Synthetic seeds are mostly needed to improve the characteristics of new embryos, which makes them beneficial for storage for longer duration. Further, they also prevent the desiccation of somatic embryos or plant propagules in the natural environment.

Earlier, only somatic embryos were used as explants for the formation of synthetic seeds in a number of plants. However, later reports by various researchers revealed the use of a variety of plant micro propagules, including monopolar axillary shoot tips as well as buds, nodal segments, embryogenic masses, and calla, along with a variety of other explants, including bulb, bulblets, hairy roots, microtubes, and protocorms or protocorm-like bodies (Chandrasekhara Reddy et al., 2012; Gantait & Sinniah, 2012).

Somatic embryo :

Somatic embryos are those that are created asexually through somatic cells alone without union of gametes. Plant somatic embryo in vitro development was initially described independently by (Reinert, 1959; Steward et al., 1958). While indirect SEs come from explanted tissues via an intervening callus phase, direct SEs grow directly from explanted cells (Williams & Maheswaran, 1986). However, unlike normal embryos, SEs do not experience desiccation or dormancy and instead begin to germinate as soon as they are completely developed (Zimmerman, 1993). Somatic embryos have been successfully produced in a number of plants thanks to advancements in tissue culture technology, making them more advantageous for the generation of artificial seeds since they are more readily available. If the relative humidity can be kept at 10% like conventional seeds by drying, the SEs can be retained in a viable form for a longer period of time.(Ara et al., 2000).

Protocorms and protocorm-like bodies:

When implanted in culture media in vitro, the tiny exalbuminous orchid seeds began to expand after one or two weeks, suggesting effective germination as a result of ingestion of nutrients and water (Nongdam & Chongtham, 2011). The embryos underwent many divisions to become spherules, which are irregularly shaped parenchymatous cell masses (Nongdam & Tikendra, 2014). Protocorms, which are oval, extended, branching, and spindle-shaped creatures that are thought to represent an intermediary structure separating embryos and plants, were formed from the hairy spherical spherules. Although protocorm-like entities are produced in vitro from plant elements other than orchid seeds, they function and morphologically resemble

protocorms. Synthetic seeds have been created in a variety of orchid species, including Cymbidium giganteum, Dendrobium wardianum, and Spathoglottis plicata, by encasing protocorms or protocorm-like structures in alginate solution (Corrie & Tandon, 1993; Nagananda et al., 2011; Sharma et al., 1992). When cultivated in vitro on nutritive media or in sterile soil and sand under greenhouse conditions, the encapsulated protocorms of C. giganteum grew into healthy plantlets. In vitro, the frequency of conversion of synthetic seeds was greater than that of seeds that had already germinated in a sand and soil combination. As PLBs have a great potential for direct plantlet formation, (Mohanty et al., 2012) used PLBs to manufacture synseeds in Dendrobium nobile and reported a conversion of synseeds that was notably high at 80%. Coelogyne breviscapa PLBs were encapsulated with a 3% sodium alginate matrix by (Mohanraj et al., 2009) and kept for 60 days before being cultivated into seedlings with MS medium supplemented including several growth regulators. With longer storage times, synthetic seed germination percentages steadily declined.

Calli and Embryogenic Masses:

For the development of clonal plants and for the investigation of genetic change, regenerative and stable embryogenic masses can be employed. However, due to repeated subculturings, keeping them for a longer period of time in bioreactors and culture containers is challenging (Ara et al., 2000). Encapsulating these embryogenic masses in sodium alginate and storing them at 40oC following 6-benzyl amino purine (BAP) treatment might avoid the time-consuming and costly subculturing method (Redenbaugh et al., 1991). The viability and initial proliferative power of synthetic seeds may be kept in storage for around two months. The effectiveness & proliferative nature of embryogenic masses may diminish with an increase in storage time, but further study is needed to determine whether this is the case with synthetic seeds. The growth of progressively randomer lines of cell division, decreased cell specializations, and the disappearance of ordered structures are all related to callus formation (Wagley et al., 1987). Calli's undifferentiated character and minimal differentiation capability restrict their adoption for explant propagules for the manufacture of synseed (Gantait et al., 2015c). For the first time, the use of calli for the formation of synseeds was successfully observed in Allium sativum (Kim & Park, 2002), exhibiting a high rate of conversion and regeneration of synseeds to plants.

Apical shoot tips/ shoot buds and nodal segment:

In order to create synthetic seeds, auxiliary shoot buds and/or apical shoot tips that lack root meristems have also been encapsulated. Recoin and Standard documented the encapsulation of shoot tips of apple clone root system M. 26 following an adequate root induction treatment using IBA (24.6 m) over 3-6 days since these structures lack root meristems and need be stimulated to regrow roots before encapsulation. When compare to micropropagation of shoot tip/buds encapsulated synseeds, traditional shoot tip culture in vitro takes more space and culture medium (Gantait et al., 2015c). The need for less space means that moving plant propagules from one location to another is simple.

Previous studies

Literature review is important to access to the most accurate details and consequences. Another important thing to use the previous research is to give the researcher knowledge of the history of the evolution of the subject, and opens his eyes on points not to pay attention to and may be key to the solution.

Synthetic seeds have potential for a considerable level of cost lowering (Kok-Siong *et al.*, 2012; Roy and Mandal, 2008) with rapid multiplication of plant with genetic uniformity (Saiprasad, 2001). Seeds are desiccation tolerant, durable and quiescent due to protective coat. Such properties of seeds are also used for germplasm preservation in seed repositories" (Patricia *et al.*, 2004). Artificial seed coating has the ability to deliver beneficial adjuvant like growth promoting plant nutrients as well as growth control agents. "The propagation of plants by artificial seeds widens the horizon of plant biotechnology and agriculture" (Kinoshita, 1992), "the technology provides methods for preparation of seed analogues from the micropropagules such as axillary shoots, apical shoot tips, embryogenic calli, somatic embryos as well as protocorm or protocorm- like bodies" (Jaiswal *et al.*, 2001). "The artificial seeds can be an alternative as more is learned about the mechanism by which this type of seed has no tolerance to desiccation" (Leprince *et al.*, 1993). . "The use of somatic embryogenesis system in these species would significantly reduce labor costs" (Chee and Cantliffe, 1992)

In ornamental plants and orchids, the synthetic seeds have very much commercial importance, because of their minute seed size and presence of reduced endosperm in seeds (Lambardi *et al.*, 2006). Ruffoni *et al.* (1994) produced synthetic seeds of somatic embryos in two ornamental species (*Eustoma grandiflorum* and *Genista monosperma*). Piccioni and Standardi

(1995) produced synthetic seeds of shoot tips in *Betula pendula and* bulbs in *Lilium longiflorum* (birch).

Coniferous forest species may be propagated cheaply, the regular breeding programs in such species are considered very time consuming because its life cycle of conifers is long. Coniferous forests are regarded as too heterogeneous. "Artificial seeds have the ability to clone those overhanging trees at reasonable cost and in minimum time" (Desai *et al.*, 1997). "The use of artificial seed technology can significantly reduce costs by reducing the labor required, time and space in case of these plants"(Chee and Cantliffe, 1992).The majority of fruit species are propagated by vegetative means due to the fact that the presence of self- incompatibility and breeding cycles very long. "The use of synthetic seed facilitates its spread" (Towill, 1998). Kok-Siong *et al.*, 2012, in their study "Production of Artificial seeds derived from encapsulated *in vitro* microshoots of cauliflower, *Brassica oleracea* var. *Botrytis*", a high number of micro shoots (21 ± 2.31) of cauliflower was obtained. The technology of artificial seed has affected almost every aspect of plant biotechnology and has the potential to become the most promising and viable technology for large scale production of plants (Dhabhai and Prakash, 2012). Kariuki (1991), in his research paper "Production of synthetic seeds from nodal segments of *Solanum nigrum*", presented an efficient protocol for the production of synthetic seeds in *Solanum nigrum*, a medicinal plant.

Production of artificial seeds for different vegetables, were started at different time from different part of the plant. The production of synthetic seeds was by the encapsulation of multiple carrot somatic embryos (Kitto and Janick, 1982). 100% germination of encapsulated axillary buds by adding 0.5 mg/l NAA and 1.0% activated charcoal and advanced synthetic seed production systems by using somatic embryos in *Ipomoea batatas* were reported (Onishi et al., 1992, 1994). Phonkajornyod et al. (2004) reported the dry synthetic seed production and desiccation tolerance induction in somatic embryos of *Capsicum annuum*. Encapsulation of nodal segments and shoot tips of *Manihot esculenta* (Cassava) germplasm was reported (Cid et al., 2009). In most of the commercial fruit crops, the seed propagation has not been successful because of heterogeneity of seeds; minute seed size and presence of reduced endosperm, low germination rate and in some crops have desiccation sensitive and recalcitrant seeds which cannot be stored for longer time (Rai *et al.*, 2009). Recently many of the crops available are seedless varieties. Propagation of *Musa paradisica* (Hassanein et al., 2005.)

Production of artificial seeds

Production of artificial seeds depend on several steps, which can be summarized as follows:

- **First** comes crop selection, which relies upon commercial and tech potential, then the assembly of a somatic embryo system.
- **The second step** consists of clonal production, system optimization and embryo production and automation of embryo production;
- **The third step** consists of treatment of mature embryos that triggers quiescence;
- **The forth is** encapsulation development and coating system, optimization and automation;
- **The fifth step** consists of determination of economic practicableness of adopting the artificial seed delivery system for a specific crop compared with alternative propagation techniques (cost–benefit analysis regarding encapsulation). In general, some procedures apply to quite one species whereas alternative steps could also be species-specific (Pond and Cameron, 2003).

Potential uses of artificial seeds

- Delivery system reduced costs of transplants
- Direct greenhouse and field delivery of elite, select genotypes, hand pollinated hybrids, genetically engineered plants, sterile and unusable genotypes, large seed monocultures, mixed genotype plantations.
- Carrier for adjuvant such as micro-organisms, plant growth regulators and pesticides protection of meiotically unstable elite genotypes.
- Analytical tools comparative aid for zygotic embryogeny
- Production of large numbers of identical embryos
- Determine role of endosperm in embryo development and germination
- Study of seed coat formation
- The synthetic seeds so developed breed true.
- These seeds can be produced within a short time (one month) whereas natural seeds are the end product of complex reproductive process and breeders have to wait for a longtime for development of new variety.

- Artificial seeds can be produced at any time and in any season of a year.
- They are useful in preserving germplasm.
- They are applicable for large scale monocultures as well as mixed genotype plantation.
- The synthetic seed provide us knowledge to understand the development, anatomical characteristics of endosperm and seed coat formation. Such seeds give the protection of meiotically unstable, elite genotype.
- Comparative advantages of artificial seeds over classical as well as micro-propagation (with short tip culture). The rapid and large scale multiplication minimal labour and low cost propagation.
- Artificial seeds can be directly delivered to the field. Thus eliminating transplantation and tissue hardening steps.
- They can also provided with various kinds of adjuvants like plant growth regulators, useful micro-organism and pesticides to tailor a field specific.
- Plantable unit for a desired crop. However, genetic uniformity is maintained in all propagation methods.
- Artificial seed technology can be very useful for the propagation of a variety of crop plants, especially crops for which true seeds are not used or readily available for multiplication (e.g Potato). The true seeds are expensive (e.g Cucumber and Geraniums) hybrid plants (e.g. Hybrid rice) and vegetatively propagated plants which are more prone to infections (e.g. day lily, garlic, potato, sugarcane, sweet potato, grape and mango)

Application of Synthetic Seeds

By combining the benefits of a vegetative propagation system with the capability of long-term storage and with the clonal multiplication, synthetic seeds have many diverse applications

- Multiplication of non-seed producing plants, ornamental hybrids or polyploids plant
- Propagation of male or female sterile plants for hybrid seed production
- Germplasm conservation of recalcitrant species
- Multiplication of transgenic

Limitations

- Limited production of viable micro-propagules that are useful in synthetic seed producer
- Asynchrous development of somatic embryos
- Improper maturation of somatic embryos that makes them inefficient for germination
- and conversion in to normal plants
- Lack of dormancy and stress tolerance in somatic embryos that limit the storage of synthetic seeds
- Somo clonal variations which may alter the genetic constituent of the embryos

Problems

Artificial seeds that are stable for several months requires the procedures for making the embryos quiescent.

- Artificial seeds need to be protected against desiccation.
- Recovery of plants from artificial seeds is often very low due to incomplete embryo formation or difficulties in creating an artificial endosperm.
- The embryo must be protected against microorganisms.

Conclusion

Synthetic seeds technique is a rapid tool of plant regeneration because of its wide use in conservation and delivery of tissue cultured plants. Procedures were optimized and proper plantlets were obtained. For critically endangered plant species, it is the rapid means of conservation and multiplication. This technique has great advantages such as: a cost-effective delivery system, minimization of the cost of plantlets, simple methodology with high potential for mass production, a promising technique for the direct use of artificial seedlings in vivo, and a high storage capacity. However further research is needed to perfect the technology so that it can be used on a commercial scale.

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